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Arup Saha

Assistant Professor,
Department of Optometry,
Swami Vivekananda
University, Barrackpore, West
Bengal, India

Bulti Saha Debnath

Consultant Optometrist and
Vision Therapist, Nabajatak
Child Development Centre, BC
Block, Salt Lake Sector -1,
Kolkata, West Bengal, India

Corresponding Author:

Arup Saha

Assistant Professor,
Department of Optometry,
Swami Vivekananda
University, Barrackpore, West
Bengal, India

Macular degenerative changes and observation in the aging population

Arup Saha and Bulti Saha Debnath

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Abstract

The objective of our study was to evaluate the current level of knowledge about the pathogenesis, ocular symptoms, diagnosis, and ancillary testing of age-related macular degeneration.

Methodology: relevant research on age-related macular degeneration published up to 2014 is used for systematic reviews.

Age-related Macular Degeneration (AMD) is a prevalent macular disorder mostly affecting the elderly in the Western world. Geographic atrophy, choroidal neovascularization, and the formation of drusen in the macula are characteristics that set it apart (CNV).

The macula is commonly affected by age-related macular degeneration, a prevalent chronic degenerative illness that mostly affects the elderly. Loss of central vision is caused by anomalies in the photoreceptor, retinal pigment epithelium, choroidal complex, Bruch's membrane, and photoreceptor. Geographic atrophy and/or neovascularization are frequently the result of these anomalies.

Advanced AMD can be divided into two primary categories: wet and dry. While dry AMD accounts for most diagnosed instances, wet AMD causes the bulk of severe visual loss and often develops over weeks to months. While neovascularization has been demonstrated to be the most common cause of severe vision loss, geographic atrophy, the most advanced form of dry AMD, can also cause a significant loss of vision.

Keywords: Geographic atrophy, choroidal blood vessel changes, retinal neovascularization, age-related macular degeneration

Introduction

The macula is commonly affected by age-related macular degeneration, a prevalent chronic degenerative illness that mostly affects the elderly. Loss of central vision is caused by anomalies in the photoreceptor, retinal pigment epithelium, choroidal complex, Bruch's membrane, and photoreceptor. Geographic atrophy and/or neovascularization are typically the result of these anomalies. Advanced AMD may be divided into two primary categories: wet and dry. While dry AMD accounts for most identified instances, wet AMD causes the bulk of severe visual loss and often develops over weeks to months. While neovascularization has been demonstrated to be the most common cause of severe vision loss, geographic atrophy, the most advanced type of dry AMD, can also cause a significant loss of vision.

Epidemiology

AMD ranks third among the world's main causes of blindness, after glaucoma and cataracts. Most of the people affected live in developed countries. In general, advanced AMD is rare in those under 55 and more prevalent in those 75 years of age and above. The frequency of neovascular AMD and geographic atrophy appears to vary globally across different ethnic and cultural groups. The incidence of advanced AMD increases every ten years beyond the age of fifty and peaks at eighty.

Risk factors

AMD In general, risk factors may be divided into two categories: environmental and personal (Such as smoking, sun exposure, and dietary intake of fish, micronutrients, and alcohol).

Personal factors can be further subdivided into the following categories: sociodemographic (Such as age, sex, race/ethnicity, heredity, and socioeconomic status); ocular (Such as iris color, macular pigment optical density, cataract and its surgery, refractive error, and cup/disc ratio); and systemic (Such as cardiovascular disease and its risk factors, reproductive and related factors, dermal elastotic degeneration, and antioxidant enzymes).

Factors that put choroidal neovascularization development at risk. The presence of five or more drusen, smoking, hyperpigmentation, systemic hypertension, and one or more large drusen (Larger than 63 μm in linear dimension) are all present.

Pathogenesis

Currently being employed to provide information on the origin of AMD include molecular dissection of histopathologic specimens and genetic linkage analysis using different populations. Early in the disease phase, lipids are accumulated in Bruch's membrane, most likely due to the RPE's incapacity to manage cellular debris associated with outer segment turnover. Only later in the course of the illness do drusen become apparent. The onset of drusen is the first evident clinical sign of AMD.

Lipids, complement factors, amyloid, and other biological components are detected by Drusen analysis^[1,2].

The development of drusen is preceded or coincident with the thickening of the collagenous layers of the Bruch's membrane, the calcification of the membrane, the degradation of collagen and elastin within the membrane, the accumulation of lipids and exogenous proteins, and the elevation of advanced glycation end products^[3]. These changes may function as a hydrophobic barrier, preventing fluid and nutrients from moving between the outer retina and choroid, leading to relative ischemia. Bruch's membrane breaks may then cause the choriocapillaris to develop and become neovascularized^[4].

Ocular manifestation

Dry age-related macular degeneration

Drusen is one of the early signs of AMD. Typical drusen in a clinical context appear as deep retinal foci with yellowish-white excrescences. Drusen deposits usually differ substantially in quantity, form, location, and size. They are located underneath Bruch's membrane and the retinal pigment epithelium. In terms of size, most drusen fall either the soft or hard categories, ranging from 20 to 100 μm .

In certain populations, hard drusen are immediately identifiable as round, distinct yellow-white spots. They are neither age linked, nor do they have an increased risk of developing neovascularization^[5,6].

Conversely, soft drusen are weakly defined, with a maximum size of 63 μm , and have non-discrete borders. Numerous research and trials have shown that large, soft, confluent drusen are age-related and associated with an increased risk of developing progressive AMD with neovascularization^[6,7].

Geographic atrophy is easily recognized clinically because it is clearly distinguishable as a well-defined area of thinner retina in comparison to the surrounding retina and has a color shift that increases the visibility of the underlying choroidal veins. There may be pigmentary changes, either hypo- or hyperpigmentation, in the area around the macular atrophy.

If the foveal center is intact, good visual acuity may be preserved, but a small central visual field may still cause reading vision impairment^[8].

Wet (Neovascular) age-related macular degeneration

One attribute of wet AMD is neovascularization inside the macula.

The formation of new blood vessels from the choriocapillaris into the sub-pigment epithelial region through a breach in the outer layer of Bruch's membrane is known as choroidal neovascularization (CNV).

Clinical indicators of neovascular AMD include subretinal fluid, intraretinal fluid, retinal, subretinal, or sub-RPE hemorrhage, lipid exudates, gray or yellow-green discoloration or plaque-like membrane, RPE separation, and RPE rupture.

Advanced disease-stage neovascularization results in an atrophic or fibrovascular macular scar known as a disciform scar, which irreversibly impairs central vision^[9-11].

Pigment epithelial detachment: The accumulation of drusen underneath the retinal pigment epithelium (RPE), hemorrhage, fibrovascular tissue, or serous fluid can all result in PEDs. Serous PED presents as a dome-shaped RPE detachment that shows increasing pooling in a specific region along with intense, diffuse hyperfluorescence^[12]. Hemorrhagic PED is characterized by a dark elevation of the RPE with suppressed fluorescence throughout all angiography stages, which is caused by underlying blood^[13].

Diagnosis and ancillary testing

A clinical examination is usually adequate to confirm a diagnosis of AMD, while additional techniques like as fundus autofluorescence, optical coherence tomography, fluorescein angiography, and indocyanine green angiography are best used to determine mild macular abnormalities.

Optical coherence tomography may be a useful additional diagnostic at any stage of AMD. In patients with dry AMD, high-quality B-scans can be performed to assess the ultra-structure of drusen and examine surrounding retinal layers that may be impacted by the disease process.

OCT can track the development of early AMD into more severe types, such as geographic atrophy. Some characteristics of wet AMD, such as the presence of intraretinal or subretinal fluid and retinal PEDs (which may be categorized as serous, fibrovascular, and hemorrhagic PEDs), can be detected using high quality B-scans.

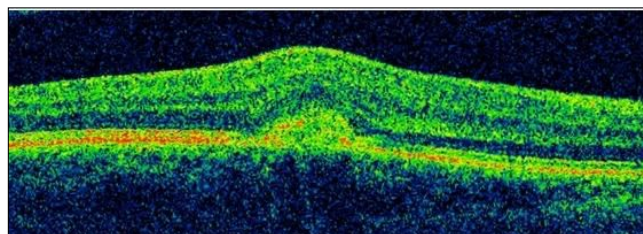


Fig 1: The figure shows an optical coherence tomography (OCT) image of the retina, displaying its cross-sectional layers with a central elevation

Detachment of the pigment epithelium

Fundus autofluorescence is one imaging method that can demonstrate the morphological changes caused by

lipofuscin metabolism. Geographic atrophy areas exhibit extremely low to extinguished fluorescence signals (black) due to the loss of lipofuscin and RPE. This results in a region where the atrophy and perilesional retina transition to a high contrast area.

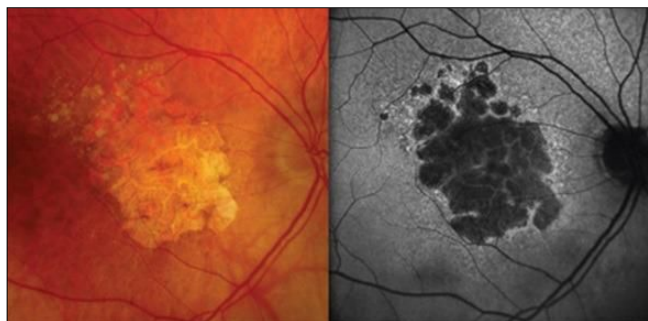


Fig 2: The figure shows a color fundus image (left) and a fundus autofluorescence image (right) depicting retinal abnormalities with central geographic atrophy

Fundus autofluorescence - geographic atrophy

Fluorescein angiography is commonly employed to verify the existence of neovascularization and to ascertain the features of the lesion, including the location and makeup of the neovascularization. The fluorescence angiographic patterns allow for the classification of the neovascular lesion as either classic or occult. Bright, uniform, early hyperfluorescence with late-phase leaking and blurring of the lesion margins are characteristics of classic CNV.

Occult CNV is differentiated by fibrovascular PED or late leaking from an unknown cause using angiography. An region of irregularly elevated RPE, which is neither as bright nor as well-defined as normal CNV, is the hallmark of fibrovascular PED. Midphase angiography may show stippled hyperfluorescence, while late-phase angiography may show leakage or staining [13].

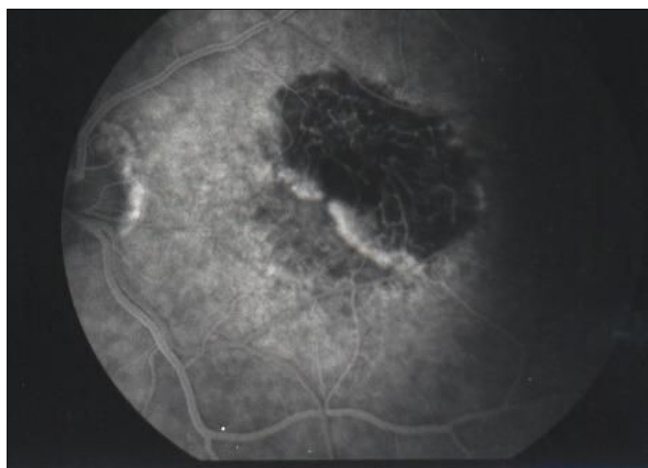


Fig 3: The figure shows a Fundus Fluorescein Angiography (FFA) image highlighting an area of hyperfluorescence and hypofluorescence, likely indicating retinal pathology

Classic CNV

The term "classical Choroidal Neovascularization" (CNV) describes the aberrant development of new blood vessels that extend into the subretinal region and originate from the choroid, the vascular layer of the eye. The most typical association between this disorder and Age-related Macular Degeneration (AMD) is with the "wet" type of the disease.

Underneath the retina, fluid, blood, and lipid exudates build up as a result of the fragility and leakiness of the nascent capillaries. If treatment is not received, this may lead to a severe and rapid loss of eyesight.

Important Features of Traditional CNV

- 1. Location:** The neovascular tissue extends into the subretinal space or subretinal pigment epithelium (RPE) after emerging from the choroid and passing through Bruch's membrane.
- 2. Appearance:** Due to dye leaking from the neovascular membrane, classic CNV often exhibits early hyperfluorescence on fluorescein angiography. Later phases are characterized by increased hyperfluorescence and leaking, which sharply define the boundaries of the CNV.
- 3. Symptoms:** Blurred vision: A progressive loss of central vision is frequently one of the early signs.
 - **Metamorphopsia:** This condition causes wavy lines to appear in straight lines and other visual abnormalities.
 - **Scotomas:** Blind areas might exist inside the range of vision.
- 4. Prognosis**
 - **Optical Coherence Tomography (OCT):** Offers precise cross-sectional pictures of the retina that highlight fluid buildup, thickening of the retina, or disturbance of the healthy layers of the retina.
 - **Fluorescein Angiography (FA):** Follows the passage of fluorescein dye through the retinal and choroidal circulation to help visualize blood vessels that are leaking.
 - **Indocyanine Green Angiography (ICGA):** Can be used in conjunction with FA to help see deeper choroidal veins.
- 5. Therapy:** Anti-VEGF Therapy: Intravitreal injections of anti-vascular endothelial growth factor (VEGF) medicines, such as ranibizumab, aflibercept, or bevacizumab, are the cornerstone of therapy. These medications serve to stabilize or enhance eyesight by reducing leakage and inhibiting the formation of new blood vessels.
 - **Photodynamic Therapy (PDT):** Due to the effectiveness of anti-VEGF medicines, PDT is currently used less frequently. In PDT, aberrant blood vessels are destroyed by laser activation after an intravenous injection of a photosensitizing dye.
 - **Laser photocoagulation:** Due to its risk of harming the surrounding healthy retinal tissue, laser photocoagulation, formerly a widespread therapy, is now hardly utilized.

Outlook

Variable: The degree of neovascularization and the promptness of therapy determine the prognosis for individuals with typical CNV. In many situations, anti-VEGF medication used early on can stabilize or even enhance eyesight.

In summary

When it comes to conditions like wet AMD, classic CNV is a crucial stage when vision preservation requires quick action. The therapy of this problem has greatly improved with the introduction of anti-VEGF medicines and advances

in imaging tools, providing afflicted individuals with hope for improved visual results.

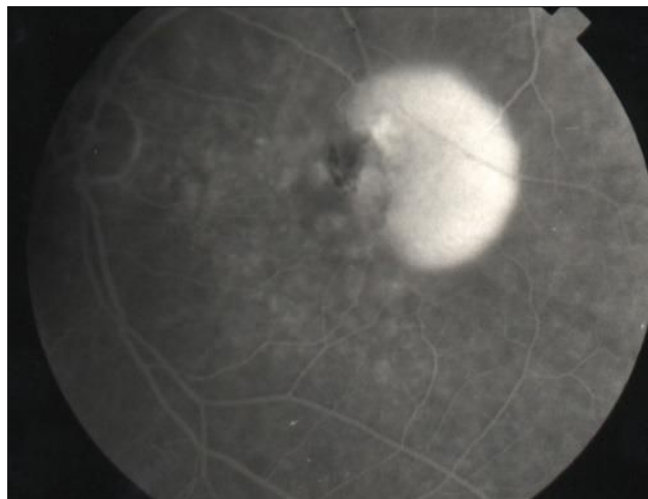


Fig 4: fluorescein angiography image of the retina, highlighting a focal point of hyperfluorescence indicative of a possible retinal condition

Unknown CNV

Indocyanine green angiography was utilized for the diagnosis and treatment of patients with AMD. Because of the characteristics of the dye, this angiography technique was able to characterize the choroidal circulation more precisely than fluorescein angiography.

In the following situations, indocyanine green angiography is highly beneficial

- Poorly defined or ambiguous CNV; • CNV linked to fluid above the exudate or hemorrhage
 - Differentiating between the vascularized and serous sections of fibrovascular PED
- Indocyanine green angiography is very useful in following circumstances:
- Distinguishing between vascularized and serous regions of a fibrovascular PED;
 - CNV associated with exudate or hemorrhage fluid above ^[14].

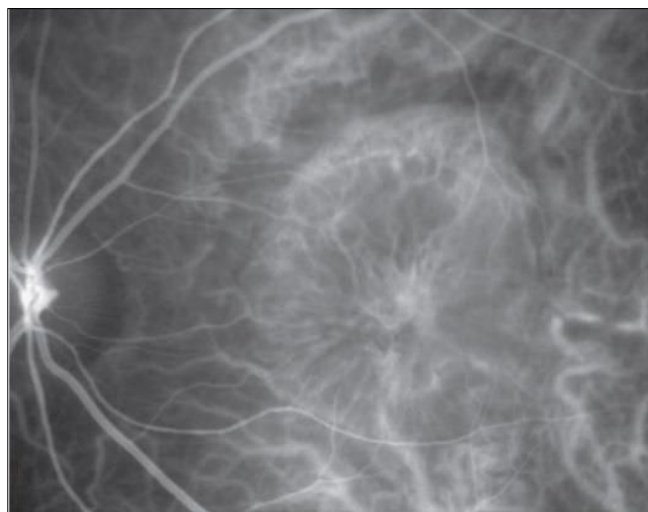


Fig 5: fluorescein angiography image showing retinal vascular leakage and possibly indicative of a macular or retinal condition

Typical neovascularization of the choroids. Indocyanine green angiography in its early phase

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