

Insights of Ophthalmic Pathology

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Ophthalmic pathology in the Philippines has come a long way since the establishment of the Philippine Ophthalmic Pathology Society in 2020. It has provided the much-needed avenue for eye doctors to explore the wonders and mysteries of different eye diseases as they affect the human body. Through the microscope, we are able to answer queries raised by complex cases, fortify our knowledge of the different disease processes of the eye, and enlighten curious minds during clinicopathologic conferences.

Ophthalmic pathology serves as the backbone for all the advancements in ophthalmology, without which we would not be able to cope with the havoc caused by diseases affecting the eyes. An ophthalmologist of any subspecialty with a strong foundation in ophthalmic pathology is armed with the basic knowledge of disease processes, which enables him to be confident, exercise good clinical judgement, and administer the proper medical and surgical management.

Case reports and case series are important as these form a pool of valuable data for future reference in systematic reviews, and can themselves inspire further research. One such example was the case series of liquid biopsy for retinoblastoma by Dr. Jesse Berry.¹ Dr. Berry obtained aqueous humor samples from enucleated eyes of retinoblastoma patients and from eyes of retinoblastoma patients prior to injection of intravitreal chemotherapeutic agent, and demonstrated tumor-derived cell-free

DNA in the aqueous humor. Dr. Berry and her colleagues later discovered gain of chromosome 6p from examining the aqueous humor of retinoblastoma eyes.^{2,3} Dr. Berry's case series has spurred similar studies by other researchers. The acquisition of chromosomal information from the tumor through analysis of the aqueous humor provides vital insights for treatment planning and prognosis without the need for the traditional tissue biopsy, which is risky due to potential tumor spread outside the eye. This new approach is particularly important as retinoblastoma is the most common intraocular tumor in childhood and direct tumor biopsy carries a significant risk of metastasis.^{4,5,6,7,8,9,10}

We have made the pharmaceutical industry flourish because most of the time the aim of treatment is to control the disease and not to eradicate it completely. Knowing the exact pathology of diseases allows us to explore other modalities of treatment. In the case of age-related macular degeneration (ARMD), there is more to just angiogenesis. Studies of the molecular constituents of drusen have shown that in ARMD, there is an immunologic component involved. Drusen exhibited signs of inflammation brought about by derivatives of the complement system, immune-associated responses, and protein by-products.^{11,12,13,14} My mentor Dr. William Green has demonstrated that macrophages engulfing Bruch's membrane (BM) cause breaks in the BM which allow choroidal neovascularization to set in,



resulting in the cascade of bleeding and scar formation.¹⁵

These are just two areas in which ophthalmic pathology has played a key role in the discovery of new modalities of treatment. An inquisitive mind unearths new discoveries which help us understand the evolution and pathogenesis of different eye diseases. Encouraging young physicians to pursue knowledge and equipping them with the right tools for research are as important as developing their clinical acumen in diagnosing eye diseases. We need to encourage the young ophthalmologist to submit ocular specimens to further our quest for knowledge. Vitreous specimens, conjunctival tissues from pterygium excisions, eyeballs from enucleations—they do not get their worth in the waste basket. Now, with the addition of molecular genetics services from the Philippine Genome Center, we have an augmented armamentarium to help us discover new diseases that may be unique to our population and further contribute to the wealth of ophthalmic knowledge.

REFERENCES

- Berry JL, Xu L, Murphree AL, *et al.* Potential of aqueous humor as a surrogate tumor biopsy for retinoblastoma. *JAMA Ophthalmol.* 2017 Nov; 135(11): 1221-1230.
- Berry JL, Xu L, Polski A, *et al.* Gain of Chromosome 6p is a molecular biomarker for prognostication of retinoblastoma ocular survival: the aqueous humor surrogate tumor biopsy. *IOVS.* 2020 June; 61(7): 2805.
- Xu L, Polski A, Prabakar R, *et al.* Chromosome 6p amplification in aqueous humor cell-free DNA is a prognostic biomarker for retinoblastoma ocular survival. *Mol Cancer Res.* 2020 Aug; 18(8):1166-1175. doi: 10.1158/1541-7786.MCR-19-1262. Epub 2020 May 20.
- Shields JA, Shields CL, Ehya H, *et al.* Fine-needle aspiration biopsy of suspected intraocular tumors. The 1992 Urwick lecture. *Ophthalmology.* 1993 Nov; 100(11): 1677-1684.
- Karcioglu ZA, Gordon RA, Karcioglu GL. Tumor seeding in ocular fine needle aspiration biopsy. *Ophthalmology.* 1985 Dec; 92(12): 1763-1767.
- Karcioglu ZA. Fine needle aspiration biopsy (FNAB) for retinoblastoma. *Retina.* 2002 Dec; 22(6): 707-710.
- Eide N, Syrdalen P, Walaas L, Hagmar B. Fine needle aspiration biopsy in selecting treatment for inconclusive intraocular disease. *Acta Ophthalmol Scand.* 1999 Aug; 77(4): 448-452.
- Eide N, Walaas L. Fine-needle aspiration biopsy and other biopsies in suspected intraocular malignant disease: a review. *Acta Ophthalmol.* 2009 Sept; 87(6): 588-601.
- Eriksson O, Hagmar B, Ryd W. Effects of fine-needle aspiration and other biopsy procedures on tumor dissemination in mice. *Cancer.* 1984 July; 54(1):73-78.
- Ali MJ, Honavar SG, Vemuganti GK, Singh AD. Fine needle aspiration biopsy of retinal tumors. *Monogr Clin Cytol.* 2012; 21:72-81.
- Hageman GS, Luthert PJ, Victor Chong N.H., *et al.* An integrated hypothesis that considers drusen as biomarkers of immune-mediated processes at the RPE-Bruch's membrane interface in aging and age-related macular degeneration. *Prog Retin Eye Res.* 2001 Nov; 20(6): 705-732.
- Johnson LV, Leitner WP, Staples MK, Anderson DH. Complement activation and inflammatory processes in Drusen formation and age related macular degeneration. *Exp Eye Res.* 2001 Dec; 73(6): 887-896.
- Mullins RF, Aptsiauri N, Hageman GS. Structure and composition of drusen associated with glomerulonephritis: implications for the role of complement activation in drusen biogenesis. *Eye (Lond).* 2001 June; 15(Pt 3): 390-395.
- Geerlings MJ, de Jong AK, den Hollander AI. The complement system in age-related macular degeneration: a review of rare genetic variants and implications for personalized treatment. *Mol Immunol.* 2017 Apr; 84: 65-76.
- Dastgheib K, Green WR. Granulomatous reaction to Bruch's membrane in age-related macular degeneration. *Arch Ophthalmol.* 1994 June; 112(6): 813-818.