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Age-Related Macular Degeneration: Current Status and Treatment

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Age-Related Macular Degeneration (ARMD) is the leading cause of irreversible vision loss over the age of 50. It affects about 15 million men and women in the United States with about 200,000 new cases diagnosed each year. About 1.7 million U.S. citizens have the advanced form of the disease, projected to grow to 3 million by 2020. About 200 million people are affected worldwide. While it does not usually cause total blindness, ARMD is the leading cause of functional or legal blindness. Risk factors include: female gender, white race, family history, obesity, hypertension, hyperlipidemia, and smoking.

"Dry" Versus "Wet" ARMD

Broadly speaking, there are two types of ARMD – non-exudative ARMD (also known as DRY or non-neovascular), and exudative ARMD (WET or neovascular). The non-exudative form accounts for 90% of all ARMD cases and is characterized by changes in the outer retina layers leading to atrophy and loss of the photoreceptor (rods and cones) function. Exudative ARMD is defined by the invasion into the retina of abnormal choroidal vessels (called choroidal neovascularization, or CNV) that results in leakage of serous fluid or hemorrhage which can be devastating to the photoreceptors. Even though only 10% of ARMD is exudative, these cases are responsible for the greatest visual disability- and thus economic burden- among all ocular diseases in developed countries. It is important to recognize that non-exudative diseases may undergo exudative conversion at any time, hence the importance of routine eye exams and patient education so that any vision change is detected as early as possible.

Symptoms

Patients with non-exudative ARMD may complain of gradual visual acuity loss or distorted vision (metamorphopsia), whereas patients with the exudative disease can have more acute onset of such complaints. Vision loss is painless and not associated with any systemic symptoms. Color vision may also be affected.

Diagnosis

The diagnosis of ARMD is made during a comprehensive eye exam, supported by imaging studies, while ruling out other causes of macular or retinal disease such as diabetic maculopathy, retinal vascular disease, and macular hole or pucker. The characteristic exam findings for non-exudative ARMD are drusen (pale yellow deposits under the retina) and pigmentary atrophy of the outer retina layer (Figure 1). Exudative ARMD eyes exhibit subretinal fluid, hard exudate, subretinal fibrosis, and/or hemorrhage secondary to choroidal neovascularization (Figure 2).

Confirmatory studies can be done in the office and include fundus photos, fluorescein angiograph, and optical coherence tomography (OCT). Fundus photos are especially useful in monitoring non-exudative ARMD, as the increase in the number and size of drusen can be very subtle and annual photos allow for side-by-side comparison. Fluorescein angiography is a series of photographs taken with special filters after the intravenous injection of fluorescein dye, which allows imaging of the retinal vasculature and the retinal layers. This imaging can help detect leakage otherwise not apparent on a fundus exam. OCT is a detailed high-resolution laser scan of the retina, showing drusen, atrophy of retinal layers, abnormal blood vessels, edema, hemorrhage and other abnormalities otherwise nearly impossible to discern. The OCT is essentially an "optical biopsy" of the retina and the choroid (Figure 5). These studies are useful for diagnosis, patient education, follow-up, and treatment guidance.

Treatment

Treatment differs greatly between non-exudative and exudative ARMD. Currently, there is no effective treatment for non-exudative ARMD, but fortunately most cases do not lead to severe visual loss. It is managed with periodic exams, self-monitoring by patients, antioxidant vitamin supplements (AREDS vitamins, which contain zinc, copper, vitamin C, vitamin E, lutein, and zeaxanthin), and low-vision aids when appropriate. A healthy diet, control of hypertension, smoking avoidance, and wearing sunglasses are recommended. Some evidence suggests a benefit from lenses blocking blue light that is emitted from smart devices and LED light bulbs. Patients are instructed to report new symptoms suggestive of exudative conversion.

Treatment of exudative ARMD is targeted at CNV to reverse retinal edema and hemorrhage. In the past, direct destruction of CNV by thermal laser was the only method. This process rarely improved vision and was associated with disease recurrences and scar formation that led to further vision loss. Another type of treatment called photodynamic therapy (PDT) involves intravenous injection of a photoactivated chemical dye, followed by laser activation of the dye to coagulate CNV. However, this treatment tends to stabilize but not reverse vision loss.

The mainstay of current treatment is an intraocular injection of anti-VEGF (vascular endothelial growth factor), which has been in widespread use since 2005. These biologic drugs work by either inhibiting VEGF receptors or by removing VEGF from the vitreal cavity. Treatment is given initially monthly and then at extended intervals depending on the patient's response. There are three anti-VEGF drugs currently in use – bevacizumab (Avastin®), ranibizumab (Lucentis®), and aflibercept (Eylea®). Bevacizumab was developed to treat colorectal cancer, but is specially formulated by compounding pharmacies in doses safe for the eye. Ranibizumab and aflibercept were designed specifically for ophthalmic uses, including ARMD, diabetic macular edema, and retinal edema associated with retinal vein occlusion. This new class of drugs has revolutionized the management, prognosis and visual outcomes for patients with exudative ARMD. Many patients are now able to regain lost vision, and almost all are stabilized. Once the diagnosis of exudative ARMD is made, anti-VEGF therapy can be given by a retina specialist in the office setting, with minimal ocular and systemic risks. Endophthalmitis is the main ocular complication which can result in blindness, but its incidence is about 1 in 5000.

Patient Counseling

ARMD patients are instructed to monitor their own disease with an Amsler Grid at home. This should be done at least once a week to detect any changes in vision or distortion. Changes should be reported to their Ophthalmologist so that the necessary treatment can be implemented quickly. With the advent of OCT technology, patients and family can now more easily understand the disease process of ARMD and appreciate the treatment impact. Patients who require anti-VEGF injections for exudative ARMD are educated about the need for frequent injections initially (i.e. every 4 weeks), but the interval between injections typically is extended to 6, 8, 10, 12 weeks, etc. once exudation is under control. Patients are reassured that while central vision may be affected, they will not lose all vision. Family members and caretakers are advised on how to assist their vision-impaired relatives. Consultation with a low vision specialist- usually an Optometrist or Vision Therapist- may be recommended so that the patient can learn to utilize low-vision aids, including illuminated magnifiers, special spectacles, closed circuit TV magnification, reading machines, large print books, large number telephones, etc. Because peripheral vision is not affected in ARMD, mobility is usually not an issue, in contrast to patients with advanced glaucoma or retinal degeneration.

On the Horizon

Imaging technologies are fast evolving: higher-definition OCT and OCT angiography are becoming commonplace. Even optometric practices are often equipped with basic OCT machines to help diagnose AMRD during routine eye exams. Future therapies for exudative ARMD include longer acting anti-VEGF drugs, an extraocular reservoir that allows anti-VEGF to enter into the eye without the need for repeat injections (thereby decreasing the risk of endophthalmitis and other complications), gene therapy that stimulates the retina to produce endogenous anti-VEGF, and viral vector delivery of genes for photoreceptor Rhodopsin production. For non-exudative ARMD and its advanced form (geographic atrophy), anti-complement therapy and stem cell transplants to regenerate photoreceptors are being studied.

Conclusion

ARMD is common and potentially blinding, but with proper diagnosis and timely treatment, it seldom has the same grim prognosis as it did two decades ago. When a patient complains of symptoms of painless central vision loss or appearance of wavy vision, they should be promptly referred to an Ophthalmologist for a thorough evaluation.

Recommended links for further reading and multimedia:

1. American Academy of Ophthalmology (AAO): https://www.aao.org/eye-health/diseases/amd-macular-degeneration
2. American Society of Retina Specialists (ASRS): https://www.asrs.org/patients/retinal-diseases/2/agerelated-macular-degeneration

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