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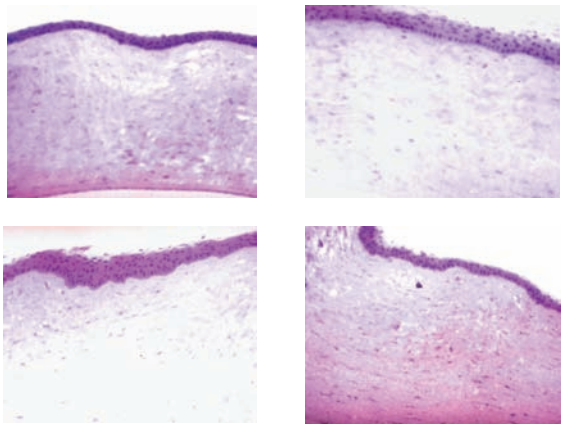

PHILIPPINE JOURNAL OF
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EDITORIAL

UP Manila Institute of Ophthalmology

Pioneer in eye research

The Institute of Ophthalmology is now known locally and internationally not only for its valuable contribution to Philippine ophthalmology through research and publication, but also for having produced the pillars of Philippine ophthalmology.

THE IDEA of a Philippine eye-research institute evolved in response to the problem of blindness in the country. To Dr. Geminiano T. de Ocampo, there was a need for an institute to study blindness among Filipinos, utilizing the basic laboratories—pathology, microbiology, biochemistry, and other scientific disciplines—to understand the disease process in the eye and its relation to the whole human-body system.[1]

The Philippine Eye Research Institute was created on June 19, 1965, through Republic Act 4593, to undertake and promote research on eye health and eye diseases in the Philippines. It was formally established by the University of the Philippines (UP) Board of Regents on October 22, 1966. As the premier eye-research center in the Philippines, it was tasked to:

1. undertake clinical, applied, and epidemiological investigations on eye diseases;
2. conduct basic studies on different eye diseases;
3. perform the research functions of the UP Department of Ophthalmology;
4. collaborate with scientific researchers in other fields of medicine;
5. provide stimulation and assistance to ophthalmic research elsewhere in the country;
6. cooperate with scientific research activities here and abroad; and
7. formulate plans, activities, or proposals and recommend policies, procedures, rules, and regulations for adoption by the Board of Regents consistent with its powers and effective operation.

What started as a small study group interested in corneal diseases and corneal transplantation has now become an organized study group engaged in basic ophthalmologic research and involved in national eye-health programs. The Philippine Eye Research Institute consolidated and directed the research activities of the Department of Ophthalmology under a separate program and management. These were pursued more aggressively and systematically, complementing the ophthalmic teaching of the university's medical students and ophthalmology residents. The first building near the Department housed the support laboratories—Experimental Ophthalmic Pathology, Experimental Ophthalmic Surgery including the Animal House, Ocular Microbiology and Immunology, Biochemistry, Ophthalmic Photography, and Administration. The ophthalmic equipment was donated by the Rockefeller Foundation through Dr. Lucien Gregg. The Institute opened its doors in June 1967 with Dr. de Ocampo as acting director.

The Institute developed and pursued its research agenda and that of the Department. It developed research programs, facilities, and expertise. Concerns included studies on corneal diseases and corneal preservation, ocular infection, cataract, diabetic retinopathy, glaucoma, malnutrition blindness/xerophthalmia, motility, uveitis, and retinoblastoma among other areas. Through the years, the Institute was able to upgrade its facilities and ophthalmic equipment and acquire funding for its research. It acquired the first argon laser in the Philippines from the National Science and Development Board for research on diabetic retinopathy; the first Konan SP 5500 Specular Microscope with cell analyzer for in vivo studies of corneal endothelium from Don Emilio T. Yap; the top-of-the-line Zeiss fundus camera with computer, and Fluron fluorophotometer for posterior-segment studies from former senator Orlando Mercado.

The Institute collaborated with other agencies in the pursuit of new knowledge in the promotion of eye health and prevention of blindness. Among the tie-ups were those with Helen Keller International in 1974–76

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for the Vitamin A Deficiency/Xerophthalmia Project, and with IMPACT UK and IMPACT Philippines in 1991–93 for the Cataract Backlog Management Project–Sight Restoration in the Philippines.

The commitment of the Institute to Philippine ophthalmology and to the World Health Organization was to define and characterize eye health and the blindness problem in Filipinos.[2] As the national eye-research center, the Institute was designated to take the lead role in planning and formulating eye-health policies. In cooperation with other nongovernment organizations, it formulated and published the National Sight Plan in 1979. It joined the global interest on blindness prevention by initiating and developing the program on Preventive/Public Health Ophthalmology and Primary Eye Care. As part of program development, it enhanced its expertise by sending two researchers to training courses abroad (Dr. Rossina Ramirez to Baltimore, Maryland, for a one-year fellowship in Preventive Ophthalmology and Dr. Evangeline Santos to London for a six-month course on Community Eye Health). At the same time, Dr. Salvador R. Salceda became a member of the World Health Organization's advisory group on Blindness Prevention and the organizing committee of the Public Health Ophthalmology course in Korat, Thailand. The Institute's commitment to blindness prevention in the Philippines is now defined and is provided by its researchers with expertise on the program.

The Institute assessed the blindness problem through the first population-based blindness survey,[3] which was done simultaneously with the National Nutrition Survey. The results provided an organized epidemiology database on local blindness, a prerequisite to the development of a national program on blindness prevention. The survey showed that cataract was the single largest remediable cause of blindness among Filipinos. The Institute did 2 more blindness surveys with the Department of Health.[4, 5] The results served as the basis for the development of prevention of blindness and eye-health programs.

After more than 35 years, the graduate program in ophthalmology is now a reality. The UP Board of Regents recently approved the Diploma in Preventive Ophthalmology, which is being offered by both the Institute and the Department of Ophthalmology and Visual Sciences of the UP College of Medicine. The new course aims to train Eye MDs on the promotion of eye health and prevention of blindness appropriate to our needs and resources. Another program aimed at delivering eye-health services in underserved areas is the Modified Residency Training Program in Ophthalmology.[6] The program is the contribution of the Institute and the Department to the campaign for reduction of blindness prevalence in the country by providing appropriate ophthalmic care, services, and manpower.

The Institute of Ophthalmology is now known locally and internationally not only for its valuable contribution to Philippine ophthalmology through research and publication, but also for having produced the pillars of Philippine ophthalmology.[7] Among them are:

- Dr. Geminiano T. de Ocampo, National Scientist (Medicine) and founding director of the Institute whose contributions to Philippine ophthalmology, particularly on ocular diseases, are immeasurable.
- Dr. Salvador R. Salceda, director of the Institute for more than 20 years and noted for his commitment to the study of fungal ulcer and the prevention of blindness in Filipinos.
- Dr. Roberto N. Sunga, expert in optics acknowledged for his PERI Color Test, a screening tool for night blindness in early xerophthalmia; he introduced visual aids to visually disabled Filipinos.
- Dr. Vitaliano B. Bernardino Jr., who established the Ophthalmic Pathology Section of the Institute.
- Dr. Alejandro S. de Leon, for his valuable input in the formulation of the National Sight Plan and the Department of Health's Prevention of Blindness.
- Dr. Romeo V. Fajardo, for his studies on uveitis in Filipinos and his contribution to ophthalmic literature by spearheading the publication of the first local *Textbook of Ophthalmology* and as founding editor of the PHILIPPINE JOURNAL OF OPHTHALMOLOGY.
- Dr. Romeo B. Espiritu, for his studies on retinoblastoma in Filipino children.
- Dr. Pacifico V. de Ocampo Jr., expert in fluorescein angiography, for his studies on diabetic retinopathy in Filipinos and for setting up the Institute's retina program and acquiring the first argon laser in the Philippines.
- Dr. Mario J. Valenton, for his studies on ocular infection and for setting up the first External Disease Clinic together with Dr. Salceda.
- Mrs. Lilia Flor C. Nievera, for her studies on ocular microbiology in Filipinos.

Membership in the International Union of Nutritional Sciences was granted to Dr. Salvador R. Salceda and Dr. Rossina Lydia A. Ramirez in recognition of their research on vitamin-A deficiency. Likewise, Dr. Ramirez introduced and formalized the teaching of Ophthalmic Epidemiology and Biostatistics, an essential requisite

in eye research. Dr. Evangeline O. Santos was awarded by the Asia-Pacific Academy of Ophthalmology for her work on the prevention of blindness in the Philippines.

After 40 years, the Institute has characterized ocular diseases and their diagnosis and treatment in Filipinos. It has conducted three population-based blindness surveys, which assessed the blindness problem in the Philippines and served as the basis for the development of eye-health and preventive-ophthalmology programs. With several awards for published and communicated research papers, and recognitions given to its researchers for their contributions to ophthalmology, the Institute is indeed the national center for eye research.

Under its present director, Dr. Manuel B. Agulto, the Institute of Ophthalmology continues to be the research arm of the Department of Ophthalmology and Visual Sciences located at the newly established Sentro Oftalmologico Jose Rizal located within the Philippine General Hospital compound. As stated in RA 4593, the Institute and the Department together play the lead role in Philippine ophthalmology in pursuit of a common agenda—eye health for all Filipinos.

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ORIGINAL ARTICLE

Third National Survey on Blindness

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ABSTRACT

Objectives

The Prevention of Blindness Program (PBP) and Vision 2020 Philippines of the Department of Health (DOH) have been implemented to address avoidable causes of blindness. Population-based surveys every 5 to 8 years are utilized to monitor and evaluate these programs. The third National Survey on Blindness in the Philippines was conducted from October 2001 to May 2002 to determine the prevalence and major causes of visual impairment in the Philippines at both the national and regional levels. The results were also compared with those of the first (1987) and second (1995) surveys.

Methods

A nationally representative sample was selected based on multistage, cluster, random sampling. The 16 administrative regions of the Philippines served as the cluster sites where 9 villages each were randomly sampled using probability proportional to size procedures. Visual acuity (VA) with or without glasses was determined using a modified Snellen acuity chart. Anterior-eye examination was performed with a penlight. The posterior-eye segment was examined with an ophthalmoscope. When indicated, eye pressures were obtained with the Schiotz tonometer. The World Health Organization's (WHO) definitions of blindness and low vision were used to categorize visual impairment. Diagnoses of eye disease were in accordance with the International Classification of Diseases.

Questionnaires were entered and analyzed using Epi Info 6.0. National and regional prevalence rates and 95% confidence intervals were computed. Chi-square test was used to detect differences among regions and compare results with the 1987 and 1995 blindness surveys.

Results

A total of 29,888 people in 6,757 households were enumerated, of which 24,624 (82.39%) were examined. Nationwide, the prevalence of visual impairment (VA worse than 6/18 in the better eye) is 4.62%; the prevalence of bilateral blindness [VA less than counting finger (CF) at 3 meters] is 0.58%, monocular blindness is 0.71%, bilateral low vision (VA worse than 6/18 but

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equal to or better than CF at 3 meters) 1.43%, and monocular low vision 0.87%. Regionally, the prevalence of blindness is from 0.16% to 1.08% and low vision 0.60% to 4.07%.

Cataract is the most common cause of blindness (62% of all persons with bilateral blindness), and error of refraction (53%) is the most common cause of low vision.

The current prevalence of bilateral blindness is 46% lower than the 1987 prevalence (1.07%, $p < 0.001$) and 17% lower than the 1995 prevalence (0.70%, $p = 0.108$).

Conclusion

There are over 400,000 bilaterally blind people in the Philippines, of which 62% is due to cataract. The prevalence of blindness has been reduced compared with the 1987 and 1995 national surveys. Vision 2020 Philippines has contributed to this reduction. With continued support and implementation of the blindness-prevention program, the prevalence is expected to be reduced to the WHO target of less than 0.5% by year 2020.

IN DEVELOPING countries, blindness remains a public-health problem. According to the World Health Organization (WHO), blindness is a public-health problem when its prevalence is 1% or higher.[1]

The first National Survey on Blindness in the Philippines conducted in 1987 showed a prevalence rate of 1.07%, making blindness a public-health problem then.[2] The number of blind Filipinos was estimated at 350,000 at the time. Cataract and vitamin-A deficiency were among the most common causes of blindness.

Because of the high prevalence, the Department of Health (DOH) has instituted preventive programs like vitamin-A supplementation for children. Nongovernment organizations have initiated the Primary Eye Care (PEC) program and the Modified Residency Training Program (MRTP) in ophthalmology, which encourage rural doctors to become eye-care providers in their respective provinces. They support the cataract programs in the country.

The 1995 survey showed a blindness-prevalence rate of 0.7%, a decline of almost 35% from the 1987 rate.[3] However, the number of blind Filipinos rose to almost half a million (475,000), an increase of almost 36% from 1987. This was largely attributed to the rise in population and an increase in the life span of Filipinos. Seventy-seven percent (77%) of blindness cases seen in 1995 were due to cataract.

The first and second surveys gave a good picture of the problem at the national level, but they were not very useful for planning at the regional level.

In the years following the second national survey, significant strides were taken in blindness-prevention programs. Among these was the formation of the National Committee for Sight Preservation composed of government and nongovernment organizations, which coordinates blindness-prevention activities and monitors cataract surgeries. The Department of Health also launched Vision 2020 Philippines in September 2000. Vision 2020 is part of the WHO global initiative to eliminate avoidable blindness by increasing the rate of cataract surgeries, providing refractive services, and planning national programs for the prevention of childhood blindness.

In the last 5 years, the MRTP, a collaborative program of the Department of Health, the University of the Philippines Manila, and Christoffel Blindenmission, has fielded 28 additional graduates (from 16 previous graduates), making ophthalmic services available in 28 additional provincial hospitals in the country.

This and future five-year surveys will serve both as baseline and evaluation tool to measure the impact of Vision 2020 Philippines and the MRTP on the blindness-prevention programs in the country.

OBJECTIVES

The third National Survey on Blindness was undertaken to determine the prevalence and causes of blindness and low vision at the national and regional levels.

The survey was also utilized as a tool to increase awareness of public-health officials on Vision 2020 Philippines as a strategy to eliminate avoidable blindness by year 2020. It was used to determine the resource needs for the attainment of the goals of Vision 2020 Philippines at both regional and provincial levels. It was also used to gather information and reference data needed for the formulation of policies on cataract surgical missions, cataract preoperative and follow-up procedures, and cost-recovery measures for cataract surgeries.

METHODOLOGY

Sampling Design

Based on the 2000 census projections, Philippine population was estimated at 79,503,675 in 2002.[4]

A multistage, cluster, random sampling was adopted to select a cross-sectional, nationally representative sample of the population. The 16 administrative regions of the Philippines (Regions 1–16) served as the cluster sites where 9 villages (known as the barangay, the smallest political unit) were randomly sampled using probability-proportional-to-size (PPS) procedures. The estimated 2002 population of the villages was used for the PPS sampling.

The sample size per region was calculated based on the objective of determining the prevalence of blindness per region and on several specifications and assumptions. The national blindness prevalence based on the 1995 national survey was 7 per 1,000 population. It was presumed that for the 2002 study, the prevalence was lower at 5 per 1,000. For each cluster, it was determined that several survey days at the village would be enough to examine 50 households (average of 5 to 6 members per household). At 250 respond-ents per cluster, the expected number of blind individuals was 1.25. Based on the previous blindness survey, and using the regions as clusters, the variance of the number of blind respondents per cluster of 250 was estimated at 0.92 persons. The relative variance (variance divided by mean) was calculated at 0.59. Specifying a desired precision of an estimate within 50% of its true value with 95% confidence, the number of clusters was calculated at 9.

The expected population using the assumptions was 36,000 individuals from 144 clusters of 250 respondents. This sample size was estimated to be sufficient to achieve a relative precision of $\pm$20% or better with 95% confidence. The calculated sample size for a simple-random-sampling design was only 19,104. It was assumed that with a design effect of 1.5%, the sample size was bigger due to the cluster sampling.

The process of selecting the barangays consisted of listing the barangays with their respective population sizes, stratified according to their region. The list of barangays with their respective population was obtained from the Department of Interior and Local Government. The barangays were randomly arranged in an array per region. In each array, a cumulative sum (k) of the population was computed. For each region, 9 random numbers from 1 to k was chosen. The barangay whose cumulative total captured any of the 9 random numbers chosen automatically were included in the study. The procedure was done in all 16 regions. Another set of 9 randomly selected barangays was also generated per region as alternates. The order of the barangays in the alternative list was the order by which they were used to replace barangays that did not satisfy a set of predetermined selection criteria. Barangays were replaced if they were in an isolated area and inaccessible by normal means of transportation or if their location would compromise the safety of the survey personnel. Barangays whose leaders did not wish to be included in the study were also replaced.

The second stage in the sampling process was the random selection of 50 households within the barangay. In very large barangays, (population more than 10,000) the barangay was divided into grids, and from one randomly selected grid (additional stage), the 50 households were selected. This was done in 2 barangays in the National Capital Region (NCR), 2 in Cebu City, and one in Legaspi City.

All individuals living in the selected households were included in the study population.

Standardization

A survey manual was prepared. All personnel involved in the data collection were given a copy of the survey manual. A two-day workshop among all data collectors was conducted to discuss the survey manual and simulate the actual data collection in the field. Inter-observer variability was measured at this point and adjustments made accordingly. Operational definitions of the clinical entities were established and incorporated to the survey manual.

Approval

Written approval of the study protocol was obtained from the Ethics Review Board of the University of the Philippines–National Institutes of Health. Signed informed consent was also sought from the household head, following explanation of the procedures to be conducted, before examining the household members.

Data-Collection Tool

A WHO-based questionnaire was devised and pretested in an arbitrary community to ensure that the data to be collected corresponded to the information required in the study.[5] Correlation and Cronbach-α analyses were carried out to determine the reliability of the data-collection-tool items. The data-collection tool underwent three revisions. A total of 50,000 questionnaires were reproduced, with at least 300 being allocated for each of the 144 barangays.

Survey Teams

Eight teams were formed. One region was assigned to one, at most two, teams. Each team was composed of an ophthalmologist, a research assistant, and an administrative assistant. Travel arrangements were made. Letters of introduction and other documents were prepared for the key leaders of the study site and sent prior to deployment of survey teams. The letter specified the date of the team's visit to the barangay and the total number of households to be surveyed, and requested for protection for the team and assistance in obtaining local transportation and accommodation.

Household Selection

Actual survey started as soon as the survey team arrived at a study site. A local ophthalmologist often joined the survey team. His role was mainly to examine patients who were not included in the study sample, as well as to advise

persons needing further ophthalmological care. After paying courtesy calls on the governor, mayor, barangay and health officials, the team proceeded to the barangay health station, where a list of all the households in the barangay and a spot map were usually found.

Guided by the household list, the team selected households for the study by simple random sampling using either a random-sample table or the random-number generator in Microsoft Excel (Microsoft Corp., Redmond, WA, USA). The survey form was then filled out, one for each household member. The forms for one household were stapled together. The batches of stapled forms numbered 50, corresponding to the 50 randomly selected households. In the few cases where the barangay did not have a listing of household heads with their corresponding members, the team met with the barangay captain or his/her representative and, with the aid of the spot map, assigned consecutive numbers on the houses prior to random sampling. The barangay captain then gave the team the names of the household heads of the selected households. The team visited each of the houses on the list of selected households.

Household Dropouts

Households randomly selected from the listing given by the barangay captain but which had transferred to another locality at the time of the survey were considered dropouts. Houses located in an area not accessible to the survey team were also considered dropouts. No replacements were made. When the household was chosen twice by random sampling, the data obtained were counted twice.

Clinical Examinations

A survey form was filled out for each member of the selected household, including those who were not available at the time of the visit. The following demographic information were obtained for each household member: name, age, gender, occupation, and civil status.

Presenting visual acuity was assessed separately for each eye using a modified Snellen chart (Figure 1). Subjects that have corrective lenses were allowed to wear them. Visual acuity was tested at 6 meters, and those unable to read the largest letter were tested at 1 or 2 meters. When necessary, testing included the ability to count fingers, to detect hand movements, or to perceive light. If vision was less than 6/18, pinhole test was done to determine if vision improved to 6/18 or better. For children and adults whose vision was difficult to assess using the modified Snellen chart, vision was measured by other means to determine whether they were blind or not.

Functional vision was also assessed in both eyes by determining whether the respondent can ambulate without difficulty, recognize faces, or read a newspaper's headlines.

Clinical examination of the external eye, anterior segment, and fundus was performed using penlight and Heine (Heine Optotechnik, Herrsching, Germany) or Welch Allyn (Welch Allyn Medical Products, Skaneateles Falls, NY, USA) direct ophthalmoscope by the team ophthalmologists. Pupils were dilated when necessary. The presence of cataract was defined as partial or complete obscuration of the red-orange reflex of an undilated normal pupil as a result of the presence of lens opacity, as assessed using direct ophthalmoscopy. Intraocular pressure was measured using Schiotz tonometer (Rheine, Germany) for those suspected of having glaucoma based either on optic-nerve characteristic or previous diagnosis or surgery. Retinal and macular findings were based on funduscopy of a dilated pupil. Diagnoses were based on the International Classification of Eye Diseases (ICD).[6] Refractive error was a diagnosis in eyes with vision improving to 6/18 or better with pinhole test. When the presenting vision was 6/60 or lower, the causes of visual impairment were marked for each eye. The most treatable cause was chosen as the main diagnosis. If all the causes were deemed no longer treatable, the most recent pathology was chosen as the main diagnosis.

All respondents who were blind or had eye diseases or low vision were referred to the nearest eye-care facility.

Nonresponders

Household members who were not available for eye examination during the entire one or two days when the survey team was at the barangay were listed as "interview only" or nonresponders. The reasons for nonexamination were recorded by the survey staff. All nonresponders were recorded as "believed blind" or "not blind" in each eye separately, depending on the answer given by the immediate or close relative or neighbor of the enumerated individual when interviewed regarding the functional vision of the subject.

Operational Definitions

The reporting of the visual status of the subject was based on the WHO categories of visual impairment and further subdivided into several categories, an expansion of the categories of blindness used in the 1995 Survey of Blindness (Table 1).[1] The subdivided categories of blindness were intended for use in the implementation of blindness-prevention programs.

Data Management

At the end of each day, the data collectors checked each of the questionnaires for missing entries or inconsistent recordings. Missing entries or inconsistent data were

verified through appropriate callbacks. All completed forms were submitted to the survey coordinator for final review. The summary sheets (summary of data for all persons per barangay) were filled out. The forms were then forwarded to the data-processing center, Applied Research Consultants Inc. (ARC), which customized a data-encoding software for the study. Data encoding was accomplished by ARC according to the guidelines agreed upon with the survey coordinator. Data-encoding forms were constructed based on the final data-collection tool. Data encoders were recruited and trained accordingly. Double encoding was done to ensure data quality. Range and consistency checks were also done.

Statistical Analysis

Crude prevalence of low vision and blindness for both national and regional data were calculated. Estimates of affected population were calculated using crude prevalence and the estimated 2002 national and regional population data published by the National Statistics Office. Since most of the people who have low vision or are blind were in the older age group, the age-standardized prevalence rates were also calculated to give a more precise estimate of the prevalence rate. They will also be used in comparing Philippine prevalence rates with other published studies in which age-standardized prevalence rates may be the norm.

Confidence intervals (CI) for age-standardized prevalence estimates were calculated taking into account design effects associated with cluster sampling. Design effects reflect the relative inefficiency of cluster sampling compared with simple random-sampling plan, and can become large when within-cluster variance is small compared to between-cluster variance for the parameter estimated.[7]

Chi-square test was used to detect differences among regions and compare results with the previous surveys.

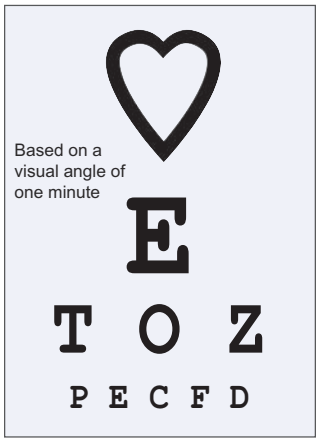

Figure 1. Modified Snellen chart

RESULTS

Demographics

A total of 29,888 respondents in 6,757 households in 144 barangays from 16 regions were enumerated. The average number of members per household was 4.42. The total number of household dropouts was 443 (6.15%). The study population consisted of 43% children under 20 years of age. Only 28% were in age group 40 years and above. The mean age was 23 years, and 49.2% were males. Forty percent of all respondents were not employed, 11% were engaged in agriculture, and 7% were employed, mainly by the government.

Examinations were performed on 24,624 subjects—an overall response

Table 1. **Categories of visual status.**

Vision	WHO Category
No Visual Impairment	**0**
Believed not visually impaired At least 6/12 both eyes At least 6/12 one eye, 6/18 other eye, 6/18 both eyes	
Monocular Visual Impairment (no visual impairment by WHO definition) (Mono BVI, Mono SVI, Mono Blind)	**0**
Monocular Low Vision *(Mono BVI),* Moderate Visual Impairment.[1] At least 6/18 one eye, 6/60 other eye Monocular Low Vision *(Mono SVI),* Severe Visual Impairment[1] At least 6/18 one eye, CF 3m other eye Monocular Blind *(Mono Blind)* At least 6/18 one eye, < CF 3m other eye	
Low Vision (<6/18, ≥ CF 3m)	**1, 2**
Moderate Visual Impairment (<6/18, ≥ 6/60)	1
Bilateral moderate visual impairment *(Bila BVI)*[2] (6/60 both eyes)	
Moderate visual impairment one eye, Severe visual impairment other eye *(BVI-SVI)*[2] (6/60 one eye, 3/60 other eye)	
Moderate visual impairment one eye, Blind other eye *(BVI Blind)*[3] (6/60 one eye,<CF3m other eye)	
Severe Visual Impairment (<6/60, ≥ CF 3m)	2
Bilateral severe visual impairment *(Bila SVI)*[2] (3/60 both eyes)	
Severe visual impairment one eye, Blind other eye *(SVI Blind)*[3] (3/60 one eye,<CF3m other eye)	
Blind *(Bilateral Blind)* (< CF 3m)	**3, 4, 5**
Blind CF 1m	3
Blind CF 2m	4
Blind NLP	5

Classification in the 1995 Survey on Blindness
[1]Monocular low vision
[2]Bilateral low vision
[3]Low vision - Blind

Table 2. **Prevalence of visual impairment, Philippines.**

Vision[1]	WHO Category	Total No.[2]	Male	Female	Crude Prevalence (%)	Age-Standardized Prevalence[3] (95% CI)	Afffected Population (2002)[4]
No Visual Impairment		**29,116**	**14,397**	**14,749**	**97.42**	**98.16 (97.98-98.34)**	**77,452,480**
Believed not visually impaired		2,170	1,076	1,094	7.26	10.52 (10.10-10.93)	5,771,967
At least 6/12 both eyes		24,912	12,349	12,563	83.35	83.04 (82.51-83.56)	66,266,313
At least 6/12 one eye, 6/18 other eye		579	248	331	1.94	1.35 (1.19-1.51)	1,542,371
6/18 both eyes		846	388	458	2.83	1.83 (1.66-2.01)	2,249,954
Monocular Visual Impairment (no visual impairment by WHO definition) (Mono BVI, Mono SVI, Mono Blind)	**0**	**609**	**306**	**303**	**2.04**	**1.42**	**1,621,875**
Monocular Low Vision *(Mono BVI)* Moderate Visual Impairment At least 6/18 one eye, 6/60 other eye[5]		307	145	162	1.03	0.64 (0.53-0.76)	818,888
Monocular Low Vision *(Mono SVI)* Severe Visual Impairment At least 6/18 one eye, CF 3m other eye[5]		91	54	37	0.30	0.23 (0.17-0.30)	238,511
Monocular Blind *(Mono Blind)* At least 6/18 one eye, < CF 3m other eye[6]		211	107	104	0.71	0.55 (0.45-0.66)	564,476
Low Vision (<6/18, ≥ CF 3m)	**1, 2**	**598**	**256**	**342**	**2.00**	**1.43 (1.26-1.60)**	**1,590,074**
Moderate Visual Impairment (<6/18, ≥ 6/60)	1	448	192	256	1.50	1.06 (0.91-1.20)	1,192,555
Bilateral moderate visual impairment *(Bila BVI)* (6/60 both eyes)		308	131	177	1.03	0.79 (0.65-0.92)	818,888
Moderate visual impairment one eye Severe visual impairment other eye *(BVI-SVI)* (6/60 one eye, 3/60 other eye)		74	26	48	0.25	0.14 (0.10-0.18)	198,759
Moderate visual impairment one eye, Blind other eye *(BVI Blind)* (6/60 one eye,<CF3m other eye)[6]		66	35	31	0.22	0.13 (0.09-0.17)	174,908
Severe Visual Impairment (<6/60, ≥ CF 3m)	2	150	64	86	0.50	0.37 (0.28-0.47)	397,518
Bilateral severe visual impairment *(Bila SVI)* (3/60 both eyes)		107	48	59	0.36	0.28 (0.20-0.36)	286,213
Severe visual impairment one eye Blind other eye *(SVI Blind)* (3/60 one eye,<CF3m other eye)[6]		43	16	27	0.14	0.09 (0.05-0.13)	111,305
Blind *(Bilateral Blind)* (< CF 3m)	**3, 4, 5**	**174**	**84**	**90**	**0.58**	**0.41 (0.32-0.49)**	**461,121**
Blind CF 1m	3	93			0.31		246,461
Blind CF 2m	4	58			0.19		151,057
Blind NLP	5	23			0.08		63,603
Total Visually Impaired		**1,381**	**646**	**735**	**4.62**	**3.26**	**3,673,070**

[1]Based on the vision of the better eye. Words in italics in parenthesis correspond to the 9 categories of blindness used in the 1995 survey:

- *Mono BVI* (Monocular Borderline or Moderate Visual Impairment)
- *Mono SVI* (Monocular Severe Visual Impairment)
- *Mono Blind* (Monocular Blind)
- *Bila BVI* (Bilateral Borderline or Moderate Visual Impairment)
- *BVI-SVI* (Borderline Visual Impairment on one eye and Severe Visual Impairment on the other eye)
- *BVI-Blind* (Borderline Visual Impairment on one eye and Blind on the other eye)
- *Bila SVI* (Bilateral Severe Visual Impairment)
- *SVI-Blind* (Severe Visual Impairment on one eye and Blind on the other eye)
- *Bila Blind* (Bilateral Blind)

[2]n = 29,888

[3]Prevalence in the Philippine population adjusted based on the age distribution of estimated 2002 Philippine population

[4]Based on crude prevalence, 2002 Population: 79,503,675

[5]Monocular low vision

[6]Monocular blind

rate of 82.4%. Nonresponders made up 17.6%, most of them under 30 years of age.

Bilateral Blindness

One hundred seventy-four persons were found to suffer from bilateral blindness (WHO Category 3, 4, and 5) on presentation. This corresponds to a crude blindness prevalence of 0.58%. Age-standardized blindness prevalence was determined to be 0.41% (95% CI 0.32-0.41%) based on the 2002 population estimates.

Bilateral Low Vision

A total of 598 respondents had bilateral low vision while 150 (0.50%; age-standardized prevalence 0.37%, 95% CI 0.28–0.47) had severe visual impairment (<6/60, ≥ CF 3m, WHO Category 2) in the better eye upon presentation. A total of 448 respondents (1.50%; age-standardized prevalence 1.06%, 95% CI 0.91–1.20) had moderate visual impairment (<6/18, ≥ 6/60, WHO Category 1).

Monocular Blindness and Low Vision

Of the 29,116 (97.42%) who had no binocular visual impairment (WHO Category 0), 609 respondents had monocular visual impairment (2.04% prevalence). Two hundred eleven of the 609 had monocular blindness (at least 6/18 one eye, < CF 3m other eye) and 398 had monocular low vision.

National Prevalence of Visual Impairment

When bilateral blindness, low vision, and monocular visual impairment were combined, the prevalence of visual impairment in the population was 4.62% (age-standardized prevalence of 3.26%). Table 2 shows the prevalence of visual impairment based on the presenting visual acuity using the WHO-defined vision categories.

Regional Prevalence of Visual Impairment

The number of bilaterally blind persons for each region surveyed ranged from 3 to 19 per region (mean = 10). The variation of prevalence between regions was statistically significant ($p < 0.001$). Regions 1, 13, 14, and 15 had the lowest prevalence (mean = 0.26%) whereas region 11 had the highest prevalence (>1.0%) (Table 3).

Age and Occupation

Figure 2 illustrates the distribution of the visually impaired persons according to their age in 10-year intervals. There was an exponential increase in visual impairment as the age increased, with peak at the 70 to 79 age interval. In terms of occupational status, most (978 of 1381, 70%) were not gainfully employed. This was followed by people who worked in agriculture (17%).

Table 3. **Prevalence of blindness[1] by region.**

Prevalence Interval (%)	Mean Prevalence (%)	Region[2]
< 0.40	0.26	Region 1: Ilocos Region 13: National Capital Region Region 14: Cordillera Autonomous Region
0.40–0.60	0.50	Region 15: Caraga Region 4: Southern Luzon Region 5: Western Visayas Region 8: Eastern Visayas
0.60–1.00	0.73	Region 12: Central Mindanao Region 2: Cagayan Valley Region 3: Central Luzon Region 5: Bicol Region Region 7: Central Visayas Region 9: Western Mindanao Region 10: Northern Mindanao Region 16: Autonomous Region for Muslim Mindanao
> 1.00	1.08	Region 11: Southern Mindanao

[1]Based on the vision of the better eye. See the individual statistics per region for detailed prevalence rates.
[2]Regions 13,14,15, and 16 were assigned the consecutive numbers in this study. In the actual reference to administrative regions in the Philippines, these numbers are not used.

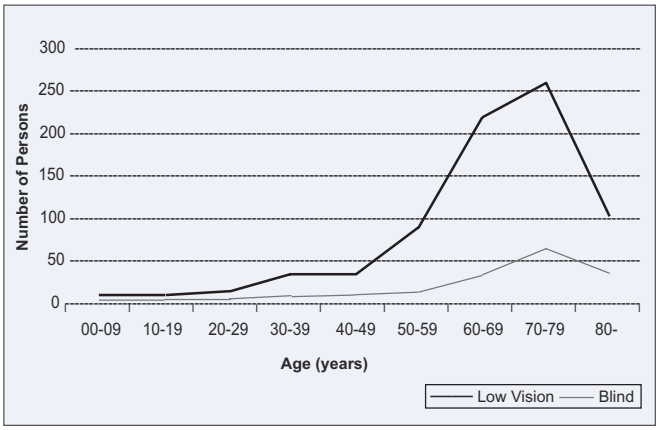

Figure 2. Linear trends of visual impairment, Philippines (n = 1,381).

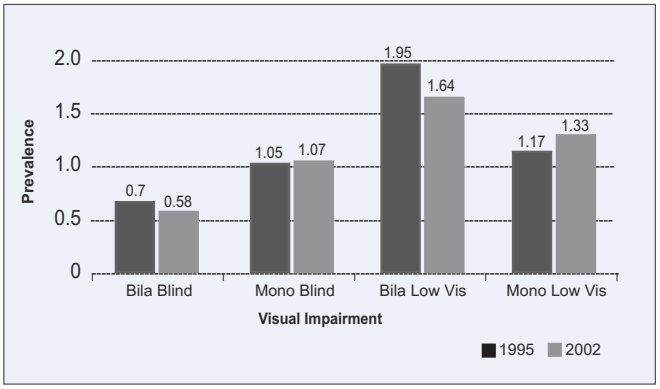

Figure 3. Prevalence of visual impairment, 1995 vs. 2002, Philippines.

Table 4. **Main causes of bilateral blindness.**[1]

Disease	Number	Percent
Cataract	108	62.1
Error of Refraction	18	10.3
Glaucoma	14	8.0
Retinopathy	7	4.0
Maculopathy	7	4.0
Corneal Opacity	6	3.5
Optic Atrophy	6	3.5
Phthisis Bulbi	5	2.9
Amblyopia	1	0.6
Others	2	1.1
Total	**174**	**100.0**

[1]Total n = 29,888

Table 5. **Main causes of low vision.**[1]

Disease	Number	Percent
Error of Refraction	317	53.0
Cataract	244	40.8
Maculopathy	13	2.2
Retinopathy	12	2.0
Glaucoma	5	0.8
Amblyopia	2	0.3
Optic Atrophy	2	0.3
Corneal Opacity	1	0.2
Others	2	0.3
Total	**598**	**99.9**

[1]Total n = 29,888

Comparison with Previous Blindness Survey

The prevalence of bilateral blindness in the Philippines based on the 1987 survey was 1.07%. This declined to 0.70% in 1995 (34.6% decrease, equivalent to a yearly decrease of 4%, $p < 0.001$). In this survey, the prevalence of bilateral blindness further decreased to 0.58% (17.1%, equivalent to a yearly decrease of 2.4%, $p = 0.194$).

Compared with the 1995 survey, the prevalence of bilateral low vision decreased from 1.95% to 1.64% ($p = 0.010$) (Figure 3). However, there was a marginal increase in the prevalence of monocular low vision from 1.17% to 1.33% ($p = 0.122$).

Causes of Visual Impairment

Table 4 outlines the ocular disorders diagnosed as the main cause of blindness among individuals with bilateral blindness. Cataract was the main cause in 108 of the 174 bilaterally blind (prevalence of 0.36%); 18 had error of refraction (prevalence of 0.06%). The other causes of blindness, in order of decreasing frequency, were: glaucoma, retinopathy, maculopathy, corneal opacity, optic atrophy, and phthisis bulbi.

Among the 598 persons with low vision (Table 5), 317 had error of refraction at presentation (prevalence of 1.06%). This was followed by cataract in 244 (prevalence of 0.82%). Other causes of low vision were maculopathy, retinopathy, glaucoma, amblyopia, optic atrophy, and corneal opacity.

Majority of the visually impaired with cataract were in the 60 to 69 and 70 to 79 age groups. Refractive error as a cause of visual impairment was common in the 50 to 59 and 60 to 69 age groups. In all regions, cataract and error of refraction were the most common causes of visual impairment. The overall prevalence of cataract as a cause of visual impairment in the 1995 survey was 2.97%; this decreased to 1.83% in the 2002 survey ($p < 0.001$). In contrast, error of refraction as the overall cause of visual impairment increased from 1.09% in 1995 to 2.06% in 2002 ($p < 0.001$).

DISCUSSION

The third population-based National Survey on Blindness in the Philippines was designed to have a nationally representative population with precision of blindness data both at the national and regional levels. The parameters used in this survey were consistent with the previous surveys to facilitate comparison. This study provides vital epidemiological data on the level of visual impairment that will be useful for the evaluation of the Vision 2020 program and for the planning and implementation of additional blindness-prevention programs.[8]

By extrapolating the prevalence of visual impairment in this study to the estimated national population for the year 2002 (79,503,675), the number of bilaterally blind people was computed at 461,121 (0.58%), those who had low vision at 1,590,074 (2.0%), and those who had monocular blindness at 1,621,875 (2.04%). These brought to 3,673,070 (4.62%) the total number of visually impaired persons in the Philippines in 2002. The average number of blind persons per region was 28,708 (range of 2,933 to 66,856; average population of 4,968,979 per region). The average number of persons with low vision per region was 105,386 (range of 12,758 to 442,918).

Visual impairment was mostly due to cataract and error of refraction, which are treatable causes. Among the bilaterally blind, 287,285 (62%) had cataract as the main cause of blindness. Of those with low vision and monocular visual impairment, 1,590,712 (49.5%) were due to error of refraction. The incidence of cataract cases is assumed to be 1/5 of those already existent.[9] Based on this assumption, around 57,242 new cases of bilaterally blinding cataract are expected to develop annually.

Blindness prevalence was found to be greater with increasing age because the most common causes of blindness are associated with diseases that are more prevalent in the elderly population. Blindness was also seen to be more prevalent among economically disadvantaged people. This finding is similar to those reported in the Asia-Pacific region.[10] This may reflect the poor access

to health care among the economically disadvantaged sector. In fact, half of the cases of visual impairment among those with low vision and monocular vision could be reduced with corrective lenses alone.

The study population was representative of the entire Philippines. It should be noted that the precision of the study might have been slightly affected by design effects associated with multistage sampling. However, this was taken into account when the confidence intervals for the prevalence estimates were calculated. In this study, an overestimation of the prevalence of blindness is possible if the listing of household or household members was replaced by the barangay officials without the knowledge of the survey team. On the other hand, because prevalence estimates were based only on central-vision requirements, some impairment for blindness associated with visual-field defects could have been missed. Overall, the effects of these factors affecting the precision of the study were expected to be minimal and were taken into account in the study design.

Compared with those in the previous surveys, the prevalence of blindness has decreased by 17% in 7 years (from 0.7 to 0.58). Unfortunately, the decrease in the estimated number of blind people was minimal because of the yearly increase in the population. On the other hand, the prevalence of blindness among children did not decrease compared with the previous surveys. This was expected because there is no program for prevention of childhood blindness in the Philippines.

The reduction in the prevalence of blindness is largely due to the efforts of ophthalmologists with the support of government and nongovernment organizations. The results of the survey reflect the overall progress in blindness-prevention and sight-preservation programs in the Philippines.

On a regional level, only 8 of the 16 regions of the country showed remarkable decrease in the prevalence of blindness. It is, therefore, important that in some of these regions, more support be given in the evaluation and implementation of blindness-prevention programs. Although it is apparent that cataract and refractive error should remain a high priority of blindness-prevention programs in the Philippines, the increasing prevalence of age-related macular degeneration and diabetic retinopathy as causes of blindness should also be addressed. Additional studies on the quality and postoperative monitoring of cataract surgeries should be done to assess visual outcome and quality of life. These are needed to determine the impact of blindness-prevention programs.

With continued implementation of the blindness-prevention program by the Department of Health with the support of nongovernmental organizations, the prevalence of blindness is expected to be reduced to the WHO's goal of less than 0.5% in the next several years.

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Annex 1. **Study population, Philippines.**

Region	Number of Households in Selected Villages[1]	Number of Households Included[2]	Percent National	Number of Study Subjects[3]	Percent National
Ilocos	3,948	414	6.13	1,807	6.05
Cagayan Valley	2,403	434	6.42	1,843	6.17
Central Luzon	7,096	432	6.39	1,894	6.34
Southern Luzon	10,962	410	6.07	1,778	5.94
Bicol Region	4,886	370	5.48	1,826	6.10
Western Visayas	5,452	420	6.22	1,775	5.94
Central Visayas	8,516	446	6.60	1,937	6.48
Eastern Visayas	3,028	438	6.48	1,885	6.29
Western Mindanao	2,196	428	6.33	1,752	5.85
Northern Mindanao	6,573	440	6.51	2,123	7.11
Southern Mindanao	11,211	435	6.44	1,756	5.88
Central Mindanao	3,750	438	6.48	2,018	6.76
National Capital Region	NA	382	5.65	1,595	5.34
Cordillera Autonomous Region	4,002	414	6.13	1,940	6.49
Caraga	7,589	436	6.45	1,846	6.18
Autonomous Region of Muslim Mindanao	4,194	420	6.22	2,113	7.08
Total		**6,757**		**29,888**	

[1]Nine villages were randomly selected per region (total of 144 villages). For each village, 50 households were randomly sampled. The average number of members per household was 4.42.
[2]Total number of household dropout: 443 (6.15%).
[3]Total number of subjects not examined; data obtained through interview of available household member: 5,264 (17.61%), 5 (0.017%) were determined blind; the rest were determined not blind, 66.77% of whom were under 30 years of age.

Annex 2. **Prevalence of visual impairment[1] by region.**

Region	Low Vision[2] (<6/18, ≥ CF 3m) WHO Category 1,2		Blind[2] (< CF 3m) WHO Category 3,4,5		Total[2]		Affected Population 2002[3]
	Number	Prevalence	Number	Prevalence	Number	Prevalence	
Ilocos	44	2.43	9	0.50	53	2.93	125,535
Cagayan Valley	75	4.07	16	0.87	91	4.94	144,421
Central Luzon	23	1.21	15	0.79	38	2.00	159,939
Southern Luzon	66	3.71	10	0.56	76	4.27	509,773
Bicol Region	46	2.52	13	0.71	59	3.23	158,830
Western Visayas	34	1.91	9	0.51	43	2.42	158,588
Central Visayas	34	1.76	12	0.62	46	2.38	137,017
Eastern Visayas	50	2.65	10	0.53	60	3.18	124,096
Western Mindanao	28	1.59	13	0.74	41	2.33	76,957
Northern Mindanao	46	2.17	13	0.61	59	2.78	80,453
Southern Mindanao	30	1.71	19	1.08	49	2.79	153,582
Central Mindanao	31	1.53	8	0.40	39	1.93	53,764
National Capital Region	13	0.81	3	0.19	16	1.00	107,289
Cordillera Autonomous Region	17	0.87	4	0.20	21	1.07	15,691
Caraga	11	0.60	3	0.16	14	0.76	17,394
Autonomous Region of Muslim Mindanao	44	2.43	17	0.80	61	3.23	72,953
Total	**592**	**1.98**	**174**	**0.58**	**766**	**2.56**	**2,035,294**

[1]Based on the vision of the better eye
[2]n = 29,888
[3]Based on crude prevalence, Y2002 Population: 79,503,675

Annex 3. **Visual impairment by age and gender.**

Age Group/ Gender	Bilateral Blind[1]	Low Vision (WHO)					Not Visually impaired (WHO)			Age Total	Age-Specific Prevalence (%)
		Low Vision-Blind		Bilateral Low Vision			Monocular Low Vision				
		SVI - Blind[2] (Monocular Blind)	BVI - Blind[3] (Monocular Blind)	BVI- SVI[4]	Bilateral SVI[5]	BVI[6]	Monocular Blind[7]	Monocular SVI[8]	Monocular BVI[9]		
0-4/M	0					1	2	1	0	6	0.22
0-4/F	2						0	0	0		
5-9/M	1				2	2	6		0	22	0.62
5-9/F	2				0	2	4		3		
10-14/M	1	0					2		4	12	0.34
10-14/F	1	1					1		1		
15-19/M	1			1	1	1	5		0	17	0.55
15-19/F	0			0	0	1	5		2		
20-24/M	0					2	4	1	2	17	0.66
20-24/F	2						4	0	2		
25-29/M	1	0			1	0	1	2	2	22	1.01
25-29/F	1	1		1	0	5	3	0	4		
30-34/M	1	1	1	1	0	0	4	1	3	33	1.69
30-34/F	1	0	0	0	1	7	5	4	3		
35-39/M	2	1		2		2	5	4	6	47	2.45
35-39/F	4	0	1	0	4	4	2	3	7		
40-44/M	2	1			1	1	9	5	6	55	3.14
40-44/F	3	0				5	6	7	9		
45-49/M	5	1		0		1	12	4	11	65	3.94
45-49/F	2	1	1	1	1	8	7		10		
50-54/M	3		2	1	1	4	4	3	19	90	6.51
50-54/F	5		1	2	2	15	4	1	23		
55-59/M	5	0	3	1	3	16	10	2	10	102	10.27
55-59/F	1	2	0	2	4	15	9	1	18		
60-64/M	4	4	2	4	7	27	9	7	28	193	20.86
60-64/F	8	4	7	8	12	16	13	5	28		
65-69/M	11	1	4	3	8	25	12	6	28	207	30.40
65-69/F	9	5	4	7	10	29	10	9	26		
70-74/M	14	4	6	7	9	20	7	12	19	216	46.45
70-74/F	17	3	5	14	14	29	16	5	15		
75-79/M	16	2	7	3	6	20	10	4	4	158	47.59
75-79/F	15	3	9	7	8	22	11	2	9		
80- /M	17	1	10	3	8	9	5	2	3	119	57.77
80-/F	17	7	3	6	3	19	4	0	2		
Total/M	*84*	*16*	*35*	*26*	*48*	*131*	*107*	*54*	*145*		
Total/F	*90*	*27*	*31*	*48*	*59*	*177*	*104*	*37*	*162*		
Total	**174**	**43**	**66**	**74**	**107**	**308**	**211**	**91**	**307**	**1,381**	
(% of 1,381)	(12.96)	(3.11)	(4.78)	(5.36)	(7.68)		(15.28)	(6.30)	(22.23)		

[1]Bilateral Blind (WHO Category 3,4,5). VA < CF 3m
[2]Severe Visual Impairment one eye, Blind other eye (Monocular Blind), 3/60 one eye, <CF 3m other eye (WHO Category 2)
[3]Moderate or Borderline Visual Impairment one eye, Blind other eye (Monocular Blind), 6/60 one eye,<CF3m other eye (WHO Cat 1)
[4]Moderate or Borderline Visual Impairment one eye, Severe Visual Impairment other eye; 6/60 one eye, 3/60 other eye (WHO Cat 1)
[5]Bilateral Severe Visual Impairment, 3/60 both eyes (WHO Category 2)
[6]Bilateral Moderate or Borderline Visual Impairment; 6/60 both eyes (WHO Category 1)
[7]Monocular Blind, At least 6/18 one eye < CF 3m other eye (No Visual Impairment, WHO Category 0)
[8]Monocular Low Vision–Severe Visual Impairment; At least 6/18 one eye, CF 3m other eye (WHO Category 0)
[9]Monocular Low Vision–Moderate or Borderline Visual Impairment; At least 6/18 one eye, 6/60 other eye (WHO Category 0)

Annex 4. **Comparative visual impairment, 1987 and 2002, Philippines.**

Type of Visual Impairment	1987[1]			2002[2]			*p*
	Number	Percent Prevalence	Affected Population	Number	Percent Prevalence	Affected Population	
Blind, Monocular	22	0.60	324,678	320	1.07	851,217	< 0.001
Blind, Bilateral	39	1.07	578,000	174	0.58	461,121	< 0.001
Total	**61**	**1.67**	**902,678**	**494**	**1.65**	**1,312,338**	

[1]Total n = 3,659, Y1987 Population = 56,921,782 (est.)
[2]Total n = 29,888, Y2002 Population = 79,503,675

Annex 5. **Comparative visual impairment, 1995 and 2002, Philippines.**

Type of Visual Impairment	1995[1]			2002[2]			*p*
	Number	Percent Prevalence	Affected Population	Number	Percent Prevalence	Affected Population	
Blind, bilateral	136	0.70	478,968	174	0.58	461,121	0.108
Blind, monocular							
a. other eye low vision[3] (low vision-blind)	82	0.42	287,381	109	0.36	286,213	0.340
b. other eye normal[4]	123	0.63	431,071	211	0.71	564,476	0.329
Low vision, bilateral[3]	379	1.95	1,334,268	489	1.64	1,303,860	0.010
Low vision, monocular[4]	228	1.17	800,561	398	1.33	1,057,399	0.122
Total	**948**	**4.87**	**3,332,249**	**1,381**	**4.62**	**3,673,069**	**0.194**

[1]Total n = 19,449, Y1995 Population = 68,424,000
[2]Total n = 29,888, Y2002 Population = 79,503,675
[3]Low Vision by WHO categorization
[4]Not Visually impaired by WHO categorization

Annex 6. **Cataract and error of refraction as causes of visual impairment, 1995 and 2002, Philippines.**

Cause of Visual Impairment	1995[1]			2002[2]			*p*
	Number	Percent Prevalence	Affected Population	Number	Percent Prevalence	Affected Population	
Cataract	577	2.97	2,032,193	547	1.83	1,455,049	< 0.001
Error of Refraction	212	1.09	745,822	616	2.06	1,638,592	< 0.001
Total	789	4.06	2,778,015	1,163	3.89	3,093,641	

[1]Total n = 19,449, Y1995 Population = 68,424,000
[2]Total n = 29,888, Y2002 Population = 79,503,675

Annex 7. **Cataract as a cause of visual impairment, 1987 and 2002, Philippines.**

Type of Visual Impairment	1987[1]			2002[2]			*p*
	Number	Percent Prevalence	Affected Population	Number	Percent Prevalence	Affected Population	
Cataract	45	1.24	744,000	547	1.83	1,455,049	0.009

[1]Total n = 3,659, Y1987 Population = 56,921,782 (est)
[2]Total n = 29,888, Y2002 Population = 79,503,675

Annex 8a. **Main causes of visual impairment, Philippines.**[1]

VISION	WHO Category	Cataract			Refractive Error			Corneal Opacity			Glaucoma		
		No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalance	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]
Monocular Visual Impairment	0	***195***	***0.65***	***518,709***	***281***	***0.94***	***747,475***	***20***	***0.07***	***53,201***	***8***	***0.03***	***21,280***
Monocular Low Vision Moderate Visual Impairment At least 6/18 one eye 6/60 other eye		65	0.22	172,903	213	*0.71*	566,591	5	*0.02*	13,300	1	*0.003*	2,660
Monocular Low Vision Severe Visual Impairment At least 6/18 one eye CF 3m other eye		30	0.10	79,801	47	*0.16*	125,023						
Monocular Blind At least 6/18 one eye <CF 3m other eye		100	0.33	266,005	21	*0.07*	55,861	15	*0.05*	39,901	7	*0.02*	18,620
Low Vision[2] (<6/18, ≥CF 3m)	1,2	***244***	***0.82***	***649,052***	***317***	***1.06***	***843,237***	***1***	***0.003***	***2,660***	***5***	***0.02***	***13,300***
Moderate Visual Impairment (<6/18, ≥6/60)	1												
Bilateral moderate visual impairment (6/60 both eyes)		98	0.33	260,685	194	*0.65*	516,050				1	*0.003*	2,660
Moderate visual impairment one eye, severe visual impairment other eye (6/60 one eye, 3/60 other eye)		29	0.10	77,141	42	*0.14*	111,722				1	*0.003*	2,660
Moderate visual impairment one eye, blind other eye (Mono Blind) 6/60 one eye,<CF3m other eye		29	0.10	77,141	36	*0.12*	95,762						
Severe Visual Impairment (<6/60, ≥ CF 3m)	2												
Bilateral Severe Visual Impairment (3/60 both eyes)		63	0.21	167,583	35	*0.12*	93,102	1	*0.003*	2,660	3	*0.01*	7,980
Severe Visual Impairment one eye, blind other eye (Mono Blind) (3/60 one eye,<CF3m other eye)		25	0.08	66,501	10	*0.03*	26,601						
Blind[2] (< CF 3m) Blind CF 1m Blind CF 2m Blind NLP	3,4,5 3 4 5	***108***	***0.36***	***287,286***	***18***	***0.06***	***47,881***	***6***	***0.02***	***15,960***	***14***	***0.05***	**37,241**
Grand Total		**547**	**1.83**	**1,455,049**	**616**	**2.06**	**1,638,593**	**27**	**0.09**	**71,821**	**27**	**0.09**	**71,821**

[1]Based on the main cause of blindness.
[2]Based on the vision of the better eye
[3]Based on crude prevalence, Y2002 Population: 79,503,675

Annex 8b. **Main causes of visual impairment, Philippines.**[1]

VISION	WHO Category	Retinopathy			Maculopathy			Uveitis			Optic Atrophy		
		No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]
Monocular Visual Impairment	0	***13***	***0.04***	***34,580***	***28***	***0.09***	***74,482***	***2***	***0.01***	***5,320***	***10***	***0.03***	***26,600***
Monocular Low Vision Moderate Visual Impairment At least 6/18 one eye 6/60 other eye		4	*0.01*	10,640	10	*0.03*	26,601				1	*0.003*	2,660
Monocular Low Vision Severe Visual Impairment At least 6/18 one eye CF 3m other eye		2	*0.01*	5,320	4	*0.01*	10,640						
Monocular Blind At least 6/18 one eye <CF 3m other eye		7	*0.02*	18,620	14	*0.05*	37,241	2	0.01	5,320	9	*0.03*	23,940
Low Vision[2] (<6/18, ≥CF 3m)	1,2	***12***	***0.04***	***31,920***	***13***	***0.04***	***34,580***				***2***	***0.01***	***5,320***
Moderate Visual Impairment (<6/18, ≥6/60)	1												
Bilateral moderate visual impairment (6/60 both eyes)		6	*0.02*	15,960	6	*0.02*	15,960				1	*0.003*	2,660
Moderate visual impairment one eye, severe visual impairment other eye (6/60 one eye, 3/60 other eye)					3	*0.01*	7,980						
Moderate visual impairment one eye, blind other eye (Mono Blind) 6/60 one eye,<CF3m other eye													
Severe Visual Impairment (<6/60, ≥ CF 3m)	2												
Bilateral Severe Visual Impairment (3/60 both eyes)		4	*0.01*	10,640	1	*0.003*	2,660				1	*0.003*	2,660
Severe Visual Impairment one eye, blind other eye (Mono Blind) (3/60 one eye,<CF3m other eye)		2	*0.01*	5,320	3	*0.01*	7,980						
Blind[2] (< CF 3m) Blind CF 1m Blind CF 2m Blind NLP	3,4,5 3 4 5	***7***	***0.02***	***18,620***	***7***	***0.02***	***18,620***				***6***	***0.02***	***15,960***
Grand Total		**32**	**0.11**	**85,120**	**48**	**0.16**	**127,682**	**2**	**0.01**	**5,320**	**18**	**0.06**	**47,880**

[1]Based on the main cause of blindness.
[2]Based on the vision of the better eye
[3]Based on crude prevalence, Y2002 Population: 79,503,675

Annex 8c. **Main causes of visual impairment, Philippines.**[1]

VISION	WHO Category	Enucleated Eye			Phthisis Bulbi			Amblyopia			Others		
		No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]	No.	Percent Prevalence	Affected Population[3]
Monocular Visual Impairment	0	***6***	***0.02***	***15,960***	***20***	***0.07***	***53,201***	***10***	***0.03***	***26,600***	***16***	***0.05***	***42,560***
Monocular Low Vision Moderate Visual Impairment At least 6/18 one eye 6/60 other eye								3	*0.01*	7,980	5	*0.02*	13,300
Monocular Low Vision Severe Visual Impairment At least 6/18 one eye CF 3m other eye								3	*0.01*	7,980	5	*0.02*	13,300
Monocular Blind At least 6/18 one eye <CF 3m other eye		6	*0.02*	15,960	20	*0.07*	53,201	4	*0.01*	10,640	6	*0.02*	15,960
Low Vision[2] (<6/18, ≥CF 3m)	1,2							**2**	***0.01***	***5,320***	***2***	***0.01***	***5,320***
Moderate Visual Impairment (<6/18, ≥6/60)	1												
Bilateral moderate visual impairment (6/60 both eyes)								2	*0.01*	5,320	1	*0.003*	2,660
Moderate visual impairment one eye, severe visual impairment other eye (6/60 one eye, 3/60 other eye)													
Moderate visual impairment one eye, blind other eye (Mono Blind) 6/60 one eye,<CF3m other eye													
Severe Visual Impairment (<6/60, ≥ CF 3m)	2												
Bilateral Severe Visual Impairment (3/60 both eyes)													
Severe Visual Impairment one eye, blind other eye (Mono Blind) (3/60 one eye,<CF3m other eye)											1	*0.003*	2,660
Blind[2] (< CF 3m) Blind CF 1m Blind CF 2m Blind NLP	3,4,5 3 4 5				***5***	***0.02***	***13,300***	***1***	***0.003***	***2,660***	***2***	***0.01***	***5,320***
Grand Total		**6**	**0.02**	**15,960**	**25**	**0.08**	**66,501**	**13**	**0.04**	**34,580**	**20**	**0.07**	**53,200**

[1]Based on the main cause of blindness.
[2]Based on the vision of the better eye
[3]Based on crude prevalence, Y2002 Population: 79,503,675

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ORIGINAL ARTICLE

Low-dose transpupillary thermotherapy for retinal-pigment epithelial detachment in Asian eyes

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ABSTRACT

Objective

This study investigated the efficacy of low-dose transpupillary thermotherapy in Asian eyes diagnosed with subfoveal retinal-pigment epithelial detachment.

Methods

Records of seven patients from different medical institutions were included in this nonrandomized retrospective series. All patients were diagnosed to have unilateral retinal-pigment epithelial detachment and underwent treatment with transpupillary thermotherapy (TTT) between January 2002 and January 2003. Minimum follow-up was 6 months.

Results

Average change in visual acuity at 1 month post-TTT revealed less than 1 (0.86) line of improvement, which increased to 1.28 lines on the third month and leveled at .42 lines on the sixth month. Overall improvement of these 7 patients at 6 months of follow-up was 2.56 lines. The average reduction in the size of the lesion was 41.54%. Total average reduction in the size of the lesion between retreatment and when lesion was deemed clinically stable was 55.67%.

Conclusion

Low-dose transpupillary thermotherapy may be a viable treatment modality for subfoveal pigment epithelial detachments based on the improvement of visual acuity, reduction in the size of lesion, and absence of complications at 6 months of follow-up.

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RETINAL-PIGMENT epithelial detachment (RPED) is among the features of neovascular age-related macular degeneration (ARMD), the leading cause of irreversible central visual loss in Caucasians 50 years old and older in most developed countries.

Patients presenting with RPEDs may have blurred vision or metamorphopsia. One third of RPEDs may resolve within 24 to 36 months.[1] However, studies have shown that 33% of serous RPEDs exhibit decreased visual acuity and 26% of eyes developed choroidal neovascularization in one year.[2] Elman and colleagues reported that 33% of serous RPEDs progress to choroidal neovascularization (CNV) within 20 months.[3]

The Macular Photocoagulation Study (MPS) is the largest randomized and controlled multicenter study to evaluate the efficacy of laser photocoagulation for the treatment of selected cases with neovascular ARMD. In this trial, RPEDs associated with CNV were excluded.[4] Results of a controlled, clinical trial by the Moorfields Macular Study Group showed that treatment of eyes with serous RPEDs using laser photocoagulation had poor visual outcomes.[5]

Neither photodynamic therapy study (TAP) nor the verteporfin in photodynamic therapy study (VIP) investigated the treatment of RPED.[6, 7]

Transpupillary thermotherapy (TTT) is an emerging form of treatment for neovascular ARMD for patients presenting with subfoveal occult choroidal neovascularization who cannot be treated with conventional techniques. In TTT, heat is delivered to the choroid and retinal pigment epithelium through the pupil using a modified diode laser (emission wavelength of 810 nm). The near-infrared wavelength is absorbed by melanin contained in retinal pigment epithelial (RPE) cells and choroidal melanocytes.[8] The aim of this treatment is to induce leakage reduction, exudate resorption, and RPE appositioning. With TTT, it is hypothesized that sealing the break in the Bruch's membrane can be achieved by cellular apoptosis during hyperthermia and RPE proliferation. By sealing the break in the Bruch's membrane, hydraulic conductivity in the fluid pump mechanism is restored leading to leakage reduction and fluid reabsorption. Additionally, with a controlled maximal temperature rise of 10°C delivered by TTT, there is no resulting damage to the level of the RPE or sensory retina. It is hoped that with early detection and treatment of RPEDs, visual improvement can be attained and the risk of developing CNV can be lowered.

This study determined the efficacy of TTT in Asian eyes with subfoveal retinal-pigment epithelial detachment.

METHODOLOGY

Records of patients of one of the authors (RKG) from different medical institutions were reviewed for this nonrandomized retrospective series. All patients were over 45 years old diagnosed to have unilateral retinal-pigment epithelial detachment who underwent treatment with TTT between January 2002 and January 2003. Minimum follow-up was 6 months. All patients developed blurring of vision or metamorphopsia.

Included in the study were patients diagnosed with unilateral or bilateral subfoveal serous RPED with best-corrected Snellen visual acuity of 20/30 or worse. They must have undergone routine angiographic studies and fluorescein angiography must reveal early homogenous filling of the serous detachment with the accumulation of dye causing persistent hyperfluorescence in the late phases and no leakage of dye beyond the confines of the RPED. Indocyanine green angiography must exhibit a well-delineated ring of hyperfluorescence that surrounded a hypofluorescent spot in the early arterial phase.

Patients who had ocular comorbidities (diabetic retinopathy and glaucoma) or significant cataract or opacity in the media that prevents visualization, who underwent previous laser photocoagulation, or whose angiographic studies showed the presence of CNV or fibrovascular-pigment epithelial detachments were excluded.

Treatment protocol

Initial clinical assessment included best-corrected Snellen visual acuity, anterior-segment examination, dilated retinal exam with a 78D or 90D fundus lens. Further assessment was done by performing colored fundus photography (Topcon, Tokyo, Japan) and fluorescein-indocyanine green angiography (Heidelberg Retinal Analyzer HRA, Heidelberg, Germany). The size of the lesion was measured using the Heidelberg Retinal Analyzer.

All patients were briefed on the procedure and asked to sign an informed consent before undergoing angiographic studies—sodium fluorescein (FA) and indocyanine green (ICG) videoangiography. Initial 30° red-free retinal images were taken prior to dye injection. Indocyanine green was prepared using 12.5 gms of ICG diluted in 0.7 cc of solvent. This was injected intravenously followed by 3 cc of normal saline solution as bolus. Timer was started and videoangiography was performed for 1 minute, 12 frames/second with a setting of 512 Hz. This was immediately followed by intravenous injection of 5 ml of 10% sodium fluorescite. Both procedures lasted 25 minutes.

Treatment was scheduled between 1 and 12 hours from the time the angiograms were performed and after informed consent was obtained. Transpupillary thermotherapy was delivered (by RKG) through a slit-lamp using a modified infrared diode laser at 810 nm with an adjustable beam width of 0.5 mm, 0.8 mm, 1.2 mm, 2.0 mm, and 3.0 mm (Iris Medical Instruments, Mountain

View, CA, USA). Topical anesthetic using 0.5% proparacaine was instilled prior to laser therapy.

Laser-power settings were computed based on the clinical experience with TTT for occult CNV—a dose of 800 mW, 60-second exposure, and 3.23 mm spot diameter on the retina (248 mW/mm) was effective for light pigmented fundi. Spot settings were converted to actual spot diameter on the retina using a Mainster standard (image magnification = 0.96). Laser-power settings were computed and adjusted accordingly, taking into consideration the size of the retinal lesion, chorioretinal pigmentation (minus 30% of the computed laser power), and the presence of hemorrhage (plus 10 to 20% of the computed laser power). Peripheral test spots were made and appropriate adjustments done in increments of 50 to 100 mW until visible color change was observed. Once visible color change on the test spot was noted, laser power was reduced to the next lower dose. Generally, TTT is applied to the entire lesion in one spot for 60 seconds. For large lesions, multiple nonoverlapping spot treatments covering the entire area of the lesion were applied.

Patients underwent ophthalmic evaluation and dilated fundus exam 1, 3, and 6 months posttreatment. Repeat FA-ICG angiography was performed after 1 month if clinical evaluation showed no reduction in the size of the lesion and vision deteriorated. Retreatment was considered if there was no reduction in size of the lesion, with stable or deterioration of visual acuity within 4 to 6 weeks. If clinical examination showed stable or improved vision and stable or decreasing size of the lesion, the patient was put under observation and repeat FA-ICG angiography was performed after 2 to 3 months to document the status of the RPED.

Outcomes measured were angiographic reduction in the size of the lesion and visual acuity. Angiographic reduction was measured by obtaining the area in mm^2, and presented as percentage reduction in size. Visual acuity was measured by the improvement in the number of lines. Mean and standard deviations were determined. T-test was used to determine significant differences.

RESULTS

Patient population consisted of 4 males and 3 females with a mean age of 57 years. All patients had unilateral serous RPED, four of them with associated hemorrhages.

Seven eyes underwent TTT with treatment parameters described in Table 1. The laser-power settings ranged from 50 mW to 220 mW and the beam size from 0.5 to 0.8 mm. Two eyes underwent retreatment within 4 to 8 weeks using the same treatment parameters.

The average change in visual acuity after TTT was 0.86 line of improvement after one month, 1.28 lines after 3 months and 0.42 line after 6 months (Table 2).

The average reduction in the size of RPED was 41.54%, with additional 15.45% reduction in eyes that were retreated. The final average reduction in size of the lesion from pretreatment to end of study was 55.67% (Table 3).

No complications were noted after TTT.

DISCUSSION

RPED usually occurs in older patients with ARMD. Its clinical course is variable. One third of RPEDs resolve within 24 to 36 months and atrophy of the RPE may occur. Poliner reported that 33% of serous RPEDs worsened to 20/200. The presence of hemorrhagic RPED is associated with more than 80% of involved eyes worsening to 20/200 or poorer vision. Choroidal neovascular formation developed in 26% of eyes by one year and 49% of eyes by three years.[2] Elman reported that 33% of serous RPEDs progressed to CNV in 20 months.[3]

RPED associated with ARMD are due to changes caused by CNV, which is noted to be leaky due to the lack of tight junctions in the newly developed blood vessels. Breaks in

Table 1. **Transpupillary thermotherapy treatment parameters.**

Patient	SLA Spot Setting	Retinal Spot Diameter (mm)	Laser Power (mW)	Power/ Diameter (mW/mm)	Number of Treatments
1	0.5	0.52	180	346	1
2	0.5	0.52	220	423	1
3	0.8	0.83	90	100	1
4	0.5	0.52	80	154	1
5*	0.8	0.83	150	180	2
6*	0.8	0.83	150	180	2
7	0.5	0.52	50	96	1

*Retreatment within 4 to 8 weeks after 1 month observation post-TTT.

Table 2. **Visual acuity pre- and posttreatment.**

Patient	Pre-TTT	1 month Post-TTT	3 months Post-TTT	6 months Post TTT
1	20/70	0	0	1
2	CF	2	2	0
3	HM	1	0	0
4	20/100	1	3	1
5*	20/100	1	1	0
6*	20/70	0	0	1
7	20/200	1	3	0
Average Total		**.86**	**1.28**	**.42**

*Retreatment within 4 to 8 weeks after 1 month observation post-TTT.

Table 3. **Lesion size of RPED measured on ICG angiography (mm^2).**

Patient	Pretreatment	Posttreatment	Retreatment
1	20.28	9.50	
2	54.29	3.13	
3	13.51	12.15	
4	2.35	1.88	
5*	16.06	9.38	8.09
6*	18.79	18.35	14.62
7	19.52	14.81	

*Retreatment within 4 to 8 weeks after 1 month observation post-TTT.

the Bruch's membrane may allow fluid to leak out into the sub-RPE space or further into the subsensory retinal space. Fibrovascular penetration may follow, setting the stage for hemorrhage and scarring.

The importance of ICG angiography cannot be overemphasized. ICG has two biophysical characteristics that provide superior imaging of choroidal pathology. The peak absorption (805 nm) and fluorescence (835 nm) wave lengths are in the near infrared spectrum and penetrate the retinal RPE to a greater degree than visible light. CNV and other abnormalities of the choroidal vasculature are well demonstrated using ICG because the vascular patterns are not obscured by progressive leakage of dye from the choroidal vessels and the RPE does not effectively block the choroidal fluorescence produced when infrared light illuminates the ICG dye. ICG is also highly protein bound (98%) and leaks less from the choriocapillaries.[9, 10] Fluorescein videoangiography in its early and late phases was valuable as a diagnostic adjunct as it aided in determining the presence of a probable choroidal neovascular membrane (CNVM). ICG videoangiography confirmed the presence of a presumed CNVM and aided identification of leakage sites.

TTT was first described in 1995 by Oosterhius et al.in the treatment of choroidal melanomas as an adjunct to radiation therapy in cases where tumor regression was noted to be insufficient.[11] The therapeutic results of TTT are caused by hyperthermia. At the cellular level, TTT may cause vascular thrombosis, sclerosis, or leukostasis. It may also cause RPE proliferation or apoptosis and even inhibit angiogenesis.[12] TTT is a low retinal irradiance, long-pulse, infrared diode-laser photocoagulation treatment. Upon delivery of heat, the end point of treatment is not tissue coagulation but hyperthermia in a controlled gradual maximal temperature rise of 10° C at the level of the lesion, causing no neurosensory damage to the site of the lesion nor to the adjacent retina compared with standard laser photocoagulation, which causes temperature rise of 45° C and complete protein denaturation.

Power settings for these patients were adjusted according to the size of the lesion, pigmentation, visible retinal burns, and the presence of hemorrhage. Melanin in the RPE and the choroid is the primary light absorber in retinal photocoagulation. Light absorption converts laser radiation into heat energy, increasing the temperature of light-absorbing tissues.

In RPED, disrupted adherence of the RPE basement membrane to the inner collagenous zone of the Bruch's membrane may be due to increased permeability of the choriocapillaries, degeneration of the Bruch's membrane, degeneration of the RPE and its basement membrane, or exudation from sub-RPE choroidal neovascularization. It is believed that TTT seals or causes thrombosis of leaky vessels, restoring the hydraulic conductivity of the fluid pump across the RPE and Bruch's membrane.

The randomized clinical trial of TTT for CNV by Elias Reichel used laser-power setting of 800 mW for a 60-second exposure and a 3.23 mm spot diameter on the retina (248 mW/mm). Based on this computation, actual power settings were applied to the first two patients in this series with 15% reduction in the power, taking into consideration that Reichel's settings for TTT was efficient for lightly pigmented fundi.

Based on the clinical experience of Okada, who used half the power (400 mW power for 60 seconds with a 3.0 diameter laser beam resulting in 124 mW/mm power/diameter ratio) to treat lightly pigmented fundi in Japanese patients,[13] the authors adjusted the power settings to treat serous RPED, which was 30% to 40% less energy from Reichel's protocol of TTT for CNV.

The results of this study suggest that TTT may be an effective and safe treatment for RPED. While not achieving statistical significance, the encouraging results of this small series provide enough evidence to justify an RCT in order to determine the optimum treatment parameters, efficacy, and safety of TTT for the treatment of RPED.

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ORIGINAL ARTICLE

Toxicity of 0.2% chlorhexidine gluconate on the cornea and adjacent structures

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ABSTRACT

Objective

To determine the toxicity of the potential fungicide chlorhexidine gluconate (as a pure 0.2% solution and as a commercially available skin antiseptic diluted to contain 0.2% chlorhexidine gluconate) to the cornea and adjacent ocular structures.

Methods

An experimental study was performed at the Animal Facility of the Massachusetts Eye and Ear Infirmary. Pure chlorhexidine gluconate 0.2% was applied to the right eye of 10 female albino rabbits 4 times daily for 14 days. Prior to treatment, all eyes underwent debridement of the corneal epithelium and were examined on days 1, 3, 7, and 14. The toxicity of the following was also determined: a commercial skin antiseptic solution diluted to contain 0.2% chlorhexidine gluconate and 0.2% isopropyl alcohol as active ingredients (4), 0.2% isopropyl alcohol (3), and sterile distilled water (2). The acute toxicity of the diluted solution was determined by application every hour for 6 hours. Histopathological examination was done.

Results

Complete reepithelialization was noted by the seventh day in all eyes. At day 14, all corneal epithelia remained intact, but mild superficial punctate keratopathy was observed in some eyes treated with pure 0.2% chlorhexidine, in all eyes treated with the diluted solution and distilled water, but none in alcohol-treated eyes. Histopathological examination revealed no signs of corneal inflammation in 6 of 10 eyes treated with pure chlorhexidene. Very mild inflammation was noted in the remaining 4 eyes, and in all eyes treated with the diluted solution, 0.2% isopropyl alcohol, and sterile distilled water. Acute toxicity studies using the diluted solution applied hourly showed mild inflammation not only of the anterior corneal stroma (2 of 3 eyes) but also of the sclera (1 of 3 eyes).

Conclusion

Multiple applications of 0.2% chlorhexidine gluconate as a pure solution and as a diluted skin-antiseptic solution did not produce severe inflammation and structural alterations in the deep layers of the cornea in rabbit eyes. This suggests that the solutions may be safe for alternative use in the prolonged and intensive treatment of filamentous keratomycosis.

Key words: *Chlorhexidine, Toxicity, Cornea, Keratomycosis, Keratitis*

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KERATOMYCOSIS is an important cause of ocular morbidity in developing tropical countries, often leading to blindness.[1] Farmers are particularly at risk because of their constant exposure to soil and plant, both rich sources of fungi. Keratomycosis due to filamentous fungi is difficult to cure even with optimal agents such as topical amphotericin and natamycin. Moreover, in developing countries, these agents are often unavailable or unaffordable for most patients. This has triggered a search for less expensive antimicrobials that would be stable in tropical climates and effective in the treatment of filamentous corneal ulcers.[2]

In two clinical studies in humans, Rahman et al. found that 0.2% chlorhexidine gluconate was as effective as natamycin in treating keratomycosis.[2, 3] Although they found no significant corneal toxicity, previous studies have.[4, 5, 6] Furthermore, they stressed that the chlorhexidine preparation used should not contain alcohol or detergent. However, pure chlorhexidine may be difficult to obtain in the Philippines and in some areas of the world, while the combination of chlorhexidine plus isopropyl alcohol is readily available as a skin antiseptic. This study evaluated the toxicity of pure 0.2% chlorhexidine, and a diluted commercial skin antiseptic containing 0.2% chlorhexidine and 0.2% isopropyl alcohol as its active ingredients.

METHODOLOGY

This experimental study was performed at the Animal Facility of the Massachusetts Eye and Ear Infirmary using 25 female albino rabbits randomly assigned to receive treatment of the right eye under phase 1 or phase 2.

Treatment of rabbit eyes

Phase 1

Nineteen female albino rabbits (1.5 to 2.5 kg) were randomly allocated to receive pure 0.2% chlorhexidine gluconate (10 rabbits), dilute scrub solution (4 rabbits), 0.2% isopropyl alcohol (3 rabbits), or sterile distilled water as control (2 rabbits). All the rabbits underwent debridement of the corneal epithelium of the right eye by marking a 7-mm disc with a disposable trephine and then gently removing the epithelium with a number 15 Bard-Parker blade. Prior to the procedure, the rabbits were anesthetized with intramuscular ketamine (40 mg/kg body weight) and xylazine (5 mg/kg body weight), and one drop of proparacaine HCl was placed on the eye.

The right eyes of the rabbits were then treated with their respective test solutions four times a day for 14 days. The left eye served as control and received sterile distilled water at the same frequency as the fellow eye. Slit-lamp biomicroscopy was performed on all eyes prior to treatment (day 0) and prior to enucleation (day 15). Examination and fluorescein staining was also done on days 1, 3, 7, and 14.

At the end of each treatment interval, the rabbits were sacrificed by intravenous injection of pentobarbital 75–100 mg/kg followed by enucleation of both eyes. Histopathological examination was performed using hematoxylin and eosin (H and E) by one masked reader (CSF).

Phase 2

The acute toxicity of the dilute chlorhexidine antiseptic solution was determined by applying the solution to the right eye of 6 rabbits every hour for 6 hours. Debridement of the epithelium was done on half of the rabbit corneas (3 eyes) prior to the treatment (Group A), while no debridement was performed on the other half (Group B) (3 eyes). The left eye of each rabbit served as control and received sterile distilled water one drop every hour. Slit-lamp biomicroscopy with fluorescein staining was performed at the end of the treatment period. The rabbits were sacrificed as described in Phase 1 and histopathological examination was performed.

This animal protocol was designed and conducted in accordance with the ARVO Resolution on the Use of Animals in Research and was approved by the Animal Care Committee of the Massachusetts Eye and Ear Infirmary.

Preparation of 0.2% chlorhexidine gluconate

100 ml of sterile water for injection was added to 1 ml of chlorhexidine gluconate 20% to create a solution of 0.2% concentration.

Preparation of dilute scrub solution containing 0.2% chlorhexidine gluconate and 0.2% isopropyl alcohol

50 ml of skin-antiseptic solution containing 4% chlorhexidine gluconate and 4% isopropyl alcohol plus inactive ingredients (Biocyde, Biomed Systems, Norwalk, CT, USA) was added to 450 ml of a 0.05M buffer solution containing potassium phosphate monobasic and sodium hydroxate (pH 7.00) to produce 500 ml of 0.4% chlorhexidine gluconate stock solution with a pH of 7.05. 250 ml of the stock solution was then diluted with 250 ml sterile distilled water to produce 500 ml of 0.2% chlorhexidine gluconate with 0.2% isopropyl alcohol test solution with a pH of 6.98.

RESULTS

Phase 1

Slit-lamp examination on days 1, 3, 7, and 14

Results of fluorescein examination at various time points are summarized in Table I. On day 1, healing of 10 to 30% of the deepithelialized cornea was noted in all rabbits, except for one rabbit in the pure chlorhexidine group, which had 90% healing. The latter was completely healed by day 3. By day 3 there was at least 70% healing in all eyes. By day 7, the epithelium had healed in all corneas.

Table I. **Fluorescein examination of rabbit eyes on days 1, 3, 7, and 14 (Trial 1): Estimated percentage healing[a] and other staining abnormalities.**

Treatment Group	Day 1	Day 3	Day 7	Day 14
Pure chlorhexidine 0.2% (n = 10 eyes)	90% healed (1 eye) 10-30% healed (9 eyes)	100% healed (5 eyes) with 2+ SPK[b] *in 4 eyes* 85-90% healed (2 eyes) 70-80% healed (3 eyes)	100% healed (10 eyes)	100% healed (10 eyes) with 1/2+ SPK in 3 eyes
Diluted antiseptic solution (n = 4 eyes)	10-30% healed (4 eyes)	70-90% healed (4 eyes)	100% healed (4 eyes)	100% healed (4 eyes) with 1+ SPK in all eyes
0.2% isopropyl alcohol (n = 3 eyes)	10-30% healed (3 eyes)	70-90% healed (3 eyes)	100% healed (3 eyes)	100% healed (3 eyes)
Sterile distilled water (n = 2 eyes)	10-30% healed (2 eyes)	70-90% healed (2 eyes)	100% healed (2 eyes)	100% healed (2 eyes) with 1/2+ SPK in all eyes

[a]Percentage healing is based on fluorescein dye uptake after a 7-mm disc diameter debridement of the corneal epithelium. There is no other fluorescein pattern abnormality unless otherwise stated.
[b]Superficial punctate keratopathy

On day 14, all corneal epithelia remained intact, but mild superficial punctate keratopathy (SPK) was observed in some eyes treated with 0.2% chlorhexidine, all eyes treated with the diluted solution and distilled water, but none in alcohol-treated eyes. No lid swelling, conjunctival injection, chemosis, or discharge was noted.

Phase 1

Histopathology of rabbit corneas

Histopathological findings are summarized in Table 2. Complete epithelialization was noted in areas debrided in all four groups. Histological examination of the pure chlorhexidine-treated eyes revealed no signs of corneal toxicity in 6 eyes, and mild anterior stromal edema in 3 eyes (Figure 1A). One rabbit cornea was normal except for two very small areas of epithelial cell degeneration (one area with infiltration of two neutrophils). Aside from this, no inflammatory cells were noted in the cornea of the rest of the eyes.

Two of the 4 eyes in the diluted-solution-treated group showed a small (2 mm) central linear scar in the new epithelium. Mild stromal edema was noted in all eyes treated with the diluted solution, 0.2% isopropyl alcohol, and sterile distilled water (Figures 1B, 1C, 1D). Neither scleritis nor limbitis was observed on pathologic studies. All control eyes were normal on histopathologic study.

Phase 2

Slit-lamp examination for acute toxicity of diluted antiseptic solution

All 3 eyes with debrided corneal epithelium (Group A) showed 2+ conjunctival injection. This was not evident in eyes with intact corneal epithelium (Group B) or in the control eyes. There was no lid swelling, conjunctival chemosis, or discharge noted in all eyes.

Phase 2

Histopathology of rabbit corneas

Histopathological findings are summarized in Table 2.

Table 2. **Histopathological findings.***

Phase 1
Pure chlorhexidine 0.2% (N = 10 eyes) No histological changes (6 eyes) Normal cornea except for two small areas of degenerating epithelial cells (1 eye) <1/2+ anterior corneal stromal edema (3 eyes)
Diluted antiseptic solution (N = 4 eyes) <1/2+ anterior corneal stromal edema (4 eyes) with 2 mm central linear scar in the new epithelium of 2 eyes
Isopropyl alcohol (N = 3 eyes) <1/2+ anterior corneal stromal edema (3 eyes)
Sterile distilled water (N = 2 eyes) <1/2+ anterior corneal stromal edema (2 eyes)
Phase 2
Group A: Debrided corneas (N=3 eyes) Inflammatory cells in the sclera (1 eye) Inflammatory cells in the anterior stromal layer of cornea (2 eyes)
Group B: Intact corneas (N=3 eyes) Conjunctival stromal inflammation at limbal area (2 eyes) Inflammatory cells in the anterior stromal layer of cornea (1 eye)

* Conjunctiva, sclera, and iris are normal on histopathology unless specific abnormalities are listed.

In Group A, inflammatory cells were seen in the sclera (1 of 3 eyes) and anterior stromal layer of the cornea (2 of 3). In Group B, there was mild inflammation of the limbus (2 of 3) and of the anterior stromal layer of the cornea (1 of 3) (Figure 2). All control eyes were normal on histopathologic study.

DISCUSSION

The choice of chlorhexidine gluconate as a promising alternative treatment for keratomycosis was made because of its ability to penetrate the deeper layers of the cornea where fungal elements are known to be located.[5, 6, 7] It is believed to bind avidly and rapidly to the corneal epithelium, with subsequent intercalation to the bilaminar membrane.[5] Disruption of tight junctional complexes then

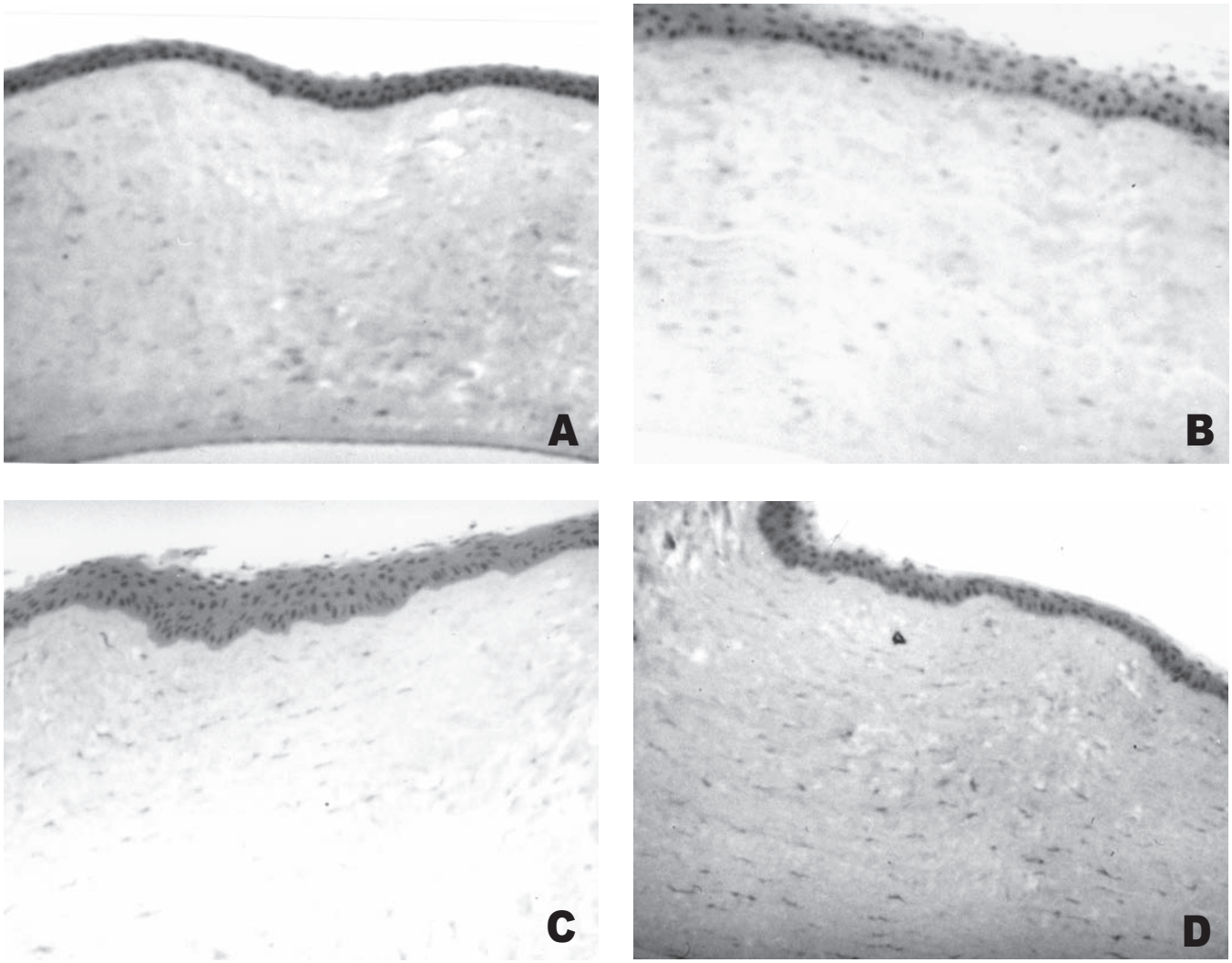

Figure 1. Histopathological sections of corneas treated for 14 days with pure chlorhexidine (**A**), diluted chlorhexidine solution (**B**), isopropyl alcohol (**C**), and distilled water (**D**) showing mild stromal edema.

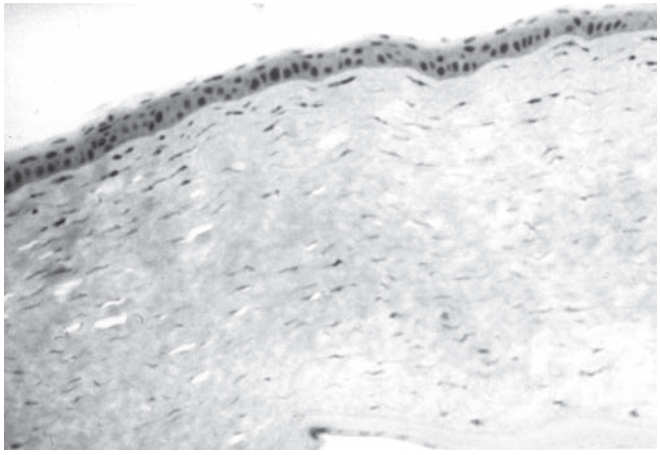

Figure 2. Histopathological section of cornea with intact epithelium treated with dilute chlorhexidine solution for 6 hours showing inflammatory cells in anterior stromal layer.

allows tear-film access to the intercellular spaces of the corneal epithelium, thereby creating a low-resistance pathway across stroma and the endothelial layer.[6] This allows chlorhexidine gluconate to reach pathogens even in the deeper layers of the cornea. The cationic antiseptic is believed to interact with the anions on the bacterial-cell wall with subsequent damage to the latter, permitting the agent to enter the cytoplasm and to precipitate its contents or to allow the entry of a synergistic drug.[8, 9] Whether this is also the manner by which chlorhexidine gluconate acts as an antimycotic is still unclear.

Four-percent chlorhexidine gluconate is a widely used skin antiseptic known to have bactericidal activity against some Gram-negative and Gram-positive organisms. It is employed for irrigation of the bladder and the pleural cavity, as well as for application to burnt skin. It is currently used as a mainstay treatment for *Acanthamoeba keratitis* at

a much lower concentration (0.02%), proving successful even against the resilient cyst stage of the amoeba.[10]

Previous studies have shown that the cytotoxic activity of chlorhexidine gluconate is not specific for microorganisms. It has been observed to damage ocular structures most notably the cornea, at concentrations greater than 0.1%. [4,5,6,11] On the other hand, Rahman et al. found that 0.2% chlorhexidine gluconate solution was effective against filamentous fungi with no toxic effects to the cornea.[2,3]

In our study, a very mild inflammation of the superficial corneal layers resulted from the application of chlorhexidine gluconate 0.2% four times a day for 14 days, as a pure solution (4 of 10 eyes), or as a diluted commercial skin antiseptic (4 of 4 eyes). More frequent applications of the diluted skin antiseptic at hourly administration for 6 hours showed mild inflammation of the superficial corneal layers and the adjacent ocular structures. We do not know whether this is due to a short-term toxicity of the solution, or represents a reaction to the introduction of a foreign substance to the eye. The edema could be part of the recovery process of the cornea and not due to the toxic effects of the test solutions since even the corneas given sterile distilled water manifested mild stromal edema. Furthermore, the adequate healing of the corneal epithelial defect, the absence of severe inflammation and structural alteration in the deeper layers of the cornea by the end of the 14-day trial is reassuring, particularly since prolonged treatment with chlorhexidine gluconate would be required for an effective antimicrobial effect.

The results of this study should be used with caution since there are some differences between the anatomy and biochemistry of rabbit and human corneas.[12] Moreover, the corneas used in this study did not have any active keratitis, thus the response to the chlorhexidine solution may be different in corneas with active keratitis. It also remains to be established if more frequent and prolonged applications of chlorhexidine gluconate at 0.2% concentration, as may be required for fungal corneal infections, would produce more severe toxicity than that observed in the study. Although the number of rabbits used in each treatment group was small, our findings are reassuring and suggest that using 0.2% chlorhexidine gluconate to treat keratomycosis may be safe. Future studies should evaluate the safety of hourly applications for prolonged periods of time.

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REVIEW

Secondary glaucoma in retinoblastoma

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ABSTRACT

Objective

To investigate the causes of secondary glaucoma in retinoblastoma (RB) and underscore the significance of glaucoma as a presenting sign of RB.

Methods

A 7-month-old boy, initially diagnosed with congenital glaucoma in the left eye (OS), revealed an intraocular RB on further work-up. The eye was eventually enucleated and histopathology showed iris neovascularization (NVI) and a large solitary posterior-pole RB tumor with total retinal detachment. Using this as an illustrative case, a literature search on the relationship of glaucoma and RB was done to determine the incidence and the most common mechanisms of RB-induced glaucoma.

Results

The most common mechanisms of secondary glaucoma in RB were: iris neovascularization (30–72%), pupillary block (27%), and tumor seeding of the anterior chamber (2%).

Conclusion

We presented a case of RB-induced glaucoma that mimicked congenital glaucoma. Awareness that RB may present initially as glaucoma is essential for appropriate evaluation and management.

Keywords: *Retinoblastoma, Secondary glaucoma, Neovascularization, Pupillary block*

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THE ASSOCIATION between retinoblastoma (RB) and secondary glaucoma was first noted in 1965[1] and reported in literature to occur in 1% to 23% of cases.[1, 2, 3, 4, 5, 6, 7] Glaucoma and iris neovascularization (NVI) are two of the anterior-segment conditions described in RB.[3, 4, 8] Certain histological features in the anterior segment of enucleated eyes with RB also suggest the presence of otherwise undetected glaucoma.[9]

Yoshizumi and colleagues found that 34 (22.8%) of 149 eyes with RB examined histopathologically had clinically proven increased intraocular pressure (IOP) (Group 1) and 38 (25.5%) of 149 eyes with RB had histopathological findings consistent with glaucoma (termed glaucoma mechanisms) but without clinically recorded IOPs (Group 2).[7] Table 1 shows that the distribution of glaucoma mechanisms in both groups was similar and the authors concluded that the clinical and histopathological concordance validates the actual existence of secondary glaucoma in RB. These authors also concluded that the actual incidence of glaucoma in eyes with RB is much higher than reported in previous studies.

In another study by Shields and colleagues of 248 patients with unilateral or bilateral RB managed during a 12-year period, 303 eyes had RB, out of which 51 (17%) developed secondary IOP elevation occurring primarily in advanced tumors that replaced most of the vitreous cavity.[10]

Walton and Grant reported that 39 (44%) of 88 eyes enucleated for RB had NVI but did not mention the frequency of glaucoma in their series. In the same study, they looked at eyes enucleated from children 5 years old or younger from 1952 to 1968 and found that NVI was most commonly associated with RB. Of the 56 eyes with NVI seen on pathologic specimens, 38 (68 %) had untreated retinoblastoma.[11]

Other older studies had also demonstrated the association of RB and secondary glaucoma. Howard and Ellsworth reported glaucoma as an initial clinical finding in only 2% of cases of RB but did not describe the frequency of glaucoma as an associated finding among the 235 RB eyes studied.[1] Stafford and colleagues reported that 14 (2.3%) of 618 cases of RB were initially misdiagnosed as primary glaucoma.[12]

METHODOLOGY

A 7-month-old boy was referred to the glaucoma service of the Massachusetts Eye and Ear Infirmary (MEEI) with the classic triad of congenital glaucoma (pain, tearing, and photophobia). He was born via caesarian section with no birth abnormalities. At 3 to 4 months, the parents noted that they could "see into the left eye" at a certain angle. The right eye (OD) was normal. The left eye (OS) was buphthalmic but not proptotic, with corneal edema, conjunctival injection, tearing, swelling, and erythema of both the upper and lower lids. Intraocular pressure (IOP) was 30 OS and 8 OD. Extraocular motility was full in both eyes. Retinal examination in OS revealed a tumor mass occupying the entire posterior pole with total retinal detachment. Computed tomography (CT) showed a 1.5 cm round, homogenous density in the mid-orbit, lateral to the superior orbital fissure. The diagnosis was retinoblastoma (RB) with secondary glaucoma OS and the eye was eventually enucleated. Histopathology showed iris neovascularization (NVI), RB cells filling the vitreous space, and a posterior-pole RB tumor with total retinal detachment.

A literature search on the relationship of glaucoma and RB was subsequently done to determine the incidence and the most common mechanisms of RB-induced glaucoma.

RESULTS

The clinical presentation of glaucoma in RB includes neovascular glaucoma with or without angle closure, pupillary-block glaucoma, or uveitic glaucoma. Symptoms, which may include pain, tearing, and photophobia are all unusual for RB. Enlargement of the globe (buphthalmos), increased IOP, corneal edema, hyphema, or eye redness may be present.

Shields and colleagues[10] noted that the most common mechanisms of IOP elevation was NVI 74% (36/51), followed by angle closure (pupillary block) secondary to anterior displacement of the lens–iris diaphragm at 27% (14/51), and tumor seeding of the trabecular meshwork at 2% (1/51). Yoshizumi and colleagues[7] found similar results. Each of these glaucoma-inducing mechanisms in RB is described in detail.

Iris neovascularization (NVI)

In 1967, Richard Schulze was the first to call attention to an association between NVI and RB.[13] Histological studies identified NVI in 30 to 72% of eyes with RB (Table 2).[7, 9, 11, 14, 15, 16] Two studies[7, 10] also reported the role of NVI in causing glaucoma in eyes harboring RB.

Clinically, iris or angle neovascularization is a spectrum that can range from the preglaucoma stage with normal IOP that progresses to an open-angle glaucoma stage with increased IOP, hyphema, vitreous hemorrhage, or fibrovascular membranes. These fibrovascular membranes may contract, causing ectropion uvea, and form peripheral anterior synechae (PAS), leading to angle-closure glaucoma with a very high IOP. In RB, synechial angle closure and NVI were closely correlated; a closed angle was observed in 61% of enucleated RB eyes with NVI compared with 5% without NVI.[16]

NVI is judged to be present histologically when an

abnormal fibrovascular layer composed of thin-walled vessels and variable amounts of fibrous tissue are found on the anterior surface of the iris. This fibrovascular layer is usually conspicuous and often associated with ectropion uveae and synechial angle closure resulting in elevation of IOP via impairment of aqueous outflow.[11] New blood vessels frequently become incorporated into the synechial growth.[9] Most eyes with RB and NVI contain large tumors located at the posterior pole with involvement of the central retinal vessels or large branch retinal vessels.[7, 10, 17] Occlusion of these large vessels results in ischemic retinopathy, which may secondarily cause NVI. However, there have been two variant cases reported of anteriorly located RBs with minimal posterior pole involvement associated with NVI as well. These cases are exceptions to the general observation that RB with large posterior-pole vascular compromise are usually associated with NVI. These cases also support the theory of the role of tumor angiogenic factor in the etiology of NVI.[18] The two cases are described in detail below:

- The first variant case described a diffuse anterior RB involving primarily the anterior ocular structures with only one microscopic focus in the peripheral retina.[19] This patient presented with glaucoma with increased IOP and anterior and posterior uveitis, but had a normal retina in the affected eye. Histopathology showed NVI and PAS with trabecular-meshwork occlusion. The retina and the optic nerve displayed glaucomatous atrophy. The RB tumor circled the lens zonules and ciliary body for a full 360 degrees, extended around the iris, invaded the ciliary body, and seeded the vitreous base and anterior chamber.[19]
- The second variant case of RB and NVI was reported in one eye where the RB tumor was limited exclusively to the retina anterior to the equator.[7] The tumor mass involved less than a 90-degree quadrant of the retina and the tumor cells were found in the anterior chamber seeding the corneal endothelium and the iris.

Table 1. **Comparison of glaucoma mechanisms present in two groups of enucleated retinoblastoma eyes.**

Glaucoma Mechanism	Group 1[a] (Percent)	Group 2[b] (Percent)
Iris neovascularization (NVI) only	41.2	36.8
Y-shaped suture detachment only	20.6	31.6
Uveitis only	0	10.5
NVI and Y-shaped suture detachment	17.6	13.2
NVI and uveitis	8.8	5.3
NVI + uveitis + Y-shaped suture detachment	2.9	0
Massive tumor involvement	5.9	0
Unusual cases	0	2.6
No glaucoma mechanisms	2.9	0

Adapted from Yoshizumi MO, Thomas JV, Smith TR. *Arch Ophthalmol* 1978; 96: 105–110.

a. Eyes with intraocular pressure >22 mm Hg by tonometry or tactile estimation.
b. Eyes with glaucoma mechanism present pathologically but without intraocular pressure readings.

Table 2. **Occurrence of iris neovascularization (NVI) in retinoblastoma.**

Author	Number of eyes	Percent with NVI
Walton & Grant (1968)	88	44
Minoda (1971)	41	44
Anderson, et al (1971)	—	48
Yoshizumi, et al (1978)	149	30
Gartner & Henkind (1978)	14	72
Spaulding (1978)	192	52

Table 3. **Incidence of iris neovascularization (NVI) in diseases clinically resembling retinoblastoma (RB).**[20]

Disease resembling RB	Percent with NVI
Retrolental fibroplasias or ROP	91
Persistent hyperplastic primary vitreous	72
Retinal dysplasia	63
Coats' disease	100
Larval granulomatosis	60
Infantile retinal detachment	100

Adapted from Moazed K, Albert D, Smith TR. *Surv Ophthalmol* 1980; 25: 85-90.

The most important factors leading to NVI are ischemia, necrosis, inflammation, and possibly tumor-angiogenesis factor.[20] Minoda observed that in RB, NVI was not always accompanied by malignant iris infiltration. He suggested that NVI might be promoted by a factor caused by tumor proliferation in the retino–vitreous cavity.[16] Studies have shown that circulating angiogenic factors produced by the RB tumor itself may play a role in the development of NVI.[21, 22, 23] Although many intraocular tumors produce diffusible tumor-angiogenic factors that stimulate both iris and retinal neovascularization distant from the tumor,[18, 24] the tumor-angiogenic factor released from RB does not cause retinal neovascularization, although it can initiate and sustain NVI, and it was suggested that a hypoxic retinal diffusible vasculogenic factor (HRDVF) accounts for NVI in RB.[25] Upregulation of an angiogenic factor, the vascular-endothelial-growth factor (VEGF), has been demonstrated within RB and has been shown to be induced in hypoxic and necrotic regions of RB tumors stimulating vascular stromal formation.[17, 26] Factors other than hypoxia may also regulate VEGF expression in RB cells.[26] Aside from the RB tumor cells producing VEGF, hypoxic normal retinal cells may also produce VEGF. *In situ* hybridization analysis using mRNA-labeled VEGF revealed VEGF in the outer nuclear layer of detached retinas in eyes with RB.[17]

Many histological features in eyes with RB are correlated with NVI. A study by Spaulding showed greater NVI in eyes with endophytic and large RB tumors.[9] Other studies[9, 11, 16, 17] showed that NVI is associated with orbital, choroidal, scleral, anterior-chamber, and optic-nerve invasion and calcifications. In addition, greater amounts of tumor necrosis and the presence of basophilic staining, which results from sedimentation of DNA from necrotic cells,

were associated with NVI.[10] In a study by Walton and colleagues of 88 patients who had anterior segment RB, 33 (38%) had NVI and 14 (16 %) had none.[11] Spaulding[9] showed in histopathologic RB specimens with vitreous seeding, that 90% had NVI and 54% had none. The presence of Flexner–Wintersteiner rosettes, which reflects a higher state of differentiation of RB and, indirectly, a less-advanced stage, is associated with less NVI.[9, 11, 17] Other histological factors such as the focality of tumor, number of mitotic figures, and seeding of the tumor cells to the vitreous and subretinal space, were not associated significantly with NVI.

Patient's age and duration of the tumor also appear to be related to the development of NVI in eyes with RB. Walton and Grant found the mean age at the time of enucleation to be 26 months for patients with RB and NVI, compared with 14 months for patients without NVI.[11] Similarly, two studies[9, 17] have shown that NVI is associated with advanced stages of RB.

Interestingly, conditions such as retinopathy of prematurity (ROP) and Coats' disease that may clinically be confused for RB are also associated with NVI. Two studies[9, 20] demonstrated that an equal or even higher incidence of NVI exists in other conditions that may clinically resemble RB (Table 3).

Pupillary block

Anterior displacement of the lens with resultant pupillary block and angle closure is the second (27%) most common mechanism of glaucoma in eyes with RB.[7, 10, 11] In one study, the most common cause of pupillary block was seen in cases with total retinal detachment with massive subretinal exudation and the retina being close to or in contact with the posterior-lens capsule, causing anterior displacement of the lens. In most cases, the tumor was present within and under the retina.[7] The tumor and subretinal fluid displace the lens anteriorly, resulting in pupillary block and angle closure.

Tumor seeding of the anterior chamber

A less frequent (2%) mechanism of glaucoma in eyes with RB is via direct involvement of the anterior chamber structures by necrotic tumor cells and/or inflammatory cells. RB tumor cells can break free from the main tumor mass in the retina and migrate into the anterior chamber. The tumor cells then can deposit in the inferior anterior chamber angle and resemble a hypopyon. Glaucoma occurs as a result of the obstruction of the outflow of aqueous humor through the trabecular meshwork by the tumor cells.[27]

In the study by Walton and colleagues, 38% (33/88) of RB specimens had anterior-segment involvement with NVI while 16% (14/88) had anterior-segment involvement without NVI but had deposits of tumor cells on the anterior surface of the iris, corneal endothelium, and trabecular meshwork.[11]

DISCUSSION

The management of glaucoma in RB is preceded by the need for instituting the appropriate management for RB. Generally, glaucoma in RB is managed medically with aqueous suppressants, but once neovascular glaucoma develops, medical management usually fails and enucleation is often required.[11] Glaucoma filtration or shunt operations are absolutely contraindicated because of the risk of extraocular spread of viable tumor cells.

The presence of a large RB with secondary glaucoma and vitreous hemorrhage is predictive of optic-nerve involvement;[27] thus, glaucoma in RB is arguably an indication for performing an enucleation.

Development of neovascular glaucoma as a consequence of obstruction or closure of the angle by fibrovascular tissue is of little practical significance in eyes that are to be enucleated for RB, but it is a considerable complication if it occurs in the better eye.[11]

Later studies seem to indicate that the actual incidence of glaucoma in eyes with RB is much higher than reported in previous studies. These studies show that increased IOP is seen in 17% (51/303)[10] to 22.8% (34/149)[7] of patients with RB. In addition, histopathologic glaucoma mechanisms are also found frequently in RB eyes with clinically increased IOPs (Table 1).[7] Moreover, in RB eyes with NVI as the sole glaucoma mechanism, a tumor involving the posterior pole was consistently present and served as a predictor for the presence of NVI on the pathological sections.

A study by Shields[28] pointed out certain unique aspects of children with RB that manifest at an older age, namely pain, inflammation, conjunctival chemosis, and glaucoma, and showed that these characteristics alert the clinician to the potential atypical presentation of the tumor in children. Another study[12] suggested that these atypical manifestations of RB carry a higher risk of death due primarily to a delay in diagnosis. Vitreous hemorrhage from NVI may also make the diagnosis and management of retinoblastoma more difficult.[29]

NVI in association with RB has received little clinical attention and the studies above have shown that NVI indicates a more advanced disease and is correlated with other histological tumor features that herald a worse prognosis for the RB tumor. The posterior pole seems to attract so much attention compared with the anterior segment that the presence of NVI often seems to be neglected or overlooked. The presence of anterior-segment involvement (i.e., raised IOP, NVI, and angle-closure configuration) in RB carries a graver prognosis.[30]

However, if slit-lamp biomicroscopy of the anterior segment, particularly gonioscopy, were done systematically and comprehensively, NVI as well as occasional clumps of RB tumor cells in the anterior chamber may be recognized more frequently. Dilated bilateral fundus examination with a 360-degree scleral depression is the most important part of the ophthalmologic examination, often done under general anesthesia.[31] Careful retinal and ciliary body examination with the procedures described above should be performed to exclude medulloepithelioma in the ciliary body region.[32, 33] Further ancillary exams such as ultrasound and CT may be needed to be certain about the diagnosis of RB since the view of the anterior and/or posterior segment may be obscured by corneal edema and/or hemorrhage.

Commenting on Minoda's study that used light and electron microscopy to study NVI in enucleated RB eyes, Henkind[16] said that since NVI may be less than 10 μm in diameter and would be virtually invisible with slit-lamp biomicroscopy, especially in dark-eyed children, it might prove instructive though somewhat difficult to perform anterior-segment fluorescein angiograms in patients with RB or entities similar to RB to ascertain whether neovascularization can be better demonstrated clinically. However, NVI itself would not seem to be a significant differentiating feature between RB and these other entities similar to RB, which also may present with NVI (Table 2)[16, 20] There also appears to be no histological difference between NVI as it occurs in RB or another disease category;[9] therefore, NVI is not pathognomonic for RB.

In conclusion, although glaucoma may be a secondary clinical issue in the shadow of a grave pediatric eye tumor, awareness of its coexistence with RB through a more thorough ocular examination, particularly of the anterior segment, can guide the clinician in assessing the overall evaluation of the affected eye.

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CASE REPORT

Cholesterol granuloma of the orbit

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ABSTRACT

Objective

To report a patient with cholesterol granuloma and describe the distinct clinical, radiologic, and histopathologic findings.

Methods

This is a case report.

Results

A 33-year-old man presented with a 12-month history of diplopia on left upward gaze. He underwent repair of wound laceration at the right fronto-temporal area 25 years prior to consultation due to a head bump sustained in a vehicular accident. Examination revealed nonaxial proptosis, inferior globe displacement, and mild limitation on left upward gaze. Orbital imaging revealed an ovoid extraconal expansile soft-tissue mass in the left orbit, slightly compressing the globe inferiorly, and thinning and widening of the superior portion of the orbital wall. Excision biopsy of the orbital mass was done through a lateral orbitotomy with bone flap. Histopathology revealed characteristic features of cholesterol granuloma including abundant cholesterol clefts, foreign-body giant cells, lipid-laden histiocytes, and hemosiderin macrophages with absence of epithelial components.

Conclusion

Orbitofrontal cholesterol granulomas have typical clinical, radiologic, and histopathologic features. Surgical excision has a high success rate with a low incidence of recurrence.

Keywords: *Cholesterol granuloma, Orbit, Orbital lesion, Diplopia, Proptosis*

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CHOLESTEROL granuloma is a rare expansile orbital lesion with an unclear pathogenesis. It presumably arises from organization of incompletely resorbed orbital hemorrhage caused by trauma, orbital surgery, foreign body, hemorrhagic diathesis, or vascular lesion, with subsequent granulomatous response to blood-breakdown products, fibrous encapsulation, and recurrent hemorrhage into the cyst.[1, 2]

We present a patient with cholesterol granuloma of the left orbit, resulting in proptosis, globe displacement, and limitation in ocular movement. This report describes the clinical, radiologic, and histopathologic features of a case of orbital cholesterol granuloma.

METHODOLOGY

A 33-year-old-man presented with a 12-month history of diplopia on left upward gaze. He had a history of gout with regular intake of allopurinol and colchicine. He underwent repair of wound laceration at the right fronto-temporal area 25 years prior to consult due to a head bump sustained from a fall. There was no history of diabetes, hypertension, tuberculosis, asthma, or allergies. On examination, best corrected visual acuity was 20/20 bilaterally; there was no periorbital edema, erythema, or tenderness. A 2.5-mm left nonaxial proptosis with inferior globe displacement was noted, as well as mild limitation on left upward gaze. There was also prominence of the left lateral brow area, noted by the patient for 20 years to have slowly progressed with time. The remainder of the ocular examination was unremarkable.

Computed tomography (Figure 1) showed an ovoid extraconal expansile soft-tissue mass with a slightly enhancing rim in the superolateral portion of the left orbit measuring approximately 2.0 x 2.5 x 2.9 cm and slightly compressing the globe inferiorly, with thinning and widening of the superior portion of the orbital wall. The bony walls of the right orbit were unremarkable. The globes, extraocular muscles, optic nerves, and visualized portions of the brain were within normal limits.

All blood-test results were normal. Radiography of the chest, electrocardiogram, and urinalysis were also normal.

The patient underwent excision biopsy of the orbital mass through a lateral orbitotomy with bone flap. After reflection of the periosteum from the orbital roof, a reddish brown mass adherent to the irregular bony defect was encountered. This was accompanied by the release of moderately thick reddish-brown fluid.

RESULTS

Histopathologic examination disclosed fragments of yellowish brown tissues measuring 2 x 2 x 1 cm in aggregates. Microscopic sections showed a nonencapsulated dense fibrous connective tissue with no evidence of epithelial elements or keratin. There were numerous cholesterol clefts scattered within a chronic inflammatory infiltrate. Foreign-body giant cells enveloped most cholesterol clefts. Aggregates of birefringent hematoidin crystals surrounded by giant cells were present. Large foamy histiocytes, hemosiderin-laden macrophages and occasional fragments of bone were scattered throughout the connective tissue (Figure 2).

The patient tolerated the procedure well and there were no complications. He was given oral antibiotics and analgesics postoperatively. There was resolution of the diplopia but persistence of the prominence of the left lateral brow area. At his last clinic visit 16 months after the surgery, there was no recurrence of the mass.

DISCUSSION

Cholesterol granuloma is an uncommon lesion that usually affects middle-aged men.[3] The largest series of cases

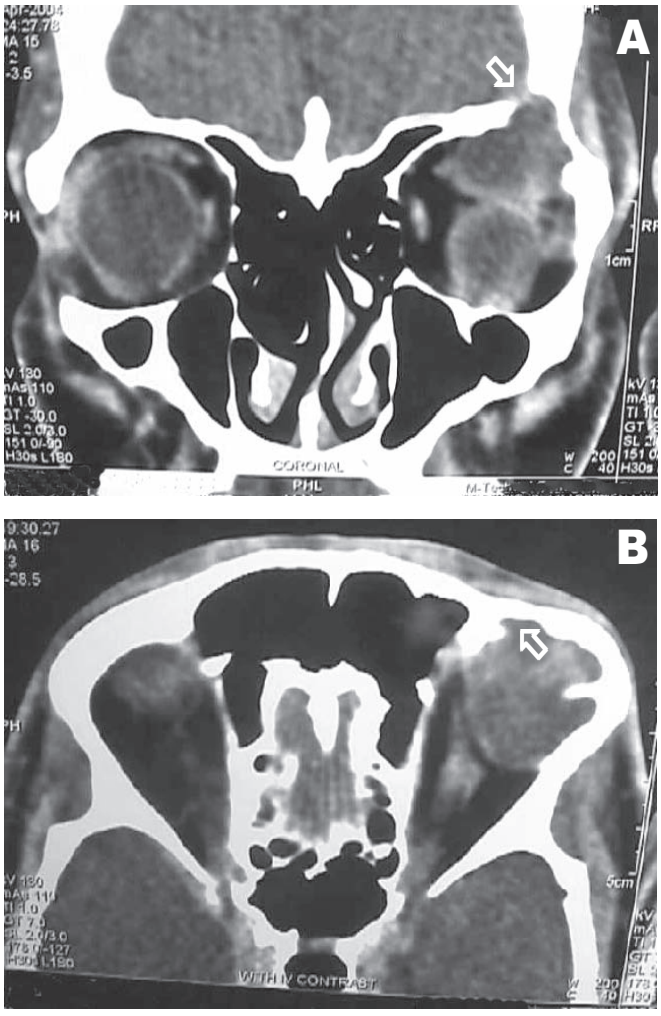

Figure 1. Coronal (**A**) and axial (**B**) sections showing a left orbital mass with thinning and widening of the superior portion of the orbital wall (⇗).

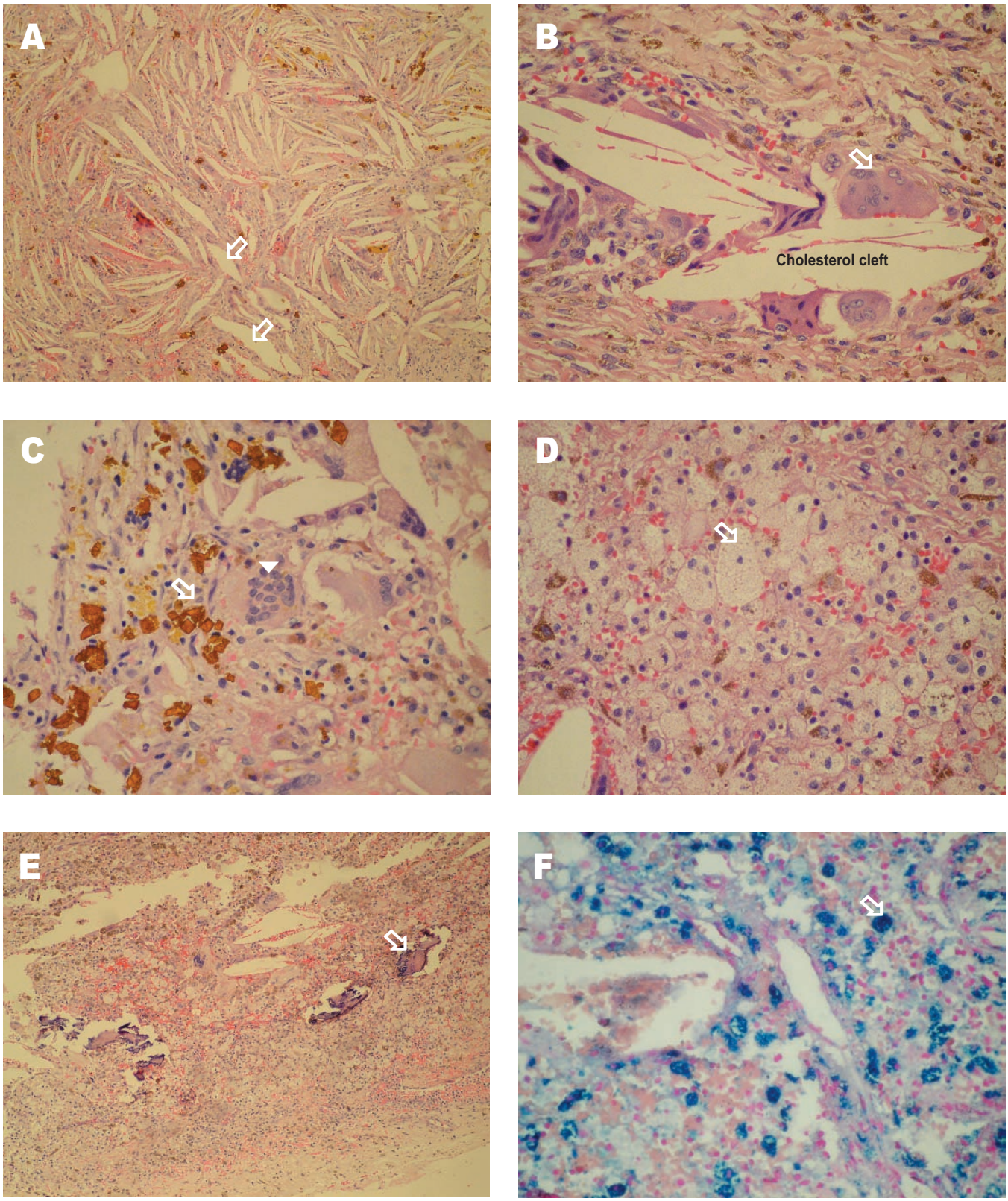

Figure 2. Cholesterol granuloma. A: Cholesterol clefts (⇖) (**H & E x 40**). B: Foreign body giant cells (⇖)surrounding cholesterol cleft (**H & E x 180**). C: Hematoidin crystals (⇖) with foreign-body-giant cell (▾) (**H & E x 100**). D: Lipid laden macrophages (⇖) (**H & E x 180**). E: Bone fragment (⇖) (**H & E x 40**). F: Hemosiderin-laden macrophages staining blue with Prussian blue stain x 80.

was reported by McNab et al.,[1] who described the clinical features and management of 27 patients with orbitofrontal cholesterol granuloma. The term "cholesteatoma" was introduced in 1838 by Muller for any lesion containing cholesterol crystals.[4] Both epidermoid cholesteatoma and cholesterol granuloma consist of cholesterol clefts and foreign-body giant cells with blood-degradation products such as hemosiderin and hematoidin. Cholesterol granuloma is distinguished from an epidermoid cholesteatoma by the lack of epithelial elements.[5]

Several reports were published using different names to describe these lesions including chronic hematic cyst,[6, 7, 8, 9] xanthomatosis of the orbit,[10] and lipid granuloma of the frontal bone.[11, 12] However, there should be a uniformity with regard to the nomenclature. Cholesterol granuloma is a better term as suggested by McNab et al. since the osteolytic changes is a result of a granulomatous reaction to cholesterol crystals.[1] Hematic cyst should be reserved to describe intraorbital accumulations of blood. Cholesterol granuloma should also be distinguished from acute subperiosteal hematomas which often result from trauma in children[13, 14] or in adults.[15]

The cholesterol in the lesion results from the breakdown of cell membranes of erythrocytes. The crystals stimulate granulomatous inflammation that sets in capillary growth and further accumulation of red blood cells and other breakdown products producing a mass effect. Suggested possible etiologies for the hemorrhage include facial or head trauma[16] and predisposing intradiploic anomaly.[3]

The frontal bone is the largest concave bony surface in the orbit. Granulomas tend to arise in the diploe of the frontal bone, causing expansion and eventual erosion of the inner and outer tables. The underlying periosteum in this area is not firmly attached as compared to other areas of the orbit. This could explain the common subperiosteal location of these granulomas.[14]

Bone resorption present in computed tomography could be attributed to prostaglandins, specifically PGE2, as seen in malignant lesions as well as in mucoceles of the paranasal sinuses and benign dental cysts.[17, 18] The transudation of red blood cells and other blood products specifically platelets provides a good source of these prostaglandins.

Osteolytic lesion with a density equivalent to the density of the brain and occasional intralesional bone fragments are characteristic features seen in computed tomography. Lesions present as high T1 and T2 signal intensities on MRI that could provide added information in difficult cases. Dermoid cysts and lacrimal-gland tumors are common lesions that should be differentiated from this entity.

Patients usually present with a superotemporal mass ranging from weeks to years as seen in our patient. This would progress and lead to displacement of the globe inferiorly and proptosis. Ocular motility restriction with associated diplopia is present in majority of patients with cholesterol granuloma.[6, 8] There may be accompanying orbital pain, which should be differentiated from a malignant process such as adenocystic carcinoma of the lacrimal gland that invades the nerve early in the disease process.

In conclusion, orbitofrontal cholesterol granulomas have typical clinical, radiologic, and histopathologic features. Surgical excision has a high success rate and leads to a low incidence of recurrence of the condition.

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BRIEF REPORTS

Choroidal melanoma in a 49-year-old female

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ABSTRACT

Objective

To describe a case of choroidal melanoma.

Methods

This is a case report.

Results

A 49-year-old female complained of blurring of vision in the right eye of five months duration. Ocular ultrasound, fluorescein angiography, and magnetic resonance imaging showed a choroidal mass with serous retinal detachment in the right eye. Standard enucleation was done, and histopathology revealed a mixed-cell type of choroidal melanoma. No further adjuvant treatment was recommended. The patient was closely followed up.

Conclusion

Choroidal melanoma, considered the most common primary malignant intraocular tumor among Caucasian adults, is rare among Asians. Enucleation alone is the current accepted treatment option for large choroidal melanomas.

CHOROIDAL melanoma is the most common primary malignant intraocular tumor in adults.[1] Its incidence is lower among Asians than Caucasians.[2] Primary choroidal melanoma arises from melanocytes within the choroid.[3] Most choroidal melanomas are believed to develop from preexisting melanocytic nevi.

At the pathology section of the Institute of Ophthalmology of the University of the Philippines–Philippine General Hospital, 15 patients were diagnosed with choroidal melanoma from January 1997 to September 2005. Females outnumbered males 2 to 1. Their ages ranged from 25 to 70 years, most of them in their 50s.

The patient is a 49-year-old female who complained of blurred vision in the right eye (OD) of five months duration. There was no history of trauma or other associated symptoms. Previous diagnosis by other ophthalmologists included tumor and retinal detachment.

On consultation, best-corrected visual acuity was hand movement with good light projection in OD and 6/6 for the left eye (OS). Pupils were 3–4 mm briskly reactive, with relative afferent pupillary defect in the right. Intraocular pressures were 8 mm Hg OD and 12 mm Hg OS. Slit-lamp examination showed clear cornea, formed and deep anterior chamber with no reaction, flat iris plane, and 1+ nuclear cataract in both eyes (OU). Gonioscopy revealed open angles OU.

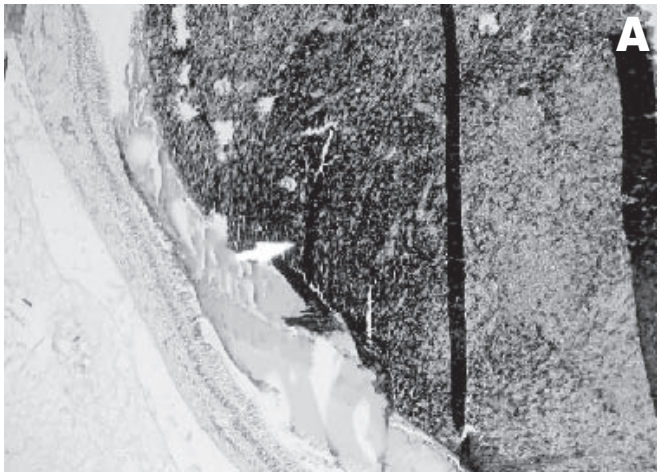
Indirect funduscopy showed an area of detached retina, with shifting fluid, more prominent at the superior half of the posterior pole and superior edge of the disc, and involving the macula. A brownish, pigmented, elevated subretinal mass measuring approximately 15 mm x 13 mm x 10 mm in the superior hemisphere was seen. The left fundus was normal.

Ocular ultrasound revealed a dome-shaped mass measuring 9.9 mm in thickness anteroposteriorly and 15.5 mm at its widest diameter, with an initial high spike and mid to low internal reflectivity. There was no choroidal excavation or extrascleral invasion.

Fluorescein angiography showed filling of the arteries and beginning enhancement and visualization of the choroidal vessels. There was complete filling of the arteriovenous (AV) channels and increased visualization of the choroidal vessels in the late venous phase. Areas of hyperfluorescence admixed with areas of hypofluorescence were seen. Magnetic resonance imaging (MRI) showed a hyperintense dome-shaped mass relative to the vitreous humor (T1) and a hypointense mass relative to the vitreous (T2) in the posterior aspect of the right globe. There was no evidence of extraocular extension. Chest X-ray was normal.

MRI of the abdomen ruled out primary malignancy and metastasis. No mass or lymphadenopathy was seen in the abdomen. Liver and renal function tests were normal.

The preoperative assessment was choroidal melanoma with serous retinal detachment (OD). The right eye was enucleated under general anesthesia, with implantation of a polymethylmethacrylate ball. The optic-nerve was severed with at least 10 mm stump. The anteroposterior cut section of the right globe showed a darkly pigmented choroidal mass measuring 15 mm at its greatest diameter



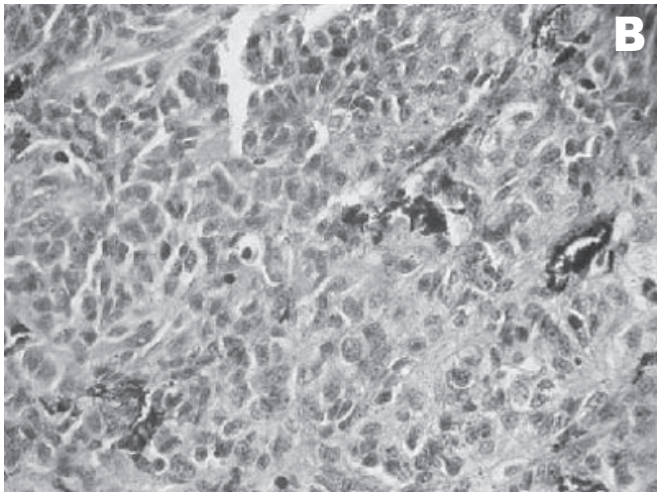


Figure 1. Low-power view showing darkly pigmented choroidal mass (A) and high-power field showing mixed population of cells (B).

and located superiorly. Based on the modified Callendar classification for the cytologic classification of uveal melanomas, a diagnosis of mixed-cell-type choroidal melanoma was made (Figure 1).

The 2004 report of the Collaborative Ocular Melanoma Study (COMS) classified posterior uveal melanomas according to basal diameter and thickness measured by ultrasound.[4] An anteroposterior thickness of 9.9 mm, which this patient had, was classified as large. Several treatment options are available, primarily based on tumor size. Enucleation is indicated for tumors greater than 15 mm in diameter and greater than 10 mm in thickness,[3] and in patients who already have irreversible loss of useful vision. Neo-adjuvant and adjuvant therapies offer no 5-year survival advantage over enucleation alone.[4]

Follow-up plans for this patient included liver-function test every 3 months, liver ultrasound every 6 months, and artificial-eye implantation after 2 months.

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Vogt-Koyanagi-Harada in a Kadazan female

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ABSTRACT

Objective

To report a case of Vogt-Koyanagi-Harada in a Kadazan girl, a member of an indigenous race of the state of Sabah, Malaysia.

Methods

This is a case report.

Results

A 23-year-old Kadazan female presented with bilateral sudden blurring of vision of two days duration associated with ocular pain, metamorphopsia, and severe headaches. Examination revealed bilateral visual acuities of 6/18 correctable to 6/12, 1+ anterior-chamber cells, and multifocal areas of exudative retinal detachments. A diagnosis of Vogt-Koyanagi-Harada (VKH) syndrome was made after excluding other differential diagnoses. She was treated with intravenous methylprednisolone with good outcome.

Conclusion

The treatment for VKH is well established, requiring the use of oral steroids in most cases. In severe cases, high-dose intravenous methylprednisolone is recommended. Early diagnosis and aggressive treatment improve outcome in VKH.

A 23-YEAR-OLD Kadazan female consulted at the Penang Hospital Eye Clinic for sudden blurring of vision in both eyes of 2 days duration, associated with redness and dull eye pain, metamorphopsia, and severe headaches. There was no history of tinnitus, hearing difficulty, ocular trauma, surgery, or menstrual problem. Family history was unremarkable. Except for gastritis, there were no other health problems.

Physical and neurological examinations were unremarkable. Ocular examination revealed bilateral visual acuity of 6/18 improved to 6/12. Pupils were round and equally reactive to light and accommodation. Corneas were clear, intraocular pressures were normal, and the conjuctivae were mildly injected. The anterior chambers contained 1+ cells.

Posterior-segment examination revealed clear vitreous and normal-looking optic discs. Both posterior poles exhibited multifocal areas of exudative retinal detachment (Figure 1). B-scan ultrasonography showed diffuse choroidal thickening (Figure 2). Fluorescein angiography (FA) showed early multiple pinpoint areas of hyperfluoresence and late pooling of fluorescein indicating multiple serous detachments.

Extensive laboratory examinations were done to rule out other ocular diseases: tuberculosis, syphilis, and sarcoidosis were excluded via chest X-ray and rapid-plasma-reagent test; connective tissue diseases via a thorough medical evaluation, negative-serum-rheumatoid factor, and antinuclear antibodies; breast and cervical cancers by gynecologic evaluation. Computed tomography (CT) of the brain and lumbar tap were normal. Hearing assessment and pure-tone audiometry were also normal.

An initial diagnosis of Vogt-Koyanagi-Harada (VKH) syndrome was made based on the presence of bilateral uveitis, multifocal serous retinal detachment, and severe headache. Under the criteria set following the first international workshop on VKH in 1999 (Table 1), the diagnosis of VKH requires the exclusion of penetrating ocular trauma or intraocular surgery (which may suggest sympathetic ophthalmia) and other ocular diseases,[1] both of which were excluded in this patient. Since neurological, auditory, and dermatological features of VKH were absent in this patient, a diagnosis of "probable VKH" was made based on three of the five criteria (1, 2, and 3). The features in this case were similar to those described by Harada, with mild anterior uveitis, multifocal choroiditis, and possible meningismus. The missing diagnostic criteria were the integumentary features. However, skin lesions are often not present in Harada's (<10%). Moreover, visual recovery generally is good in contrast to the poor visual outcome of Vogt-Koyanagi syndrome.[2] This patient's visual acuity improved to 6/9 with treatment.

VKH syndrome is a disorder affecting mostly Asians (Japanese and Chinese), Hispanics, and Native Americans (particularly Cherokee Indians). It generally occurs in individuals between 20 and 50 years old.[3-5] The youngest reported case involved a 4-year-old.[6] Both sexes are affected, but Rubsamen and Gass found more females in their case series.[7]

VKH is a multisystem, granulomatous inflammatory disorder affecting the eyes, meninges, skin, and auditory system. Vogt and later Koyanagi described patients with bilateral anterior uveitis, vitiligo, poliosis, alopecia, and dysacousia; Harada described patients presenting with posterior uveitis, exudative retinal detachment, and cerebrospinal-fluid pleocytosis. It is now accepted that these two entities are spectrums of the same disease, currently termed VKH syndrome.[2] The etiology is largely unknown. The pathogenesis is related to an immune reaction against uveal tissue, similar to sympathetic ophthalmia. The underlying mechanism of tissue damage is probably a Type IV autoimmune response against uveal antigens, possibly associated with melanocytes.[8] Histopathology shows uveal infiltration with B and T-lymphocytes, multinucleated giant

Table 1. **Diagnostic criteria for Vogt-Koyanagi-Harada (VKH) syndrome.**

1. Exclude intraocular surgery or penetrating ocular trauma
2. Exclude other ocular diseases
3. Bilateral ocular involvement (A or B)
   - *A. Early manifestations*
     1. Evidence of diffuse choroiditis
        - a. focal areas of subretinal fluid or
        - b. bullous serous retinal detachment
     2. Equivocal fundus findings, both of the following must be present
        - a. Fluorescein angiography (in order of appearance): focal areas of delay in choroidal perfusion, multifocal areas of pinpoint leakage, large placoid areas of hyperfluorescence, pooling within subretinal fluid and optic-nerve staining
        - b. Ultrasonography: diffuse choroidal thickening without evidence of scleritis
   - *B. Late manifestations*
     1. History suggestive of prior presence of findings from 3A or either or both 2 and 3 below or multiple signs from 3.
     2. a. Sunset-glow fundus
        b. Suguira sign
     3. a. Nummular chorioretinal depigmented scars or
        b. Retinal pigment epithelium clumping or
        c. Recurrent or chronic anterior uveitis
4. Neurologic/auditory findings such as
   - a. meningismus (headache, malaise, fever, nausea, abdominal pain, stiff neck)
   - b. tinnitus
   - c. cerebrospinal-fluid pleocytosis
5. Integumentary findings
   - a. vitiligo
   - b. alopecia
   - c. poliosis

1, 2, 3, 4, and 5	—	Complete VKH
1, 2, 3, and 4	—	Incomplete VKH
1, 2, 3	—	Probable VKH
Else	—	Not VKH

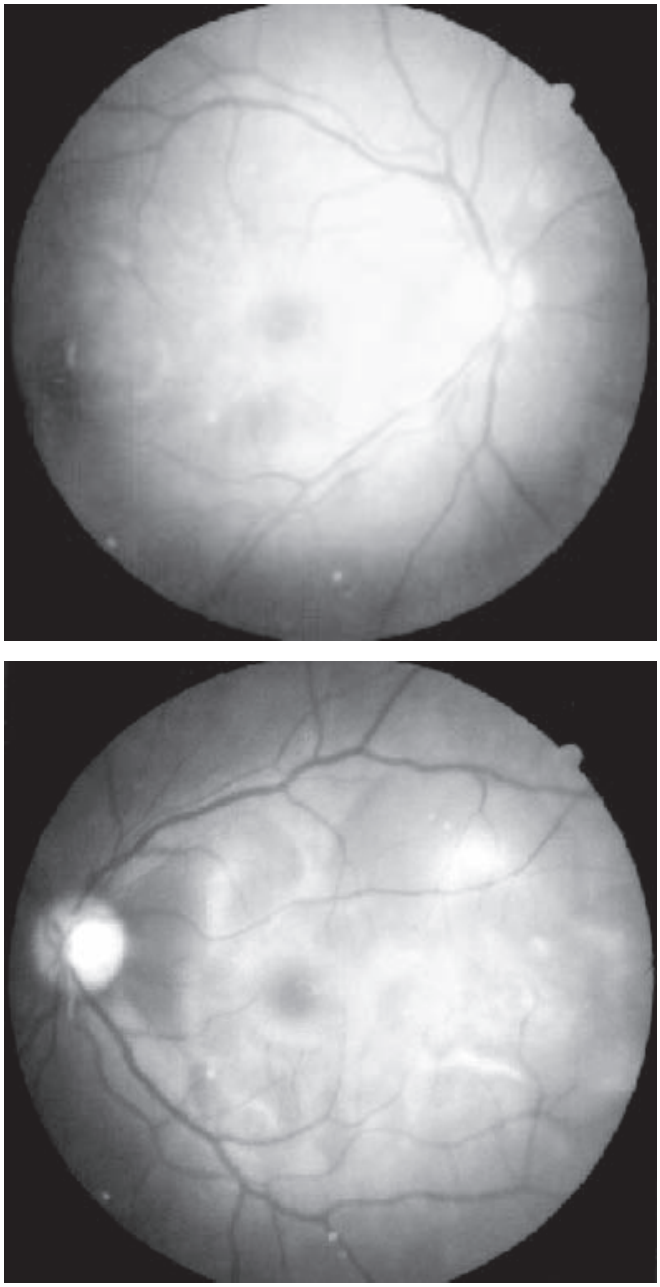

Figure 1. Right and left fundus photographs on admission show multifocal areas of exudative retinal detachment.

cells, epitheloid cells, and plasma cells suggesting that both cell-mediated and humoral immune mechanisms are involved.[9] Norose and Yano demonstrated the involvement of cytotoxic T lymphocytes.[10] Belfort et al. showed that T lymphocytes are the predominant cell type in aqueous of patients with VKH.[11] Association with several leukocyte antigens such as HLA-DR4, HLA-DRw52, HLA-DRw53 and HLA-DRw54 have been demonstrated.[3–5, 12, 13] Genetic predisposition is also suggested by cases of monozygotic twins presenting with the disease.[14]

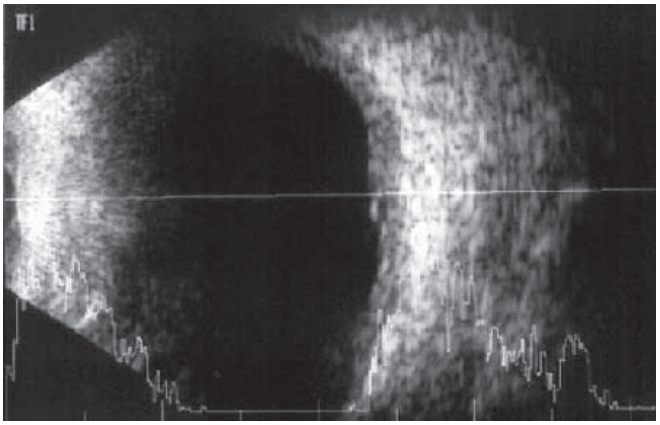

Figure 2. B-scan shows diffuse choroidal thickening.

VKH follows four clinical stages: prodromal, uveitic, chronic, and recurrent.

Prodromal stage is characterized by headaches, meningismus, vertigo, deep orbital pain, nausea, slight fever, photophobia, and lacrimation lasting for a few days. Cerebrospinal-fluid (CSF) pleocytosis occurs in 80% of patients during this stage. Melanin-laden macrophages are responsible for the pleocytosis.[15]

Uveitic stage, which follows the prodromal stage, is characterized by sudden bilateral blurring of vision with choroiditis, exudative retinal detachments as seen in this patient, disc swelling, mutton-fat keratic precipitates, and iris nodules, which may last for several weeks.

Chronic stage, which may last for months to years, is the convalescent phase when uveal and dermatologic depigmentation occurs. Sugiura's sign or perilimbal vitiligo is the earliest depigmentation seen. Depigmentation of the choroid may occur resulting in the "sunset glow" fundus. Dalen–Fuchs nodules may also be present.

Recurrence, which may interrupt the chronic stage, is often associated with anterior, rarely posterior, uveitis.

Investigations useful in diagnosing VKH are FA showing multiple areas of punctate hyperfluorescence and B scan demonstrating thickening of the choroid, sclera, or episclera posteriorly.[16] Indocyanine green (ICG) shows dark background in the early phase, indicating delayed choriocapillary perfusion and nonuniform hypofluorescent lesions in midphase that persist in the recovery.[17]

After infective etiologies were excluded, the patient was given intravenous methylprednisolone 500 mg every 12 hours 3 days after admission, together with topical betamethasone and homatropine 2%. After 5 days of methylprednisolone, there was complete resolution of the subretinal fluid in the right eye and near-complete resolution in the left. The headaches were also relieved. The patient was subsequently discharged and prescribed oral prednisone at tapering doses.

After 6 months, her vision was 6/9 in both eyes. Some

pigmentary disturbances at the posterior pole were present with no evidence of active choroiditis or subretinal fluid.

The treatment for VKH is well established, requiring the use of a steroid in some cases for up to 1 year to prevent recurrence. Oral prednisone may be used, but in severe cases high-dose intravenous methylprednisolone is recommended.[2] In steroid-resistant cases, cyclosporin A has been successfully used.[18] Refractory cases have also been documented to respond to newer immunosuppressive agents such as FK506,[19] which has been isolated from the fermentation broth of *Streptomyces tsukobaensis*. Long-term studies, however, are needed to fully evaluate the efficacy and safety of this drug.

To our knowledge, this is the first reported case of VKH among the Kadazans, the largest ethnic group in Sabah, a state of Malaysia north of Borneo.

Early diagnosis and aggressive treatment improve outcome. Treatment must be initiated early to prevent chronicity, which may result in such complications as retinal and disc neovascularisation that may lead to vitreous hemorrhage and tractional retinal detachment,[20] choroidal neovascularization,[20, 21] cataract, and glaucoma.

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Acute post-cataract-surgery endophthalmitis after suture removal

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ABSTRACT

Objective

To report a case of acute post-cataract-surgery endophthalmitis after suture removal.

Methods

This is a case report.

Results

A 77-year-old Chinese male presented with sudden painless blurring of vision in the left eye (OS) of 3 days duration 22 days after cataract surgery and 15 days after corneal-suture removal. OS was injected with corneal striae and had a visual acuity of 1/60, 3+ anterior-chamber cells with small hypopyon, and hazy vitreous. Endophthalmitis was considered and immediate vitreous tap with intravitreal antibiotics were given. Intensive topical antibiotics were instituted, followed by a repeat intravitreal antibiotic injections 3 days later. Postoperatively, there was massive fibrin formation with cyclitic membrane and seclusio pupillae that required two peripheral iridotomies. Visual acuity slowly recovered from hand movement to 6/18.

Conclusion

Endophthalmitis can be successfully treated without pars plana vitrectomy, following the Endophthalmitis Vitrectomy Study (EVS)

guidelines. Removal of corneal sutures must be followed with topical antibiotics to prevent the possibility of endophthalmitis secondary to introduction of microorganisms into the anterior chamber via the suture tract.

A 77-YEAR-OLD Chinese male, with multiple health problems including ischemic heart disease, congestive cardiac failure, systemic hypertension, type 2 diabetes mellitus, and benign prostatic hyperplasia underwent phacoemulsification cataract extraction with foldable-acrylic-intraocular-lens implantation in the left eye (OS) in 2003. A clear corneal temporal incision was made, which was closed with one 10/0 nylon suture. The surgery was uneventful with no immediate postoperative problem. The eye was treated with neomycin, polymyxin B, and dexamethasone drops for 1 week.

Seven days postoperatively, vision was 6/24. The tight suture was removed. Treatment with dexamethasone eye drops was continued for another week.

Twenty-two days postsurgery, patient complained of sudden painless blurring of vision in OS of 3 days duration. Ocular examination revealed vision of 1/60 in OS and 6/30 in the right eye (OD). The left conjunctiva was injected and the cornea had striae. There was no elevation of intraocular pressure (IOP). There were 3+ cells in the left anterior chamber with a small hypopyon. The left fundus revealed hazy vitreous with only a glimpse of the optic disc as seen with indirect ophthalmoscope. The right anterior segment was normal with an immature senile cataract. The right fundus was essentially normal.

A presumptive diagnosis of endophthalmitis was made. A vitreous biopsy was performed and patient was given intravitreal antibiotics consisting of ceftazidime 2.5 mg and vancomycin 1 mg plus subconjunctival injection of ceftazidime 100 mg. In addition, hourly topical antibiotics consisting of vancomycin 5% and ceftazidime 5% were given, and topical atropine 1% QID. Gram stain and cultures of vitreous samples did not isolate any fungus or bacteria.

After 72 hours, a repeat intravitreal antibiotic injection was given when no significant change was noted in the patient's condition. After 5 days, the hypopyon resolved with fibrin present on the surface of the intraocular lens (IOL). Topical dexamethasone was initiated. The fibrin slowly contracted and anterior-chamber cells progressively decreased. On day 20, iris bombe developed and a sequential argon-YAG peripheral iridotomy (PI) was created, relieving the pupil block. On day 25, the anterior-chamber cells decreased to 1+ and patient was discharged with visual acuity of hand movement.

On day 38, iris bombe recurred and sequential argon-YAG laser was performed to enlarge the peripheral iridotomy. B-scan showed retrolental vitreous opacities (Figure 1). On day 70, iris bombe recurred and a second sequential argon-YAG laser peripheral iridotomy was made at 5 o'clock, which relieved the pupil block. Ten months later, visual acuity in OS was 6/18 and fibrin on the IOL surface had resolved significantly. Cyclitic membrane and seclusio pupillae were still present, but the anterior chamber was deep with two patent peripheral iridotomies. Repeat B-scan showed the retina was attached and no vitreous opacities.

Sudden blurring of vision within weeks of cataract surgery should alert the ophthalmologist to the possibility of endophthalmitis, the most feared of all postoperative complications. Pain is a prominent feature of severe endophthalmitis, but early in the course of the infection, the pain may be mild as seen in this case.

Apart from pain and blurring of vision, features of endophthalmitis include lid edema, chemosis, conjunctival injection, corneal haze, numerous cells or hypopyon in the anterior chamber, vitritis, absent red reflex, and inability to visualize the fundus even with the indirect ophthalmoscope.

Systemic diseases such as diabetes mellitus are risk factors for endophthalmitis. Those caused by Gram-positive, coagulase-negative staphylococci occur more frequently among diabetics than nondiabetics. Thus, good diabetes control is important before proceeding with any intraocular surgery.[1, 2]

Another risk factor is ruptured posterior capsule, which provides intraoperative contact with the vitreous cavity.[3, 4]

Advanced age and being male have been associated with increased risk of postoperative endophthalmitis.[2] Silicone polypropylene foldable lenses have also been associated with a higher rate of endophthalmitis than polymethyl-methacrylate lenses.[5] However, no difference has been seen in the rate of contamination between extracapsular cataract extraction and phacoemulsification.[6] Poor surgical techniques such as inaccurate wound closure, increased operating time, and excessive surgical manipulation can contribute to the risk.[7] Temporal sutureless clear cornea incision has been postulated to be associated with a higher risk of endophthalmitis because the incision site is not protected from the environment by the upper lid.

The removal of suture one week after cataract surgery without any antibiotic coverage or other factors such as inaccurate wound construction and closure may have predisposed this patient to endophthalmitis.

Early diagnosis and prompt institution of antibiotics are important. Intravitreal vancomycin is used in all cases of Gram-positive organisms introduced exogenously, which has been noted to be sensitive to this antibiotic.[8, 9] Doses up to 2 mg have been found nontoxic to the retina.[7] Although a dose of 0.2 mg was found to be sufficient in maintaining intravitreal vancomycin concentration above the minimum

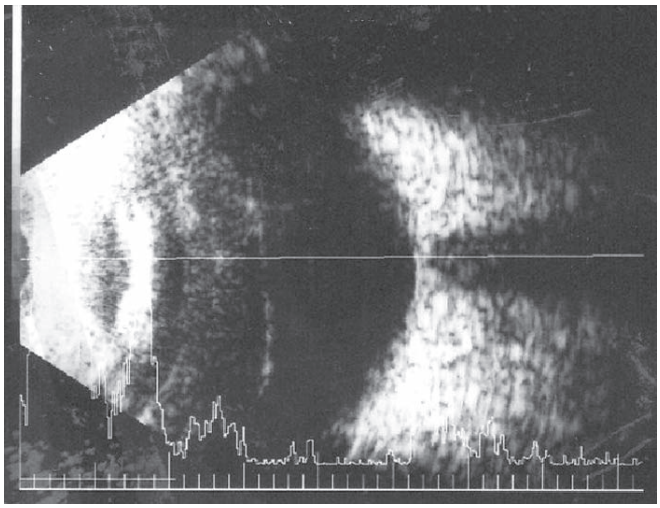

Figure 1. Day 38 after admission: B-Scan showed retrolental vitreous opacities.

inhibitory concentration for most organisms for 4 days, we adhered to the Endophthalmitis Vitrectomy Study (EVS) recommendation of using 1 mg.[8, 10]

Intravitreal ceftazidime was used to cover possible gram-negative organisms.[10] Amikacin is another option for the Gram-negative bacteria. Both exhibit equivalent activity with little difference in the likelihood of drug resistance.[11, 12] Amikacin, an aminoglycoside, has the advantage of synergistic effect with vancomycin. However, there have been reported cases of macular infarcts at therapeutic doses.[13, 14] Ceftazidime, a third-generation cephalosporin is safe but is physically incompatible with vancomycin, requiring injection via separate syringes to prevent precipitation of the drugs.[15]

The current universally accepted intravitreal antibiotic treatment to provide best coverage for endophthalmitis microorganisms is the combination of vancomycin and either amikacin or ceftazidime,[10, 16, 17] which was given in this case.

Subconjunctival ceftazidime provided antibacterial coverage to the anterior segment. Ceftazidime, like vancomycin, offers very low vitreous concentrations when given subconjunctivally.[18]

In the Endophthalmitis Vitrectomy Study (EVS), confirmed microbiologic growth was demonstrated in only 69.3% of intraocular specimens.[11] Bascom Palmer Eye Institute reported a slightly higher culture-positive rate of 75%.[19] Therefore, it is not unusual that no organism was isolated from the patient's vitreous sample.

In endophthalmitis, samples from both aqueous and vitreous should be sent for microscopy and culture even though the vitreous yields more positive cultures.[20] Vitrectomy also offers no advantage in terms of culture yield when compared with vitreous tap or biopsy.[20] No aqueous samples were taken from this patient. But it should have been recommended as it is a safe procedure in experienced hands.[21] Introduction of new organism via the paracentesis is unlikely when it is performed using sterile techniques. When initial cultures are negative, such as in this case, a repeat vitreous biopsy with aqueous tap is recommended prior to the second intravitreal injection of antibiotics.

Prior to the EVS guidelines, treatment of endophthalmitis involved various combinations of topical, subconjunctival, systemic, and intravitreal antibiotics. Pavan et al. subsequently demonstrated that using intravitreal with no systemic antibiotics resulted in reasonable outcome.[22, 23] In the early 1980s, intravitreal antibiotics became established as the mainstay treatment, while the use of systemic antibiotics and pars plana vitrectomy remained controversial.[24]

The 1995 landmark prospective EVS concluded that intravenous ceftazidime and amikacin did not alter the final visual acuity and media clarity.[10] It also found that pars plana vitrectomy was beneficial only in patients who present with vision of "perception to light" only.[10] Omission of intravenous antibiotics and performing pars plana vitrectomy only in patients presenting with vision of "perception to light" offer considerably savings in treatment cost without affecting final visual outcome.[25]

This patient was diagnosed with acute bacterial post-cataract-surgery endophthalmitis and managed according to the EVS guidelines. He was treated with repeated intravitreal vancomycin and ceftazidime and intensive topical vancomycin and ceftazidime. No pars plana vitrectomy was performed and no intravenous antibiotics were given. The final visual outcome was 6/18.

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Use of preservative-free multidose dispenser (Comod system) for glaucoma medications

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ABSTRACT

Purpose

To describe our experience in the use of preservative-free Comod system in glaucoma patients.

Methods

120 glaucoma patients were recruited and randomly assigned to group I (conventional system) or group II (Comod system). Schirmer's test, tear-breakup time (BUT), and culture and sensitivity (CS) tests were performed. A self-administered questionnaire was given to participants to evaluate ease of application, ocular stinging, and dryness.

Results

The Comod system did not cause any ocular stinging ($p < 0.01$) and was easy to use. Tear BUT and Schirmer's test were not different between the 2 groups. CS tests of the Comod at week 11 did not yield any organism.

Conclusion

The Comod system was more comfortable, easy to use, and can be used as a multidose system in administering glaucoma medications.

A PRESERVATIVE is important for two reasons: to prevent the patient from introducing microbiologically contaminated drugs into his eye(s) and to maintain the potency of the ophthalmic drug.[1, 2] The inclusion of preservatives in eye-drop dispensers, however, does not guarantee sterility. A high contamination rate was reported by Schein et al.[3] (29%), Marion and Tampert[4] (27%), Hovding and Sjursen[5] (12.9%).

The Comod eye-drop dispenser, introduced recently in Malaysia, has a shelf life of 2 years and can be used for 12 weeks after it has been opened.[6] As a sealed system, it has an "airless pump" that works without air equalization and prevents the reflux of external air and liquid when the solution is dosed. It also has an average drop size of 32.5 ± 2.5 ul, which is equivalent to the capacity of the inferior conjunctival fornix.

Timolol, a commonly used maintenance medication for glaucoma, comes in both the conventional eye-drop dispenser and in Timo-Comod system. We evaluated our experience using both systems. We performed the Schirmer's test, tear-breakup time (BUT), and graded the conjunctival injection by fluorescein. Culture and sensitivity for bacterial contamination were done for the Comod system.

One hundred twenty patients with open-angle glaucoma were randomly assigned to conventional Timolol 0.25% (Group I, 60 patients) or Comod system (Group II, 60 patients). Patients in both groups were instructed on the correct method of application especifically in avoiding any contact between the dropper tip and the eye or lid to maintain sterility.

This open-label study was divided into two phases: a comparison of the Comod system with the conventional system in phase 1, and determination of sterility of the Comod system in phase 2. Patients were also given a self-administered questionnaire to grade the convenience of application, severity of ocular stinging, and dryness of eyes.

Convenience of application was graded as follows: (1) Difficult—frequent spillage, (2) Moderately difficult—spillage of more than 10 times in a month, (3) Easy—spillage less than 10 times in a month, and (4) Extremely easy—no spillage. Spillage was defined as any drop that

overflowed from the conjunctival sac after application.

Ocular stinging was graded as: Grade 0—no stinging, Grade I—mild, Grade II—moderate, and Grade III—severe.

The conjunctival injection was graded as area of injection involving the bulbar conjunctiva: Grade 0–nil, Grade I–1 quadrant, Grade II–2 quadrants, Grade III–3 quadrants, Grade IV–4 quadrants, Grade V–4 quadrants with upper or lower palpebral conjunctival involvement.

An assistant wearing a mask and sterile gloves collected samples for culture and sensitivity test. Each bottle was uncapped, the tip swabbed with alcohol and allowed to dry. The first drop of the solution was discarded and the second drop placed onto blood agar plate and sent to the microbiology lab. The plates were incubated at 37°C and bacterial growth was assessed at 24 and 48 hours. Any growth was subjected to standard microbiological testing for identification and antibiotic-sensitivity testing.

Data analysis was done using Statistical Products and Services Solution software. The Schirmer's tests, tear film BUT, and intraocular pressures (IOP) in the two groups at 3 weeks were compared using the Student's t-test. The Chi-square test was used to analyze grade of convenience and ocular stinging. A level of significance of $p < 0.05$ was used.

Results indicated no difference in the distribution of the patients in the 2 groups in terms of ethnicity, gender, duration, and types of glaucoma. The mean IOP for both groups at baseline and 3 weeks were similar. Mean tear film BUT were also comparable (Table 1). The Schirmer's test values indicated diminished tears (< 10 mm) in both groups at baseline, with mild improvement in group II when compared to group I (Table 2) at 3 weeks, but not statistically significant.

No group II patients reported ocular stinging during the study, in contrast to those in group I who reported mild (58%) and moderate stinging (25%) ($p < 0.001$).

Table 1. **Mean tear-breakup time.**

Eye/Treatment Period	Tear-Breakup Time (seconds)		p
	Group I (n=60)	Group II (n=60)	
Right eye at baseline	12.53 ± 6.17	12.02 ± 5.61	0.632
Left eye at baseline	12.30 ± 5.98	11.57 ± 4.70	0.457
Right eye at 3 weeks	12.80 ± 6.05	12.75 ± 5.70	0.963
Left eye at 3 weeks	12.03 ± 5.76	12.48 ± 5.23	0.655

Table 2. **Mean Schirmer's test.**

Eye/Treatment Period	Schirmer's Test (mm)		p
	Group I (n=60)	Group II (n=60)	
Right eye at baseline	10.8 ± 0.89	8.2 ± 0.77	0.71
Left eye at baseline	10.6 ± 0.96	8.8 ± 0.80	0.29
Right eye at 3 weeks	10.1 ± 0.88	9.7 ± 0.81	0.79
Left eye at 3 weeks	9.3 ± 0.77	9.6 ± 0.79	0.88

Conjunctival injection was negative in both groups and cultures were also negative, even at 11 weeks.

Although several patients initially complained of some difficulty in using the Comod system, it becomes easier with repeated use.

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Tuberous sclerosis in a 17-year-old female

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ABSTRACT

Objective

To report a classic case of tuberous sclerosis complex.

Methods

This is a case report.

Results

A 17-year-old female presented with bilateral blurring of vision with left temporal headaches and seizures. Physical examination showed she had adenoma sebaceum, ash-leaf spots, and shagreen patches. Computed tomography revealed hydrocephaly, tubers, and subependymal nodules while magnetic resonance imaging revealed a giant-cell astrocytoma, later confirmed through histopathologic examination. Renal ultrasound showed findings consistent with an angiomyolipoma. Ophthalmologic findings included left cortical cataract, papillidema, and retinal astrocytoma.

Conclusion

The findings were consistent with tuberous sclerosis.

TUBEROUS sclerosis complex (TSC) is a multisystemic and neurocutaneous, autosomal-dominant disorder

characterized by hamartomatous growths that occur mostly in the skin, brain, kidneys, heart, and eyes. The classic triad of this disorder described by Vogt in 1908 includes epilepsy, mental retardation, and adenoma sebaceum. Its clinical manifestations are now known to be more diverse and inclusive.

Comprehensive diagnostic criteria set out initially by Gomez in 1988 now form the consensus statements from the Diagnostic Criteria Committee of the National Tuberous Sclerosis Association (USA)[1] (Table 1).

Diagnosis of TSC is confirmed if one or two major features plus two minor features are met. Diagnosis of TSC is probable when one major and one minor feature are met. If either one major feature or two or more minor features are met, possible diagnosis of TSC may be considered.

This patient presented with a 4-month history of gradual progressive blurring of vision associated with diplopia, esotropia, and occasional eye pain, particularly left temporal headache radiating to the occipital area. He satisfied 8 of the criteria: facial angiofibromas or forehead plaque, hypomelanotic macules (>3), shagreen patch, renal angiomyolipoma, cortical tuber, subependymal nodule, subependymal giant-cell astrocytoma (main cause of symptoms), and retinal hamartoma.

Table 1. **Diagnostic criteria for tuberous sclerosis.**

Major features
• Facial angiofibromas or forehead plaque
• Nontraumatic ungual or periungual fibroma
• Hypomelanotic macules (> 3)
• Shagreen patch (connective tissue nevus)
• Multiple retinal hamartomas
• Cortical tuber
• Subependymal nodule
• Subependymal giant cell astrocytoma
• Cardiac rhabdomyoma, single or multiple
• Lymphangioleiomyomatosis
• Renal angiomyolipoma
Minor features
• Multiple, randomly distributed pits in dental enamel
• Hamartomatous rectal polyps
• Bone cysts.
• Cerebral white matter radial migration lines
• Gingival fibromas
• Nonrenal hamartoma
• Retinal achromic patch
• “Confetti” skin lesions
• Multiple renal cysts

These findings were confirmed by the dermatology, renal, neurosurgery, and ophthalmology services.

Ophthalmic features of TSC may be divided into retinal and nonretinal.[2] Retinal features were first described by Van der Hoeve in 1921 who termed these lesions phakomas (Greek for spot), and thus introduced the concept of phakomatosis.[3] These retinal lesions, now known as retinal hamartomas, are the best-known ocular manifestations of TSC. Nonretinal features are less common. In this patient, there was a cortical cataract in the left eye and papillidema in both eyes. Only 3 cases of cataract associated with TSC have been reported.[4, 5] The papilledema was due to the increased intracranial pressure caused by the astrocytoma blocking cerebrospinal fluid (CSF) at the level of the foramen of Monroe.

The patient underwent aggressive intracranial-pressure (ICP) lowering initially, followed by right paramedian craniotomy and excision of tumor. Intraoperative findings showed a highly vascular, grayish cystic, and pinkish-white tumor embedded at the septum and at the anterior horn. Histopathological results confirmed subependymal giant-cell astrocytoma.

Prior to surgery, the patient’s vision deteriorated to “no light perception” in both eyes. The operation was done to prevent further seizures and relieve the headaches. Thus, prompt diagnosis is recommended so that early and appropriate management can be instituted to prevent vision loss.

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