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Opinion Article

Macular Degeneration and Chronically Elevated Cortisol Levels. A Clinical Case

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Abstract

Elevated maternal cortisol levels during pregnancy have been related to possible effects on infant ocular development. Studies suggest that cortisol, the classical stress hormone, can affect the development of the eye and visual system, influencing so much its structure as its function. While increased cortisol levels can be harmful, advised levels are necessary for normal development, especially in the third trimester of pregnancy.

The remission and healing of age-related macular degeneration is unusual. This is even after being treated with intraocular injections in both eyes for 10 years in the left eye and 5 years in the right eye. Treatment had to be interrupted due to the COVID-19 pandemic in 2020-2023. The patient completely forgot about the problem, and when he went to the ophthalmologist to test his visual acuity, he found scarring in the left eye and inactive macular degeneration in the right eye. Possible benefit of rest in this condition.

Keywords: Cortisol; Dry; Humid; Macular Degermation; Retina; Stress

Abbreviations

OCT: Ocular Coherence Tomography

ARMD: Age Related Macular Degeneration

Introduction

The average incidence of dry macular degeneration (MD) in Caucasians over 65 years of age is 9%. Approximately 10% of those with dry MD develop the wet form. Dry or non-neovacular MD typically presents first, but wet or neovascular MD may arise first. The overall prevalence of age-related macular degeneration (AMD) is 1% in people aged 65 to 74, 5% in the 75 to 84 age group, and 13% in those over 85. When reading ability is affected, job or driver's license loss occurs, faces are incapable to recognize, and daily activities are difficult to realize, it's moment to consider whether central vision is impaired by wet AMD. Wet AMD is the least common but most serious form of AMD and one of the main causes of blindness in the general population.

AMD is the most common cause of blindness in developed countries, especially in people over 60 years of age. It accounts for 8.7% of all types of blindness worldwide. The disease is estimated to affect approximately 196 million people by 2020 and 288 million by 2040. In 2015, AMD was the fourth most common cause of blindness worldwide and the third most common cause of moderate to severe vision loss.

Macular degeneration changes affect the fovea, the central part of the retina. Then, central vision is affected, causing difficulty reading, writing, driving, walking, dressing, eating, bathing, etc.

Concerns about personal or family finances and the inability to live independently can cause stress, depression, and anxiety. When a person is diagnosed with AMD, the feeling of uncertainty transforms into a new and unexpected worry. There is also concern about how quickly the disease will progress and what limiting impact it will have on daily activities. The future becomes uncertain, and the ability to enjoy the present begins to disappear [1].

Etiology and Pathophysiology

In this disease, lipofuscin accumulates in the retinal pigment epithelium, which disrupts the metabolism of degraded photoreceptors. This leads to the accumulation of deposits (drusen) beneath the retinal pigment epithelium.

Age-related macular degeneration is classified into two clinical variations: dry or non-neovascular, and humid or neovascular. Vision loss is gradual if it occurs in the early or intermediate dry stage of AMD. Atrophy of the retinal pigment epithelium occurs in the advanced stage of the disease, known as geographic atrophy. Geographic atrophy affecting the center of the macula causes important visual loss. Geographic atrophy is known to increase over time and tends to occur bilaterally. People with unilateral geographic atrophy are also at risk of developing neovascular or exudative AMD in the second eye. The retinal pigment epithelium and photoreceptors overlying the drusen area undergo progressive degeneration.

Neovascular or humid AMD is characterized by a choroidal neovascular membrane and features such as retinal pigment epithelial detachment, retinal pigment epithelial tears, or disconformed scarring.

Symptoms observed by patients include blurred vision and distortion, especially in near vision. Other symptoms include decreased vision, micropsia, or scotomas. Photophobia, also known as light

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sensitivity, is an abnormal intolerance to light that causes discomfort or pain in the eyes when exposed to sunlight or artificial light. It is not a fear of light, but rather an eye sensitivity that causes discomfort or even pain in bright light.

Several risk factors have been identified associated with this disease. These factors can be social, lifestyle-related, cardiovascular, hormonal and reproductive, inflammatory, genetic and ocular. Social factors include age, sex, race and socioeconomic status. Several studies have shown an increase in the prevalence and progression of AMD with age. Both early and late AMD are known to be common in the Caucasian population, compared to the Black population and other communities [2,3].

Symptoms of Visual Stress

Various common lifestyle factors and activities can induce stress, such as long work hours and constant use of digital technology. With today's technology, it's difficult to avoid the need to use your eyes more frequently and for longer periods. Common symptoms of eye stress include: Seeing stars, blurs, flashes, shadows, halos or fog; double, tunnel, or narrow vision; darkened or illuminated vision; unusual visual pulsation; visual distortions; eye muscle pain; eye strain; uncontrolled sleepiness.

Furthermore, stress-related cortisol fluctuations can disrupt blood flow to the eyes, which could contribute to conditions such as stress-related macular degeneration. Many people are unaware that stress can affect their vision. It's important to emphasize that the main aspect to consider is when the entire body is chronically stressed, which affects vision, and even worse when chronic eye stress in particular is added [4].

Retina

The retina begins to differentiate in the early stages of embryogenesis. From 26 to 33 days of gestation, three to four rows of cells are initially observed, and between 32 and 33 days, five to six rows line the inner layer of the optic cup. Maturation and myelination of the retinal pigment epithelium begins later, at the site of the presumptive macula, and continues peripherally. The development and differentiation of the retinal nerve layer takes place until the eighth month of gestation, when the eye becomes sensitive to light and the axons of retinal neurons extend to the brain, forming the optic nerve. Myelination of the optic nerve occurs between the fifth and eighth month of gestation and progresses from the geniculate bodies to the eyeball.

The retina is the neurosensory component of the eye that sends light signals to the brain for visual recognition. The neural retina is made up of different types of cells—such as photoreceptors—that convert captured photons into a nerve signal that the brain interprets as vision—a phenomenon known as phototransduction—and which, together with glial cells, serve the function of maintaining the retinal environment in optimal functional conditions. Retinal capillaries maintain retinal tissue homeostasis in a steady state, promoting angiogenesis and regeneration during tissue repair [5,6].

Prenatal, Natal and Postnatal Stress

Prenatal stress can be intense (panic about an unwanted pregnancy or a baby being born sick), moderate (common in young women and single mothers), or mild (almost every pregnancy). All three can have adverse effects on both the pregnancy and the offspring. The main psychosocial stressors are financial hardship, unemployment, inadequate housing, aggressive neighborhoods, and increasing domestic violence. While, psychosocial stress refers to unexpected social events such as a car crash, an earthquake, or a flood; unexpected adultery; the burden of caring for children; insufficient nutrition; smoking; lack of sleep; emotional instability due to anxiety and depression; job loss or divorce due to pregnancy; and newborn illnesses due to inadequate or absent pediatric care. All of these prenatal, natal, and postnatal stressors affect the course of the pregnancy and the development of the unborn child [7-9].

Stress, Inflammation and AMD

Stress can trigger the release of cortisol, a stress hormone, which can contribute to inflammation. AMD is an inflammatory disease, and increased inflammation can accelerate its progression. Stress can affect blood circulation, and decreased circulation can disrupt retinal health and potentially contribute to AMD. Preexisting stress can further contribute to making impaired vision an even greater challenge. However, stress is a part of life and affects the body in various ways. For example, it can affect vision in one or both eyes, permanently or intermittently, such as dry eyes, blurred vision, or double vision.

The body naturally responds to any threat to its normal state. This can be physical, drug-induced, emotional, mental, visual, or a combination of all of these. When stress arises from an external threat, the pupil dilates, allowing lighter into the eye to locate the potential threat. Added to this is the release of adrenaline and cortisol, which puts more pressure on the eyes [10].

Cortisol, the Eyes and Stress

Stress comes in many forms, and its effects can manifest both physically and mentally. When the body is under stress, it releases a hormone called cortisol, which increases heart rate, breathing, muscle tension, blood pressure, and blood glucose. Excess cortisol in the body affects different parts of the body. For example, it disrupts blood flow from the eyes to the brain, which can lead to stress-related macular degeneration. This eye condition causes blurred vision or blind spots in the visual field and often affects older adults.

Cortisol is a very potent hormone, invariably linked to stress, and is the first hormone linked to vision problems. The body gradually releases it in response to stress and can increase heart rate, breathing, blood pressure, and muscle tension. Cortisol can also temporarily regulate the reproductive and digestive systems during periods of intense stress. Lack of oxygen to retinal cells is very risky as it can lead to cell death. Therefore, in times of intense stress, relaxation or breathing exercises, for example, are recommended.

Elevated cortisol levels, often associated with stress, can negatively affect eye health and contribute to the development or worsening of various eye diseases. Additionally, stress-related cortisol fluctuations can disrupt ocular blood flow, which may contribute to conditions such as stress-related macular degeneration, common in people over 60 [11,12].

Brief Clinical History

The 21-year-old surrogate mother married while pregnant with a partner other than her husband. Upon learning of this situation, her husband responded with intense verbal, physical, and psychological domestic violence. Her first illegitimate child was born, who was also

rejected and harassed by the husband and stepfather. During a second pregnancy, the husband's constant hostility continued, causing the surrogate mother constant anxiety with alternating bouts of depression, in addition to a state of intense and permanent stress. With physical symptoms such as headaches, fatigue, difficulty sleeping, frequent nightmares, decreased appetite, and, despite the pregnancy, weight loss. Emotionally, she was irritable, anxious, desperate, and confused. Cognitively, she had difficulty concentrating or memorizing, was distracted, and often forgot everything.

The husband was always harsh in his dealings and a tyrant as a husband and father, becoming intolerant and aggressive at the slightest pretext. Ultimately, she was frivolous and ignorant, and she perceived herself as pretty; he was vain, and he perceived himself as short and ugly.

Effects of Intense Maternal Stress on Her Legitimate Son

Her second son was born eight months old, weighing 2.250 kilograms, with difficulty suckling at the breast and frequent fever due to respiratory symptoms or diarrhea. This led the father to declare that "this child will not wake up." He began to babble after the age of 2.5 and showed the same difficulty walking, to the point that his paternal grandmother used to take him to the bank of a nearby river to massage his legs with the warm sand. To treat him, his father decided to move the family to a larger city in search of more effective medical care. The boy's respiratory problems only resolved after he underwent a tonsillectomy.

He always had attention deficit disorder and difficulty socializing. The rest of the family considered this son to be the father's favorite. He always led a life with an irritable tendency toward isolation. However, since childhood, he has been a very good observer of his surroundings and natural events. He exhibited a peculiar indifference or disinterest toward minors, both boys and girls. He had little or no interest in pets. Although his parents didn't expect him to take an interest in academic pursuits, he steadily advanced through the academic levels until, unexpectedly, he earned a bachelor's degree, a specialty degree, and a master's degree.

He acknowledges that he always retains the feeling that his professional achievements have been unexpected, despite the difficulty of being consistent and concentrating. He's always rushing to get things done; nothing can wait until tomorrow or later. Everything was for yesterday. His body learned to produce cortisol at the slightest stressful provocation. He's always been stressed, likely generating excessive amounts of cortisol. High levels were already circulating in his nascent circulatory system during gestation and have continued throughout his life, primarily since adulthood. During his undergraduate studies, his stress level increased and never decreased in intensity.

The left eye had always shown particular susceptibility to temperature, with reddening of the sclera upon transition from room temperature to a cold environment. At age 55, she suffered a spontaneous right retinal tear measuring ≈100 microns in length in the upper medial region of the eye, which was treated with a circle of ten laser beam pulses. At age 68, he was diagnosed with wet AMD in the left eye, which was treated with 25 intraocular injections. At the same time, he was diagnosed with dry AMD in the right eye, which years later became wet and was treated with 10 intraocular injections.

When the COVID-19 pandemic hit in 2020-2023, he had to self-isolate and completely forgot about her eye conditions. Until recently, when he noticed a decrease in visual acuity, he returned to the ophthalmologist and found the AMD in her right eye inactive and the AMD in her left eye healed.

What happened during that 2 to 3-year period when he didn't receive intraocular injections and yet the AMD in both eyes was controlled or healed? The noticeable decrease in activity and the enforced rest for several years were surely surprising and greatly beneficial.

Effects of Intense Maternal Stress on the Illegitimate Child

This illegitimate son had a stormy and disastrous existence. He was constantly rejected and harassed by his stepfather. He had convergent strabismus in his right eye and chronic overweight since childhood. As a sociopath, he engaged in aggressive gang activities in the inner city, allowing himself to be influenced by the most psychopathic and criminal gangs. Although he was intelligent, he dropped out of school early. However, when he was already unstable, thanks to the support of his legitimate son, he returned to school, finished his bachelor's degree, and pursued postgraduate studies abroad. He never got along with his legitimate brother, with whom he constantly competed. He was also unable to practice his profession profitably, he started a family that never stabilized, and he ended up abroad where he was used as merchandise so that a second wife could trick him, get him a life insurance policy in her favor as the beneficiary, then she poisoned him, he died and she herself collected the insurance.

Common occurrences in that country, with no one addressing these crimes—except on very rare occasions. Thus ended the tragic story of someone who should never have been born.

Elevated Cortisol Levels during Pregnancy

High cortisol levels during pregnancy, often a result of stress, increase the risk of premature birth, low birth weight, and potential developmental problems. These include delayed cognitive development, behavioral problems such as attention deficit hyperactivity disorder, and even mental disorders later in life; immune system problems that increase vulnerability to infections, for example; and, of course, more than 40, 50, or 60 years later, difficulty managing the constant and/or increasing stress that the person suffers.

High cortisol levels during sensitive periods of embryonic development appear to be neurotoxic, leading to uncontrolled responses to stress, poor cognitive performance, and alterations in brain development, particularly in the underdevelopment of hippocampal volume. It is also often accompanied by poorly developed lungs and emotional problems in childhood. Elevated maternal prenatal cortisol levels during the third trimester have been shown to be associated with delays in mental development at 3 months and in motor development at 3 and 8 months of age [13-17].

Conclusion

- To protect vision, it is important to understand the relationship between elevated cortisol levels from pregnancy and almost permanent levels after birth, as well as intense chronic stress and visual function.
- Wet ADM is the least common but most serious form of ADM and one of the leading causes of blindness in the general population.

- Dry or non-neovacular AMD typically presents first, but wet or neovascular AMD can also present early.
- The average incidence of dry AMD in Caucasians over 65 is 9%. Approximately 10% of those with dry AMD develop the more severe wet AMD.
- The marked decrease in activity, coupled with the mandatory rest for several years due to the COVID-19 pandemic 2020-2023, was likely both surprising and beneficial.
- People over 50 years of age should undergo an eye evaluation by an ophthalmologist to rule out the presence of age-related macular degeneration. Physicians should also recommend an eye exam for their older patients. This is especially important for recognizing patients with early AMD, as these patients are often asymptomatic.
- Regarding visual function, the patient can only read with his right eye and with prescription lenses. He cannot read with his left eye. Macro vision is normal in both eyes (80%) with prescription lenses for each eye.
- As a result of the latest series of consultations with the medical specialist, four intraocular injections were scheduled for the right eye, which stabilized it with modest improvement. The scar in the left eye remains unchanged. The doctor recommended ophthalmic checkups with OCT every two, three, or six months, depending on the stability of the AMD in both eyes.

Patient Consent

Granted

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Conflicts of Interest

None

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