FOUNDERS LECTURE AT ARDS 2023

Gregg T. Kokame, MD, MMM, shares his expertise on AMD subtypes.

BY DANIEL WANG, MD

The 2023 Aspen Retinal Detachment Society (ARDS) meeting in Snowmass, Colorado, included the annual Founders Lecture. This year, we honored Gregg T. Kokame, MD, MMM, for his extensive work with AMD subtypes, and polypoidal choroidal vasculopathy (PCV) in particular. Below you will find a robust summary of his lecture, which included several clinically relevant pearls.

Registration is open for ARDS 2024, set for March 2-6. Visit aspenretina.com *for more information and get ready to hit the slopes!*

- Timothy G. Murray, MD, MBA

We have made significant progress in the diagnosis and management of AMD, but it continues to be a complex condition with substantial ocular morbidity on a global scale. During the 2023 ARDS Founders Lecture, Gregg T. Kokame, MD, MMM, provided a review of the categorization and management of wet AMD (Figures 1 and 2). This update encompassed the condition's anatomic variations and how he customizes his treatment approach based on the specific subtype. Dr. Kokame underscored the significance of ethnic disparities in AMD and highlighted the subtype of PCV.

ETHNIC CONSIDERATIONS

Dr. Kokame emphasized the distinctions between Asian and non-Asian AMD patients, noting that AMD in Asian patients typically manifests with smaller lesions and a slower growth rate. This raises questions regarding the efficacy of certain therapies, particularly newer treatments such as Syfovre (pegcetacoplan, Apellis), in the Asian population. Dr. Kokame stressed the importance of clinically relevant classification systems, specifically mentioning the consensus nomenclature for categorizing wet AMD proposed by Richard F. Spaide, MD. This framework outlines the subtypes of choroidal neovascularization (CNV): type I, type II, type III, and PCV.[1]

THE SUBTYPES

For initial patient evaluations, Dr. Kokame employs a variety of imaging techniques, including fundus photography, fluorescein angiography, ICG angiography, OCT, and OCT angiography.[2] Subsequently, patients are typically monitored using OCT alone, he said.

Type III CNV includes an intraretinal neovascular component, termed *retinal angiomatous proliferation*, and is exceptionally sensitive to anti-VEGF treatment, leading Dr. Kokame to recommend as-needed treatment for patients with this subtype of AMD. He suggested that treatment can be extended aggressively and stopped in some, but not all, cases.[3,4]

Type II CNV, found above the retinal pigment epithelium (RPE) and under the retina, is often enveloped by a layer of RPE. This type is also highly responsive to anti-VEGF therapy, often enabling a quick treat-and-extend protocol and eventual discontinuation of treatment.[3,4]

Type I CNV, beneath the RPE and above Bruch membrane, is the most common CNV and has the most variable therapeutic response. Among the subtypes of wet AMD, type I CNV is the most prevalent but exhibits variable sensitivity to anti-VEGF treatments, sometimes proving resistant.[3-5]

Dr. Kokame discussed several case studies to illustrate the differences in treatment response among the various AMD subtypes.

PCV UNDER THE MICROSCOPE

PCV received significant attention in Dr. Kokame's presentation due to its clinical importance. PCV has a varied prevalence among different ethnic groups and is often underrecognized and misdiagnosed. Dr. Kokame asserted that identifying PCV is crucial due to its effect on treatment and its predictive role in anti-VEGF resistance.

ICG angiography remains the standard for diagnosing

ABOUT THE SPEAKER

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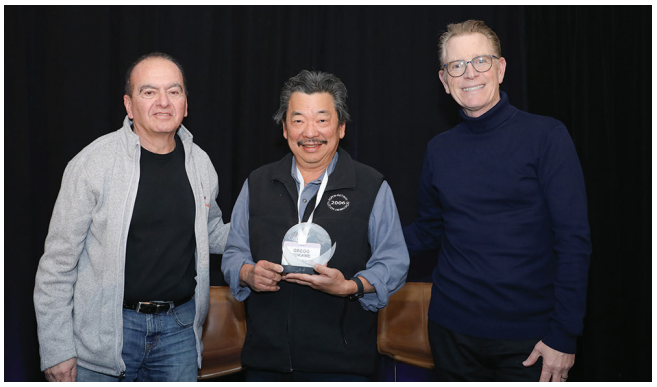

Figure 1. Program Directors Donald J. D'Amico, MD, (left) and Dr. Murray (right) present Dr. Kokame (center) with the 2023 Founders Lecture Award.

Images courtesy of Kevin Caldwell Photography

Figure 2. Dr. Kokame discussed the different subtypes of AMD, including polypoidal choroidal vasculopathy.

PCV, demonstrating typical aneurysmal polyps at the edges of the choroidal neovascular network, Dr. Kokame said.

PCV can manifest as either type I or type II CNV; the more common type I has a well-defined branching vascular network (both feeder and draining vessels), whereas type II has polyps but no defined branching vascular network.[3-5]

Notably, PCV exhibits a 50% prevalence of anti-VEGF resistance, with the closure of polyps serving as a predictor of clinical response. Given its relatively high prevalence, particularly among Asian patients, PCV demands careful consideration when evaluating patients with wet AMD.[3-5]

In Asian regions, aflibercept (Eylea, Regeneron) is often recommended for the treatment of PCV, although ranibizumab (Lucentis, Genentech/Roche) and bevacizumab (Avastin, Genentech/Roche) are often also employed. Dr. Kokame reviewed the EVEREST II study, which demonstrated that a combination of photodynamic therapy (PDT) and anti-VEGF therapy with ranibizumab yielded improved visual outcomes, increased odds of complete polypoidal lesion regression, and fewer treatments compared with anti-VEGF monotherapy.[6]

Dr. Kokame also discussed distinctions between anti-VEGF agents, including aflibercept, ranibizumab, brolucizumab (Beovu, Novartis), and faricimab (Vabysmo, Genentech/Roche). Aflibercept is typically favored in Asia for PCV, showing better visual gains in the PLANET study compared with data from the EVEREST II study. The HAWK study showed that brolucizumab administered every 8 or 12 weeks resulted in consistent visual acuity gains that were comparable with aflibercept dosed every 8 weeks.[7] Anatomic outcomes favored brolucizumab over aflibercept, with 76% of patients treated with brolucizumab receiving a dose every 12 weeks after the initial loading phase.[7] While faricimab holds promise for treatment, it requires further study in the context of PCV patients, according to Dr. Kokame.

Dr. Kokame then shared his current treatment algorithm for PCV, which involves monitoring patients with inactive PCV and treating patients with active PCV with leakage or bleeding based on location and severity. Laser or PDT treatment may be considered for extrafoveal PCV, while subfoveal PCV (depending on vision and the presence of dense subretinal hemorrhage) may be treated with anti-VEGF monotherapy or a combination of PDT and anti-VEGF. An FDA-approved laser for PDT (ML6710i, Modulight) is anticipated to expand access to this treatment option, he added.

KEY PEARLS

A thorough understanding of AMD subtypes is vital, Dr. Kokame concluded, as it can predict treatment responses and influence treatment decisions. PCV remains a crucial but often overlooked subtype of wet AMD, particularly in individuals of Asian descent. This knowledge helps inform tailored treatment approaches, optimizing the efficacy of planned interventions. ■

1. Spaide RF, Jaffe GJ, Sarraf D, et al. Consensus nomenclature for reporting neovascular age-related macular degeneration data: Consensus on Neovascular Age-Related Macular Degeneration Nomenclature Study Group. *Ophthalmology*. 2020;127(5):616-636.
2. Mettu PS, Allingham MJ, Nicholas PC, Cousins SW. Neovascular morphology by IC angiography and response to loading-dose anti-VEGF therapy in patients with neovascular AMD. *Invest Ophthalmol Vis Sci*. 2016;57(12).
3. Kokame GT, Liu K, Kokame KA, Kaneko KN, Omizo JN. Hawaii Causcasian PCV study. *Ophthalmologica*. 2020;243(3):178-186.
4. Kokame GT, deCarlo TE, Kaneko KN, Omizo JN, Lian R. Asian and Caucasian PCV study. *Ophthalmol Retina*. 2019;3(9):744-752.
5. Kokame GT, deCarlo TE, Kaneko KN, Omizo JN, Lian R. Anti-vascular endothelial growth factor resistance in exudative macular degeneration and polypoidal choroidal vasculopathy. *Ophthalmol Retina*. 2019;3(9):744-752.
6. Lim TH, Lai TYY, Takahashi K, et al; EVEREST II Study Group. Comparison of ranibizumab with or without verteporfin photodynamic therapy for polypoidal choroidal vasculopathy: the EVEREST II Randomized Clinical Trial. *JAMA Ophthalmol*. 2020;138(9):935-942.
7. Ogura Y, Jaffe GJ, Cheung CMG, et al. Efficacy and safety of brolucizumab versus aflibercept in eyes with polypoidal choroidal vasculopathy in Japanese participants of HAWK. *Br J Ophthalmol*. 2022;106(7):994-999.

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