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Review article

The effect of Rheumatoid Arthritis on Eye Health

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Abstract

An autoimmune disease called rheumatoid arthritis (RA) mostly affects the joints, but it can also damage the skin, eyes, and lungs. RA patients can have dry, irritated, or gritty eyes. When the body's immune system unintentionally targets healthy tissues, RA develops. It primarily targets the collagen-containing connective tissues in joints. Collagen is also present in certain areas of the eye, including the cornea, which is the transparent tissue in front of the eye, and the sclera, which is the white component of the eye. These tissues can also occasionally be impacted by RA. Certain drugs that physicians take to treat RA may potentially aggravate eye disorders. This post will examine the symptoms and illnesses that RA may produce, how it affects the eyes, and how medical professionals handle them.

Keywords: Rheumatoid arthritis, RA, eye health, gritty eyes.

Introduction

Though there are several rheumatic conditions, rheumatoid arthritis is arguably the most well-known. Rheumatoid arthritis is an inflammatory and autoimmune disease that causes several persistently inflamed joints. It is caused by the immune system mistakenly attacking healthy cells in its body, which results in inflammation (painful swelling) in the affected areas of the body.

The good news is that many therapies can reduce discomfort and possibly halt the disease's progression.

It is possible to stop joint deterioration by receiving early diagnosis and therapy.

Definition of Rheumatoid arthritis

The most prevalent autoimmune condition linked to dry eye syndrome is rheumatoid arthritis (RA), which is also linked to conditions that might cause blindness in the eyes, including scleritis, corneal burns, and peripheral ulcerative keratitis. In people with RA, tissue damage on the surface of the eyes is caused by the immune system. Research on people with dry eye has linked the pathophysiology of the condition to abnormalities in innate immunity (Toll-like receptors, S100A, and resident antigen-presenting cells), cytokines, chemokines, and T helper (TH)-cell subsets (TH1 and TH17). Certain characteristics are likely significant in RA-related dry eye, which can manifest independently of articular illness and is more severe clinically than idiopathic dry eye. Figure (1) illustrates the distinction between hands that are normal and aberrant, because of the impacts of autoimmune disease on the body (1).

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Figure (1): Difference between normal and Rheumatoid arthritis cases (6).

The immune components present on the ocular surface might be impacted by the overall immunological environment within the body. The therapy options for ocular inflammation in rheumatoid arthritis (RA) vary depending on the severity of the condition. These treatment modalities may include ciclosporin, topical corticosteroids, tacrolimus, autologous serum, and systemic immunosuppression. The treatment of tissue damage involves the inhibition of matrix metalloproteinases. Enhanced comprehension of ocular surface immunology can contribute to the advancement of potential therapeutic approaches, such as the selective targeting of T-cell subsets, modulation of B-cell signaling, or manipulation of cytokine activity (2).

Epidemiology of rheumatoid arthritis

The present study aims to examine the contemporary patterns of mortality in individuals diagnosed with rheumatoid arthritis. Building upon the preceding data, additional research conducted up until 2008 has indicated that there is no statistically significant decrease in mortality rates among various groups affected by rheumatoid arthritis (RA) around the globe (3). Several publications have documented a rise in mortality attributable to rheumatoid arthritis (RA) among older individuals, commencing in the mid-1990s (4). In contrast to the significant secular declines in overall mortality rates found in the general population, there has been a notable increase in the disparity between observed and anticipated mortality rates in individuals with rheumatoid arthritis (RA) over a while (5). Consequently, there has been an increase in the disparity in death rates between individuals with rheumatoid arthritis (RA), namely those who test positive for rheumatoid factor (RF), and the overall population (6). The initial documentation of this occurrence may be traced back to the year 2007, when a team conducted retrospective investigations on a population-based incidence cohort of individuals with rheumatoid arthritis (RA) who were residents in Olmsted County, MN. This information is presented in Figure 2. Subsequently, a comparable pattern of an expanding disparity in mortality rates between individuals afflicted with and without rheumatoid arthritis (RA) was documented in a prospective investigation conducted on a European cohort. This study revealed no discernible advancements in the survival rates of individuals with RA over the previous two decades (7). On the other hand, a recent study conducted in Finland proposed that there was no significant rise in mortality rates among patients who had rheumatoid arthritis (RA) between 2000 and 2007, and were then monitored until 2008 (8). The implications of these findings are not definitively established, as they could either indicate a novel pattern of decreased mortality or merely validate the earlier discovery that there is no heightened mortality in patients within the initial years following the onset of RA. Subsequently, there may be an elevated risk of mortality in later stages (9). Indeed, the limited duration of the subsequent assessment (up to a maximum of 8 years) and the absence of verification of rheumatoid arthritis (RA) diagnoses based on established classification criteria indicate that these findings are conjectural and necessitate

additional substantiation. Despite the lack of an increase, there has been no apparent decrease in relative cardiovascular (CV) mortality in recent decades. A recent study conducted in Sweden has indicated that there was no statistically significant reduction in cardiovascular mortality among two groups of successive rheumatoid arthritis (RA) patients who began in 1978 and 1995, as compared to the general population (10). some meta-analyses have synthesized the findings from studies conducted over the past five decades, reaffirming the significantly elevated risk of cardiovascular (CV) mortality in individuals with rheumatoid arthritis (RA) ranging from 50% to 60%. Notably, there is no discernible indication of any change in CV mortality rates over time (11). Nevertheless, a meta-analysis that incorporated an RA inception cohort study indicated that there was no observed rise in cardiovascular mortality (12).

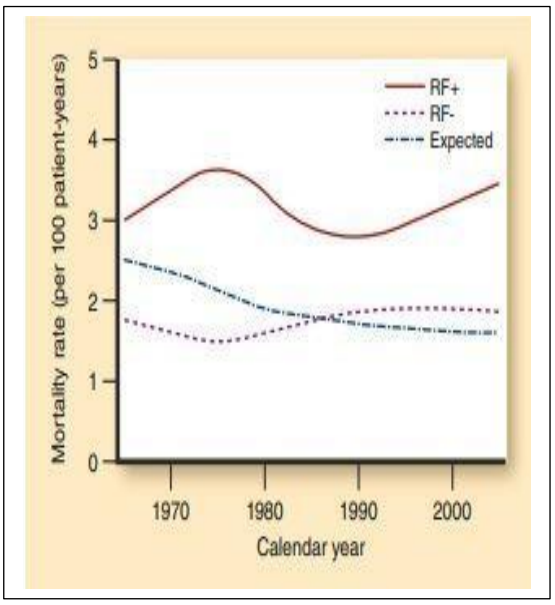

Figure (2): Observed and expected mortality in patients with rheumatoid factor–positive (RF+) and rheumatoid factor–negative (RF−) rheumatoid arthritis. Expected mortality is based on the Minnesota Caucasian population (13).

In brief, the current body of literature does not offer sufficient empirical support to definitively establish a decrease in premature death, particularly cardiovascular mortality, among those diagnosed with rheumatoid arthritis. Several studies have indicated the presence of a notable and expanding disparity in mortality rates between patients diagnosed with rheumatoid arthritis (RA) and the broader community. The promising emergence of evidence indicating no heightened risk of mortality in certain initial cohorts of patients with rheumatoid arthritis (RA) is encouraging; nonetheless, additional clarification is necessary to fully understand this phenomenon (14). While it is conceivable that the progress in enhancing survival rates has not kept pace with the current advancements in managing rheumatoid arthritis (RA), it is important to acknowledge that other disease-specific elements likely play a role in the lower survival rates observed in individuals with RA when compared to the general population. In the subsequent sections, we shall examine probable factors that may contribute to the heightened mortality observed in individuals with rheumatoid arthritis (RA) (15).

Causes

Rheumatoid arthritis is classified as an autoimmune disorder, characterized by the immune system's aberrant response in targeting and damaging healthy bodily tissues. Nevertheless, the specific causative factors for this phenomenon remain unknown at present. The immune system often produces antibodies that target bacteria and viruses, aiding in the defense against infections (16). Individuals diagnosed with rheumatoid arthritis experience an autoimmune response in which their immune system erroneously directs antibodies towards the synovial lining of their joints, resulting in an assault on the surrounding joint tissue. This phenomenon induces inflammation and soreness in the synovium, a thin layer of cells that envelops the joints, subsequently leading to the release of chemicals that inflict harm on adjacent tissues.

Bones are connected by cartilage, a flexible connective tissue, while tendons serve to connect bones to muscles. Additionally, ligaments are responsible for connecting bones to cartilage.

In the absence of treatment, rheumatoid arthritis can lead to progressive joint deformity and misalignment due to the cumulative impact of these chemical processes. Over time, it has the potential to cause full destruction of the joint (17). Several hypotheses have been proposed to explain the etiology of immune system-mediated joint attacks, including the possibility of an infectious trigger. However, none of these theories have been substantiated by empirical evidence.

Possible risk factors

There exist various factors that may contribute to an increased susceptibility to rheumatoid arthritis. One such factor is genetic predisposition, as there is limited evidence suggesting a familial association with the condition. However, it is important to note that the hereditary influence is believed to be minimal, as genes are considered to have a relatively minor impact on the development of rheumatoid arthritis. Hormonal Factors: Rheumatoid arthritis exhibits a higher prevalence among women compared to men, which may be attributable to the influence of the estrogen hormone. However, it is important to note that the causal relationship between estrogen and rheumatoid arthritis remains unestablished. Smoking: Existing research indicates a potential association between smoking and an elevated susceptibility to rheumatoid arthritis.

1.5 Signs of disease:

The enduring presence of signals and symptoms

Drug resistance is a phenomenon in which microorganisms, such as bacteria or viruses, develop the ability to withstand the effects of drugs that were previously effective in treating infections caused by microorganisms.

The individual exhibits a lack of response to two or more biological therapies.

The individual has a lack of response to anti-rheumatic medications that possess varying mechanisms of action (20).

Factors contributing to difficult-to-treat disease:

1. Environmental factors (diet, smoking, physical activity)
2. Overweight and obese
3. Genetic factors

1.6 Genetic risk factors

Genetic variables, specifically the HLA-DR1B1(21) allele, have been identified as influential in this context. The genes TRAF1, PSORS1C1, and microRNA 146a (22) are linked to refractory rheumatoid arthritis, whereas other genetic variants appear to be associated with the response to biologic modifying antirheumatic medications (bDMARDs). The FOXO3A gene region was shown to be related to a severe disease. The presence of the minor allele at the FOXO3A gene elicits a distinct reaction in monocytes among individuals with rheumatoid arthritis (RA). The transcription factor FOXO3A can induce upregulation of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNFα). Several gene polymorphisms, including STAT4, PTPN2, PSORS1C1, and TRAF3IP2, are associated with the responsiveness to TNF inhibitors.

HLA-DR1 and HLA-DRB1 gene

The HLA-DRB1 gene is a constituent of the human leukocyte antigen (HLA) complex, which encompasses a group of genes. The human leukocyte antigen (HLA) complex corresponds to the major histocompatibility complex (MHC) in humans. To date, a minimum of 2479 distinct variants of the HLA-DRB1 gene have been found (23). The existence of HLA-DRB1 alleles appears to be indicative of radiographic damage, maybe influenced by the production of anti-citrullinated protein antibodies (ACPA), as well as increased levels of inflammation in the blood and a high count of swollen joints. The greatest risk allele HLA-DR1 encodes HLA-DRB1, which exhibits a conserved 5-amino acid sequence that is associated with the

emergence of anti-citrullinated protein antibodies (24). The HLA-DRB1 gene exhibits a higher degree of association with the development of diseases. The susceptibility to and prognosis of rheumatoid arthritis (RA) are potentially linked to specific HLA-DR alleles. However, it is important to note that these alleles exhibit variation among different ethnic groups and geographic regions (25).

MicroRNAs (miRNAs)

MicroRNAs have a significant role in the pathogenesis of the mentioned disease. MicroRNAs typically function as a suppressor of target protein expression, and their levels tend to increase with the administration of biological disease-modifying antirheumatic medicines (bDMARDs) or other antirheumatic medications. The potential utility of pre-and post-treatment levels of miRNA as novel biomarkers for predicting and monitoring the outcome of anti-TNFa/DMRADs combo therapy is worth investigating. For example, certain genes were observed to have a notable increase in expression levels following treatment with a combination therapy using anti-TNFa and DMRADs. As an illustration, the following microRNAs were examined: miRNA-16-5p, miRNA-23-3p, miRNA-125b-5p, miRNA-126-3p, miRNA-146a-5p, and miRNA-223-3p. It is worth noting that the observed rise in the mentioned miRNAs following therapy was exclusively observed in patients who responded to the treatment. This increase was found to be consistent with the concurrent reduction in levels of TNFα, interleukin (IL)-6, IL-17, rheumatoid factor (RF), and C-reactive protein (CRP) (26).

THE EYE

The structure of the eyeball can be conceptualized as the integration of a small, highly curved spherical segment with a larger, less curved spherical segment. The smaller segment, which constitutes approximately one-sixth of the entire structure, possesses a radius measuring 8 mm (equivalent to 0.3 inches). This particular segment, known as the cornea, exhibits transparency. In contrast, the remaining portion, referred to as the scleral segment, is opaque and possesses a radius of 12 mm (equivalent to 0.5 inches). The region where the two distinct sections converge is referred to as the limbus. When observing the eye from a frontal perspective, one can observe the white sclera that surrounds the transparent cornea. Due to the cornea's transparency, it is not directly visible, but instead, a circular tissue located within it may be seen. (27)

The Structure of the Eye

The human eye, namely the iris. The iris is the anatomical feature responsible for determining the pigmentation of the eye. The central region of this ring is commonly referred to as the pupil. The perception of darkness arises from the limited reflection of light that enters the eye. The inside lining of the eyeball can be observed with an ophthalmoscope, which is a tool that allows the observer to illuminate the interior while seeing via the pupil. The fundus oculi, also known as the ocular lining, is distinguished by its prominent blood vessels responsible for supplying blood to the retina. These vessels are particularly noticeable as they traverse the pale optic disk, sometimes referred to as the papilla. This area serves as the point of exit for the optic nerve fibers from the eyeball. (30).

The ocular dimensions exhibit a very consistent pattern, with minor variations of approximately one to two millimeters observed among individuals in good health. The sagittal dimension, which refers to the vertical diameter, typically measures around 24 mm (equivalent to approximately one inch) and tends to be smaller than the transverse dimension, which pertains to the horizontal diameter. During the initial stages of life, the sagittal diameter measures approximately 16 to 17 mm (equivalent to approximately 0.65 inches). Subsequently, there is a rapid increase in size, reaching approximately 22.5 to 23 mm (approximately 0.89 inch) by the age of 3. Between

the ages of 3 and 13, the globe achieves its maximum size. The weight of the object is around 7.5 grams (equivalent to 0.25 ounces), while its volume measures 6.5 mm (equivalent to 0.4 cubic inches).

The ocular structure comprises three layers that encompass the optically transparent aqueous humor, lens, and vitreous body. The outermost layer of the eye is comprised of the cornea and the sclera. Moving inward, the middle layer, known as the uvea, contains the primary blood supply to the eye. This layer is composed, in order from the posterior to the anterior, of the choroid, the ciliary body, and the iris. The retina, situated above the choroid, obtains most of its sustenance from the blood vessels within the choroid. Additionally, the retinal vessels, which are observable through an ophthalmoscope, contribute to the remaining nourishment of the retina. The ciliary body and iris are covered by a thin layer known as the ciliary epithelium and posterior epithelium of the iris, which maintains continuity with the retina (30).

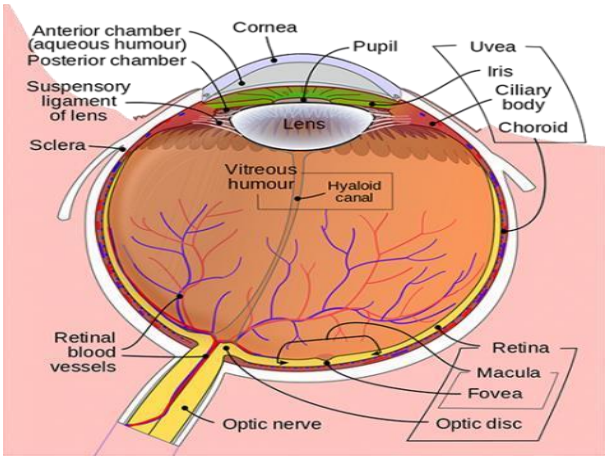

Figure (3): Anatomy of the eye

HUMAN EYE ANATOMY AND PHYSIOLOGY

A hard, transparent layer called the cornea forms the front of the eyeball. Surrounding this is the opaque sclera, inside of which the blood vessels form the choroid. On the front side, under the cornea, the iris extends the choroid. The iris has a round aperture in the middle called pupil. The eyeball is filled with a glasslike humor, the vitreous body. And finally, the inside of the choroid holds the retina (31).

Eye muscles

The eye is rotated by two pairs of direct muscles and a pair of oblique muscles functioning as antagonist pairs, The rotations are approximately symmetrical. The muscles control the six degrees of freedom of the eye. The lateral rectus abducts the eye toward the nose and the medial rectus abducts the eye away from the nose. These muscles move the eye in the horizontal plane. The remaining four muscles, the superior and inferior rectus (elevating and depressing the eye) and the superior and inferior oblique (controlling intorsion and extorsion) control the vertical motion of the eye. The optic nerve is encased by the muscles of the eye as it is lead backward from the eye (32)

Scope

- Optical Structure
- Optical Structure and Image Formation
- Optical Structure – cornea and sclera

The outer layer of the eye is in two parts: the anterior cornea and the posterior sclera. The cornea is transparent and approximately spherical with an outer radius of curvature of about 8 mm.

The sclera is a dense, white, opaque fibrous tissue that is approximately spherical with a radius of curvature of about 12 mm.

~ Optical Structure – uveal tract

The middle layer of the eye is the uveal tract. It is composed of the iris anteriorly, the choroid posteriorly, and the intermediate ciliary body The iris plays an important optical function through the size of its aperture.

The ciliary body is important to the process of accommodation (changing focus) (33)

~ Optical Structure – retina

The inner layer of the eye is the retina, which is an extension of the central nervous system and is connected to the brain by the optic nerve.

The topic of discussion pertains to the optical structure known as a lens.

The intraocular lens is situated at a depth of approximately 3 millimeters within the ocular cavity.

The zonules, which are suspensory ligaments, establish a connection between the ciliary body and another structure.

The topic under consideration is the optical structure of compartments.

The interior of the eye is anatomically partitioned into three distinct compartments.

The anterior chamber is the space located between the cornea and iris, and it is filled with a fluid called aqueous humour.

The posterior chamber, situated amidst the iris, the ciliary body, and the lens, is known to house the aqueous humour.

The anatomical structure situated between the lens and the retina is referred to as the vitreous chamber. This chamber is filled with a gel-like substance known as the vitreous humour.

The topic of discussion pertains to optical structure and the process of image formation.

The principles governing the generation of images by the human eye are analogous to those observed in man-made optical devices. The eye receives light through the cornea and undergoes refraction because of the cornea and lens. The cornea possesses a higher degree of refractive power. The shape of the lens can be modified to adjust its optical power, enabling the eye to accommodate and focus on varying distances. The diameter of the beam is regulated by the iris, which serves as the aperture stop inside the optical system. The aperture within the iris is commonly referred to as the pupil. The aperture stop holds significant importance inside an optical system, exerting influence over a broad spectrum of effects (35).

The topic of discussion pertains to optical structure and the process of image formation. The optic disc, also known as the optic nerve head, is a region located in the retina of the eye where the optic nerve fibers exit the eye and connect to the brain. It is characterized by a lack of photoreceptor cells, resulting in a blank spot in the visual field.

The optic disc is the point at which the optic nerve exits the eye. This geographical area lacks visual perception.

The dimensions of the optic disc are around 5 degrees in width and 7 degrees in height, with its location being approximately 15 degrees nasal to the fovea.

The term used to denote the specific area in the visual field that lacks visual perception is referred to as the blind spot (36).

Ocular Movements

Eye movements can be classified into two primary categories.

There are two types of eye movements involved in visual perception: stabilizing movements and saccadic movements. Stabilizing movements aim to maintain fixation on a certain point, ensuring that the picture is projected into the retina. On the other hand, saccadic movements involve rapid shifts of the eye around the visual field, allowing items of interest to be brought into the area of acute vision. The stabilization of eye movements encompasses three main types: fixations, smooth pursuit movements, and nystagmus. Saccadic eye movements encompass two distinct types of ocular motions, namely saccades and vergence movements. The measurement of eye movements is

commonly conducted in terms of degrees of visual angle. A single unit of visual angle, when measured at 57 cm from the viewer's eye, corresponds to an approximate length of 1 cm (37).

The impact of rheumatoid arthritis on ocular health
Rheumatoid arthritis is a persistent inflammatory condition that predominantly impacts the joints. Nevertheless, it is worth noting that rheumatoid arthritis can, on occasion, impact several regions of the body, including the ocular system.

Dryness is the predominant ocular manifestation associated with rheumatoid arthritis. The susceptibility of dry eyes to infection is well-documented, and in the absence of proper treatment, the presence of severe dry eyes can lead to detrimental consequences for the cornea. The cornea, being the transparent and convex outer layer of the eye responsible for facilitating visual focus, is particularly vulnerable to such damage. Sjogren's syndrome, an inflammatory condition frequently linked with rheumatoid arthritis, can manifest as dry eyes (38).

On occasion, rheumatoid arthritis may induce inflammation in the sclera, leading to symptoms such as ocular redness and discomfort. Individuals diagnosed with rheumatoid arthritis who encounter symptoms such as ocular discomfort, alterations in vision, or other ocular complications are advised to seek professional assessment from an ophthalmologist. Timely intervention can effectively mitigate the risk of ocular problems that may pose a threat to eyesight.

Rheumatoid arthritis is a persistent inflammatory condition that has the potential to impact bodily regions beyond the joints. The illness has the potential to adversely affect multiple bodily systems, encompassing the integumentary system, ocular structures, respiratory system, cardiovascular system, and vasculature (39).

Rheumatoid arthritis is classified as an autoimmune condition, characterized by the immune system's erroneous targeting and attack on the body's tissues. In contrast to the degenerative nature of osteoarthritis, rheumatoid arthritis primarily impacts the synovial membrane of the joints, leading to an inflammatory response characterized by severe edema. Over time, this inflammatory process can lead to the erosion of bone tissue and subsequent deformity of the affected joints. The pathogenesis of rheumatoid arthritis involves the inflammatory process, which has the potential to inflict harm on several anatomical structures beyond the joints. Despite significant advancements in medication, severe rheumatoid arthritis can still result in physical limitations (40).

Conclusion

In conclusion, it may be inferred that the mentioned evidence supports the notion that...
Rheumatoid arthritis is a chronic autoimmune inflammatory illness that impacts various organs, including the liver, bones, heart, lungs, and eyes.

The optimal approach for safeguarding ocular health involves timely identification and subsequent monitoring of ocular conditions and overall eye well-being.

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