

ORIGINAL ARTICLE

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Epidemiological pattern of retinoblastoma at the Philippine General Hospital

ABSTRACT**Objective**

To evaluate the epidemiological and clinical patterns of retinoblastoma in a tertiary government hospital.

Methods

This is a retrospective case series of new retinoblastoma patients seen at the University of the Philippines-Philippine General Hospital (UP-PGH) in three periods: 1967 to 1977, 1985 to 1995, and 1997 to 2001. The demographic and clinical characteristics of retinoblastoma over the three periods were compared.

Results

The incidence of retinoblastoma increased from 40/100,000 new cases in 1967 to 1977 to 237/100,000 new cases in 1997 to 2001. The average age at onset did not change over time but the age at consultation decreased from 1.5 years to 1 year. The most common initial ocular manifestation at onset was cat's eye reflex (77 to 79%) with findings of leukocoria (67 to 77%). Extraocular findings of proptosis and orbital mass declined through the years. Bilateral retinoblastoma comprised 30% in this series and showed no change in distribution over the years.

Conclusion

The epidemiological and clinical patterns of retinoblastoma cases at the Philippine General Hospital may be changing over time and requires continuous monitoring of incidence and characteristics.

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RETINOBLASTOMA is the most common primary ocular tumor in the Philippines. This paper analyzes the demographic and clinical characteristics of retinoblastoma patients over three periods:

Series I : 1967 - 1977¹
Series II : 1985 - 1995²
Series III : 1997 - 2001 (unpublished data)

These three series can be considered comparable because they:

- were conducted in the same location (UP-PGH) with the same catchment area,
- were performed by the same senior author using the same screening procedures, and
- compared only new retinoblastoma patients referred to the UP-PGH eye department.

METHODOLOGY

All suspected retinoblastoma cases referred to the Retina-Oncology Service from 1967 to 1977, from 1985 to 1995, and from 1997 to 2001 were included in the study. A detailed medical and family history was obtained. All patients underwent comprehensive eye examination, which included anterior segment evaluation, dilated fundus exam with the indirect ophthalmoscope, and when necessary, B scan, computed tomography (CT), magnetic resonance imaging (MRI), spinal fluid exam, or bone-marrow evaluation. Results were classified according to a system described in a previous study³ as follows:

Stage 1: *Intraocular stage*. Tumor is confined within the retina.

Stage 1a: Early intraocular (tumor less than half of the retinal surface)

a1 – tumor size < 4DD*

a2 – tumor size 4 DD to 10 DD

a3 – tumor size >10DD to 15 DD

Stage 1b: Late intraocular (tumor more than half of the retinal surface or >15 DD).

Stage 2: *Intraocular far advanced stage*. Tumor and/or pathologic changes have spread to other ocular structures.

Stage 3: *Intraorbital and/or metastatic spread*. Tumor has extended out of the eyeball into the orbit (intraorbital) or to distant tissues (metastatic).

Statistical analysis was performed using MS Excel (Microsoft Corporation, Redmond, WA, USA).

RESULTS

Incidence

The average number of new cases per year increased from 5 in 1967-1977 to 16 in 1985-1995 and 33 in 1997-

2001. To adjust for the increase in population growth, the figures were converted to new cases per 100,000 new eye cases seen during the period. This yielded an incidence of 40/100,000 new cases for 1967 to 1977, 80 for 1985 to 1995, and 237 for 1997 to 2001.

Age of onset

The average age of onset is the approximate age when the symptoms first appeared, a better index than the age at consultation which may be affected by nonmedical factors such as accessibility of health care. The age at onset did not significantly change over time: 12 months for 1967 to 1977, 18 months for 1985 to 1995, and 14 months for 1997 to 2001.

Analysis of the data on age at consultation revealed a decrease in the average delay of consultation from 1.5 years to 1 year. The delay was 19 months for 1967 to 1977, 11 months for 1985 to 1995, and 13 months for 1997 to 2001. This means that the onset of the disease has not changed through the years but the patients are now being brought earlier for consultation.

Gender Distribution

For the period 1967 to 1977, the ratio of male to female cases was 1.7:1. The ratio dropped to 1.3:1 in 1985 to 1995 and 1.2:1 in 1996 to 2001, closer to the international ratio of 1:1.

Tumor stage at consultation

From 1967 to 1977, the number of cases seen in all three stages were similar (Table 1). From 1985 to 1995, almost half of the cases were in stage 3 at consultation. From 1996 to 2001, however, 45 percent were seen at stage 1 indicating that more cases were seen earlier during the period.

Ocular manifestation at onset

The most common initial eye complaint was cat's eye reflex (77 to 79%), followed by strabismus (11 to 14%). These did not change over the years. Other symptoms included proptosis, orbital mass, and ocular redness (Table 2).

Ocular manifestation at consultation

From 1967 to 1977, there were no cases of strabismus at first consultation (Table 3). Most Stage 1 cases consisted of partial leukocoria (tumor size less than 1/2 of retinal surface), which still required enucleation. From 1985 to 1995, strabismus as initial presentation on consultation appeared with more cases of partial leukocoria. Extraocular findings such as proptosis declined from 16% in 1967-1977 to 6% in 1985-1995 and 3% in 1997-2001, while findings of orbital mass dropped from 27% to 11% to 3% respectively (Table 3).

*disc diameter

Table 1. Tumor stage at consultation.

| Stage | Number of New Cases (Percent) | | |
|---------|-------------------------------|-----------|-----------|
| | 1967-1977 | 1985-1995 | 1997-2001 |
| Stage 1 | 19 (34) | 58 (35) | 76.0 (45) |
| Stage 2 | 16 (29) | 29 (17) | 29.0 (17) |
| Stage 3 | 21 (37) | 80 (48) | 64.0 (38) |

Table 2. Ocular manifestation at onset.

| Signs & Symptoms | Number of Cases (Percent) | | |
|------------------|---------------------------|-----------|-----------|
| | 1967-1977 | 1985-1995 | 1997-2001 |
| Cat's eye | 44 (79) | 130 (78) | 130 (77) |
| Strabismus | 8 (14) | 23 (14) | 19 (11) |
| Others* | 4 (7) | 14 (8) | 19 (12) |

* Proptosis, Orbital Mass, Redness

Table 3. Ocular manifestation at consultation.

| Signs & Symptoms | Number of Cases (Percent) | | |
|------------------|---------------------------|------------------|------------------|
| | 1967-1977 | 1985-1995 | 1997-2001 |
| Leukocoria | 15 (27) | 112 (67) | 130 (77) |
| Strabismus | - | 10 (6) | 19 (11) |
| Orbital Mass | 15 (27) | 19 (11) | 5 (3) |
| Redness/Swelling | 9 (16) | 8 (5) | 5 (3) |
| Proptosis | 9 (16) | 10 (6) | 5 (3) |
| Buphthalmos | 5 (9) | - | - |
| Others | 3 (5) | 8 (5) | 5 (3) |
| Total | 56 (100) | 167 (100) | 169 (100) |

Table 4. Familial Incidence.

| Pedigree | Number of Cases (Percent) | | |
|--------------|---------------------------|------------------|----------------|
| | 1985-1995 | 1996-2001 | Percent Change |
| None | 154 (92) | 157 (93) | no change |
| Parents | 3 (2) | 7 (4) | |
| Siblings | 8 (5) | 3 (2) | { 7-8 |
| Others | 2 (1) | 2 (1) | |
| Total | 167 (100) | 169 (100) | |

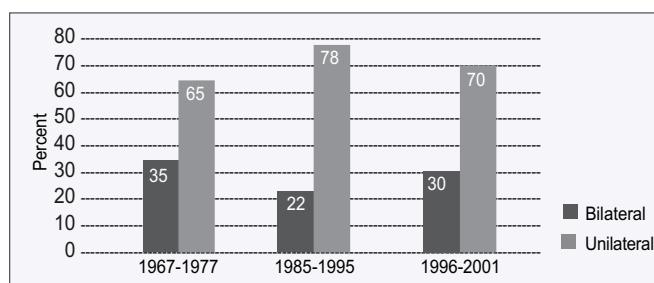


Figure 1. Distribution of cases by laterality.

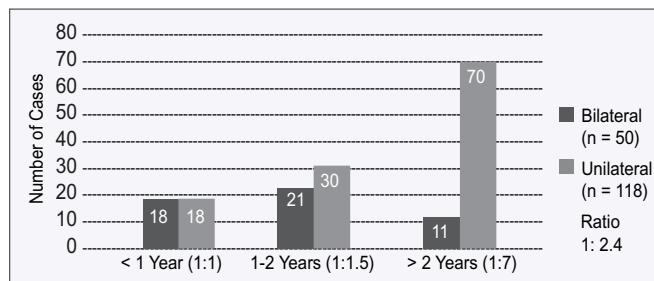


Figure 2. Age of onset of bilateral and unilateral cases (1996-2001 series).

Familial incidence

Familial incidence remained at 7 to 8%, the same as the international rate (Table 4).

Laterality

Bilateral cases comprised 30% of the series, which showed no change in distribution over the years (Figure 1). This is important as all bilateral cases are considered hereditary.⁵ In our series, most of the bilateral cases presented early, before 2 years of age (Figure 2). Below the age of 1 year, the ratio of bilateral to unilateral cases was equal (1:1). At 1 to 2 years, the ratio was 1:1.5. After 2 years, the ratio decreased to 1:7.

DISCUSSION

In contrast to the usual epidemiologic surveys that cover short duration, this study has a long observation period. Prolonged follow-up data are available, and changes and variations in trend can be detected.

One of the significant findings is the five-fold increase in incidence of retinoblastoma over the periods covered. This may be attributed to advances in disease evaluation and therapy, allowing more survivors to reach childbearing age. Gene mutations, which comprise 40% of all new cases, continue to add to the genetic pool. This may explain the higher incidence despite advances in medical technology.

The male-female ratio declined from 1.7:1 to 1.2:1, which is closer to current international data. There is no reported gender bias in retinoblastoma.

The average age of onset, clinical course and frequency of ocular manifestations remain unchanged. However, the average delay in consultation had been shortened by 6 months from 1.5 years to 1 year of age. This may be a result of greater public awareness, better communication systems, and improved public-health programs. These translated to early consultation and detection of cases and corresponding decline of advanced cases. More cases of partial leukocoria (tumor less than 1/2 of retina) were seen, allowing vision to be saved in some cases. Ocular findings of strabismus, previously noted only in the family history, were present at the time of consultation in the last two series, indicating that earlier cases of retinoblastoma were seen. The percentage of ocular proptosis and intraorbital mass, which were late manifestations, also decreased. All these will lead to better rate of therapeutic success.

The familial incidence remained the same in these series. However, with the increase in survivors for the past 10 to 15 years, an increase in familial incidence is predicted in the coming years as more of these survivors reach childbearing age.

The data on laterality showed no change over the years

studied and showed that bilateral cases have earlier age of onset. Other studies also showed a more rapid course and a greater tendency for secondary tumors in the later years of life especially if the patients were subjected to radiotherapy or radiomimetic chemotherapeutic agents.⁵

In summary, a 35-year longitudinal study of retinoblastoma incidence in the Philippines showed the following trends:

1. A fivefold steady increase in incidence from 48/100,000 eye cases to 237/100,000 eye cases.
2. A decreasing male preponderance from male-female ratio of 1.7:1 to an almost equal 1.2:1.
3. No change in average age of onset, clinical course, clinical manifestations, and familial incidence.

4. Decrease in the average delay in consultation by six months from 1.5 years to 1 year.

5. More cases of early detection and fewer cases of late presentation.

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