Early Detection and Intervention

An Unmet Need in Age-Related Macular Degeneration

by Francesco Bandello, MD

While cutting-edge innovations are in development to improve the diagnosis and treatment of age-related macular degeneration (AMD), improving patients' ability to recognize symptoms and doctors' ability to diagnose and intervene as early as possible is a strategy that can be implemented immediately to improve patient outcomes.

Figure 1. Fundus photo OS of intermediate-stage AMD. Drusen are apparent throughout the macula and appear as light-orange spots.

Clinical Manifestations of AMD

Age-related macular degeneration is a debilitating ocular condition that is estimated to affect nearly 9% of the global population.[1] Its early manifestations are subtle, with the greatest loss of vision typically occurring at advanced disease stages.[2] Initially, the condition presents with drusen on fundus exam and mild symptoms, such as blurred or distorted vision that progressively worsens with time (Figure 1). Interestingly, the ALSTAR Study at University of Alabama at Birmingham has shown that dark adaptation is impaired at least three years before AMD is clinically evident.[3] Therefore, as the earliest recognizable symptom, night vision issues or complaints could lead to detection of subclinical AMD by means of dark adaptation testing.

In the advanced stages, the condition manifests as two distinct forms: vascular ('wet') AMD and avascular ('dry') AMD. As the name implies, wet AMD is characterized by choroidal vascularization in the retina. The integrity of the new vessel walls is not sound, leading to h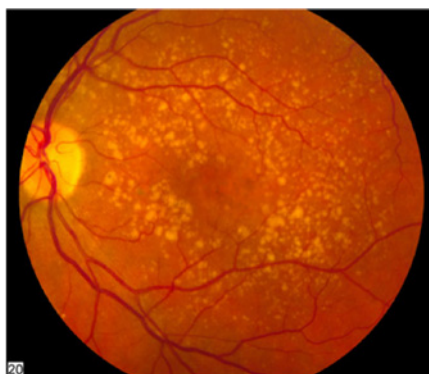emorrhage of blood and lipids into the subretinal space. This fluid may then form a disciform scar that rapidly and permanently reduces visual acuity. Contrastingly, advanced dry AMD is typically characterized by geographic atrophy, wherein the retinal pigment epithelium, choriocapillaris, and photoreceptors begin to atrophy, resulting in a gradual yet unrelenting loss of vision.

Diagnosis and Current Treatment Options

Typically, AMD is diagnosed based on fundus exam, angiography, optical coherence tomography (OCT), and best corrected visual acuity (BCVA). Despite the diverse availability of imaging modalities, a challenge for reducing the global burden of AMD lies in the fact that patients often do not consult a physician until they are already experiencing symptoms associated with intermediate to advanced AMD. As a result, patients may already be well on their way to developing advanced wet or dry AMD by the time the disease is diagnosed.

For patients who unfortunately advance to the wet form of AMD, they can now be well managed if they are diagnosed and treated early enough. While this condition used to be a lifelong sentence of blindness, drugs that act as antagonists of the vascular endothelial growth factor (VEGF) have been shown to not only halt the progression of the condition, but to improve visual acuity as well.[4] It has since been estimated that in some countries, AMD-related legal blindness has been reduced by as much as 50% since the introduction of anti-VEGF therapy. However, if the condition is not diagnosed early enough, subretinal macular hemorrhage can lead to permanent damage that cannot be reversed by VEGF antagonists.

The Need for Earlier Diagnosis, Intervention and Awareness

It is currently estimated that 8% of the world has early-stage AMD, although 15% of this cohort is expected to progress to late-stage disease within 15 years of diagnosis.[5,6] These data, combined with statistics revealing a shift in demographics towards an aging population, speak to a need for earlier diagnosis and intervention. This is especially true given the burden this condition places on the individual as well as the healthcare system. Individuals with late-stage disease often experience severe loss of independence, depression, and an increased risk of falling. Total annual direct costs from AMD-related United States medical claims were estimated to total 575 to 733 million USD.[7] These statistics point to a need for improvements in diagnosis and treatment, with earlier intervention promising more favorable outcomes.

Dark adaptation testing is gaining attention as a means of earlier diagnosis of AMD. Dark adaptation is the ability of the eye to transition from light to dark settings, which is impaired in patients with some ocular conditions, including AMD. Functional changes have been shown to precede structural changes, and thus, assessing dark adaptation is a useful strategy for detecting subclinical AMD several years before changes in the fundus are observable. While older dark adaptation modules were time consuming and infrequently used in standard clinical practice, recent advances have led to the availability of next generation technology. Nowadays, devices available include: the Portable Field Dark Adaptometer (PFDA) and the AdaptDx (MacuLogix, Inc, Middletown, PA, USA). In my practice I use the AdaptDx which can perform an objective assessment of a patient's ability to dark adapt in less than 6.5 minutes. Dark adaptation testing can now be integrated into the clinical setting to quickly and easily assess AMD suspects who present with multiple risk factors and/or a night vision complaint.

Patients whose dark adaptation outcomes are abnormal can take several steps to slow or halt the progression of the disease. Lifestyle modifications such as weight loss, smoking cessation, and increased consumption of nutrient-dense foods like dark green leafy vegetables may decrease the risk of disease progression. For patients with intermediate-stage AMD, one proven prophylactic is micronutrient therapy. It was found that an oral supplement containing antioxidants and zinc can significantly reduce the risk of patients with moderate AMD from progressing to late-stage disease.[8] Supplements containing lutein and zeaxanthin may also help restore macular pigment and improve visual performance, even at the earliest stages of the disease. This is a particularly vulnerable cohort, and identifying and treating these patients before further progression is critical to preventing irreversible vision loss or blindness.

In addition to early diagnosis, increased awareness will be an important and complementary step for improving outcomes among at-risk and AMD patients. Ideally, public health legislation should prioritize the education of every individual over the age of 50 regarding the common symptoms associated with AMD, such as trouble seeing or driving at night. Additionally, emphasis on AMD should be brought to the attention of general practitioners, who can also assist in educating patients and referring them to a retina clinic for AMD testing based on risk factors and symptoms.

Conclusions

While ongoing efforts are being made to develop effective treatments for dry AMD and improve existing treatments for wet AMD, there are already abundant opportunities to improve the current status of AMD globally. Improving awareness of the condition and its symptoms, not only for the patients and their families, but for general practitioners as well, can help increase early AMD diagnoses and reduce unnecessary vision loss. These efforts could greatly improve patient outcomes with little to no additional expenditure and can be implemented immediately, simply by enhancing communication between doctors and patients.

Editor's Note: This article was submitted to PIE Magazine by Dr. Bandello after getting a copy of PIE issue 03 distributed at ESCRS 2017 in Lisbon, Portugal. We are [always] looking for eye docs who can contribute articles to PIE Magazine. If interested, send us an email at enquiry@ mediamice.com.

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About the Contributing Doctor

Dr. Francesco Bandello is a professor and chairman at the Department of Ophthalmology University Vita-Salute, Scientific Institute San Raffaele, Milan, Italy. He is the academic dean of "Corso di Laurea Specialistica/Magistrale in Medicina e Chirurgia" at the same university. Professor Bandello is past president of EURETINA, president of Academia Ophthalmologica Europea and vice-president of EuroLam. Prof. Bandello is editor-in-chief of the European Journal of Ophthalmology and former board member of the Club Jules Gonin and Macula Society. He is a member of the Executive Board of ESASO Foundation (European School for Advanced Studies in Ophthalmology), member of the Academia Ophthalmologica Internationalis and the Accademia Nazionale di Medicina. Prof. Bandello is co-author of 11 books and he serves as a peer reviewer for grant applications for the National Eye Institute (NEI). He has authored or co-authored 473 Pub-Med articles and has served as trained Principal Investigator in several clinical trials performed following ICH/GCP and mainly concerning retinal diseases. [Email: bandello.francesco@hsr.it]