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Age Related Macular Degeneration

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Abstract

This paper is a literature review on the subject Age-Related Macular Degeneration (AMD) with a focus on its etiology, pathophysiology, clinical features, diagnosis, treatment, and prevention. AMD is the leading cause of severe and irreversible central vision loss in in individuals over the age of 55. There are two subtypes of AMD referred to as dry and wet respectively. The etiology of this disease is multifactorial and complex, with no hallmark of disease definitively identified. The distinct pathophysiological features differing in dry and wet AMD are explored in this review as well as its diagnosis and treatment. This disease is primarily untreatable, other than stabilizing wet AMD. Although untreatable there are methods of slowing the progression of AMD. These methods are also explored in this review. The final portion of this paper features a “Patient Focus” section in which the disease is humanized via an interview with an Optometrist who regular treats patients with AMD.

Keywords

age related macular degeneration, etiology, pathophysiology, diagnosis, treatment, prevention

Disciplines

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Comments

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In the developed world, Age-Related Macular Degeneration (AMD) is the leading cause of severe and irreversible vision loss in individuals over the age of 55. This disease accounts for 6-9 % of legal blindness worldwide and is expected to affect over 288 million individuals by 2024 (Ambati and Fowler, 2012; Fleckenstein et al., 2021). There are two distinct types of AMD with the first being referred to as dry AMD and the second being wet AMD. Since this disease manifests in the macula, a part of the retina that is responsible for central vision, patients primarily experience loss in central vision due to macular thinning and warping as tissues in the macula age (Duker et al., 2015). Wet AMD is characterized by neovascularization and is often found to cause more severe damage and faster progression of blindness due to blood leakage as well as vessel expansion into the rods and cones of the retina (Ambati and Fowler, 2012). The earliest descriptions of this disease were not made until around 1850, and it was not until over 150 years later than a clearer concept was formulated. This disease, although well documented and studied over history, has a cause that is still not completely understood (de Jong, 2016).

Etiology

The etiology of AMD is multifactorial, complex, and consists of an interplay between age, genetic susceptibility, and environmental factors (Fleckenstein et al., 2021). Primary modifiable risk factors include smoking, improper diet, excessive alcohol intake, and cumulative UV light exposure (Mizra and Coombes, 2013; Fleckenstein et al., 2021). Non-modifiable risk factors include age, sex, race, genetic abnormalities, and the presence of other conditions such as hypertension, heart disease, and hyperopia. Caucasian females over the age of 50 with a history of hyperopia, hypertension, and family history of macular degeneration are at the greatest risk of developing this disease. These is no clear reason for the increased prevalence among Caucasian

females however the connection is observed. Individuals with cardiovascular/circulatory conditions are at higher risk of developing AMD because of changes in blood flow in the small vasculature in the eyes (Ambati and Fowler, 2012). Hyperopia, or farsightedness, is suspected to be related due to lower intensity of light forming the macular image, but this connection is not entirely understood (Mirza and Coombes, 2013; Ambati and Fowler, 2012). Each of the aforementioned risk factors are associated with AMD, however, they are only observed as implicated causes of the disease. No hallmark of disease progression has been identified (Ambati and Fowler, 2012; Fleckenstein et al., 2021).

Pathophysiology

In AMD, the relationship between tissues of the photoreceptors, retinal pigment epithelium, Bruch's membrane, and the choriocapillaris is lost within the macula, resulting in dysfunction and overall death of these components (Fleckenstein et al., 2021). In both dry and wet AMD histopathological changes consistent with the tissues aging leads to decreased macular elastic layer integrity and the development of drusen (Duker et al., 2015). The first clinically visible change in the ocular fundus caused by AMD is represented by the development of drusen, of which there two types, hard and soft. Histologically, both types are composed of excess minerals, lipids, and protein particles (Spindler et al., 2018). Hard drusen consist of hyaline material, in addition to the previous particles listed, and appear smaller but are often more numerous. Soft drusen are amorphous with indistinct edges, are larger than hard drusen, and pull on the retinal pigment epithelium leading to retinal atrophy, detachments, and neovascularization (Duker et al., 2015; Spindler et al., 2018). As previously stated, if neovascularization occurs the AMD is classified as wet. The formation of this vasculature is triggered by an overall decrease in perfusion of the macula either due to soft drusen pulling on tissues, or a change in systemic

blood pressure/flow caused by conditions like hypertension or atherosclerosis (Kodjikian, 2022; Fleckenstein et al., 2021).

Clinical Features and Diagnosis

The clinical features of this disease vary greatly based on a dry or wet AMD diagnosis. Patients with dry AMD often are asymptomatic, however common signs and symptoms of dry AMD include, but are not limited to, gradual worsening of central vision, metamorphopsia (slight distortion of straight lines), or the development of scotomas (dark patches in the central vision). Patients with wet AMD experience these signs and symptoms at an accelerated and more severe rate and experience rapid loss in central vision (Lim et al., 2012) Approximately 71% of individuals with a family history of AMD will develop the disease in adulthood (Fleckenstein et al., 2021). This genetic connection is suspected to be associated with abnormalities in chromosomes 1 and 10 however this has not been definitively observed. The development of AMD is also connected to abnormalities in the inflammatory response, immune response, lipid metabolism, protein transport, and cellular stress (Fleckenstein et al., 2021; Lim et al., 2012). Patients with a history of obesity, sleep problems, and insufficient exercise also have a greater susceptibility to AMD. Any history of smoking dramatically increases the risk of AMD and can increase the severity of the progression if smoking continues after diagnosis (Kodjikian, 2022).

Age Related Macular Degeneration is primarily diagnosed and monitored using different types of retinal imaging, with the most popular forms being fundus fluorescein angiography and optical coherence tomography (Lim et al., 2012). Both are beneficial imaging tools; however, fundus fluorescein angiography (FA) is considered the gold standard for diagnosis primarily because it can detect dynamic and convoluted patterns of blood flow in the macula (Gong et al., 2016). Although the gold standard, FA is considered an invasive and time-consuming procedure

in which fluorescein dye is injected intravenously as imaging is taken for ten minutes post-injection (Prall et al., 2022). Optical Coherence Tomography (OCT) is a non-invasive imaging test that is widely accessible in Optometric and Ophthalmologic offices. This software takes less than 5 minutes and creates a cross-sectional map of the macula (Spirn et al., 2015). The disadvantage to OCT is that it provides a less detailed image of the retinal vasculature and cannot clearly map the area of a hemorrhage as well as FA. The use of these procedures is often based on what the doctor has access to and what the patient can withstand (Gong et al., 2016).

Treatment

Unfortunately, AMD is a primarily untreatable disease with the only methods of treatment available existing to reduce wet AMD to a stable state. Two popular treatments include intravitreal anti-vascular endothelial growth factor therapy (anti-VEGF) and thermal laser therapy. Anti-VEGF is a revolutionized treatment of wet AMD and can eliminate leakage of fluid/blood in the macula and prevent or slow the growth of choroidal neovascularization (Holz et al., 2014). In this method of treatment anti-VEGF medications are injected to the sclera of the eye. These medications bind to and prevent the action of aptamers, types of protein molecules in the retina, which encourage abnormal neovascularization (Lazarus, 2020). Thermal laser therapy is also commonly used. This procedure involves targeted photocoagulation and tissue destruction directed towards centers of neovascularization in the macula. If used, this treatment is typically administered in conjuncture with rounds of anti-VEGF drugs. The disadvantage of this treatment is that the laser is not specific to the abnormal vessels and will also destroy healthy tissues of the macula resulting in areas of blindness or blurry vision (Duker et al., 2015; Fleckenstein et al, 2021).

Prevention

AMD cannot be prevented however its progression can be managed or slowed using nutraceuticals and lifestyle changes. The most popular nutraceuticals recommended by ocular specialist is the AREDS-2 vitamin (Lim et al., 2012). The AREDS-2 formulation contains a balanced mixture of antioxidants such as Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc, and Copper (Cabral de Guimaraes et al., 2021). Other important nutrients necessary for healthy eyes include B-carotene and Omega-3 (DHA and EPA) which are primarily suggested to be acquired via dietary modifications. Managing the intake of these micronutrients is crucial to maintaining a healthy retina and is directly associated with decreased drusen formation. It is suggested that the intake of these micronutrients is most beneficial to those with a family history of AMD as they can begin monitoring their supplementation early in their diagnosis (Kodjikian, 2022).

Other methods of slowing the progression of AMD include lifestyle modifications which minimize risk factors associated with aging. Smoking cessation is a necessary change for patients diagnosed as it is estimated that the risk of developing AMD is 2-3 times larger in smokers than non-smokers (Kodjikian, 2022). Modifications to activity levels are often suggested to reduce inflammation and excess body fat which put patients at a greater risk of developing circulatory issues linked to AMD (Duker et al., 2015). It is suggested that BMI values should remain within 18.5-24.9 and waist circumferences should be monitored. In addition, at least three hours of moderate- to low-intensity physical activity should be maintained per week. Sleep duration has also been directly associated with retinal health and it is suggested to sleep for 7-8 hours per night. These lifestyle modifications and vitamin supplementations can slow the progression of AMD (Duker et al., 2015).

Patient Focus – Healthcare Professional Interview

I conducted a phone interview with Dr. Kara Cook-Ritchey, an Optometrist at Huntingdon Vision Center in Huntingdon, Pennsylvania. Dr. Ritchey completed her undergraduate education at Bucknell University with a major in English and received her graduate degree at the Ohio State University School of Optometry. Huntingdon Vision Center sees patients from a wide range of backgrounds and degrees of ocular health, but one consistency in the practice is an inflow of patients with Age-Related Macular Degeneration (AMD). Dr. Ritchey suspects they have many patients with this diagnosis due to the older population of the area as well as because the practice is celebrating its 50th year of service to the community. Due to how long the practice has been open, some patients have been making appointments since it was opened by her father and are now entering their late 70s or 80s. Patients at this age are at an extremely high risk of developing AMD, if it has not developed already.

Since dry AMD is so common, OCTs are used regularly in patient examinations to assess macular health and track the progress of present drusen. Making this a "normal" test in the practice also helps with not worrying patients as much when assessing their macular health. If there are abnormalities, Ritchey stated that the first step to a diagnosis is to calmly explain what is going on to the patient and express that it is a normal part of the eye aging. She starts by showing the patient imaging of their own eye and compares it to her own, since she does not yet show signs of AMD. It is extremely important to use comparison and photos for patients so that they have a visual representation of what exactly is going on in their eye. Another key point Ritchey made was to not assume anyone's intelligence. Speaking at a level that is informative without using "Optometrist jargon" can make the patient feel more comfortable asking questions as well as feel more involved in the diagnosis.

The next most important thing is to stress to the patient that they are not going blind. Their central vision will degrade however the progression will be slow and they will not lose their sight all at once. The psychological repercussions of telling someone that they are going blind can be extreme and for a slow developing disease such as AMD it is important to keep the patient informed of their vision loss but not automatically jump to worse case-scenario. If the diagnosis is wet AMD rather than dry, then an automatic referral to an Ophthalmologist would need to be made and the conversation will be a little heavier in content since the neovascularization has a large chance of causing extensive damage if left untreated. Dr. Ritchey stated that years ago wet AMD may not have been an immediate referral but now that anti-VEGF injections are widely used, getting the patient in as soon as possible will yield the best results. This is also something that Dr. Ritchey will mention to patients. Although the thought of ocular injections is terrifying, the benefits heavily outweigh the costs.

The most difficult parts of treating AMD for Dr. Ritchey are seeing her patients slowly lose the ability to do the things that really bring them joy and lose their ability recognize faces. In these cases, there is not much that she as a physician can do other than suggest lifestyle changes and vitamin supplementation. Even so, some patients with severe central vision loss will still want to come to appointments to see if treatments have changed. In these appointments they express their hopes they may be able to see their grandchildren, read a book, or even cook again. I can imagine myself in their shoes slowly losing the ability to make out the details of my loved ones faces and not being able to do some of my hobbies like knitting, reading, and painting. As a student wanting to pursue a career in Optometry, this empathy and understanding will help me to interact with patients on a more personal level. Trying to understand what the thought-process of

a patient during their diagnosis will help me empathize and communicate with them better during throughout their care.

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