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Mini Review

Anterior Uveitis Associateted Reumathologics Diseases: Mini Overview

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Abstract

The present text proposes a review of rheumatologic diseases that may occur with anterior uveitis, epidemiology, pathogenesis, clinical presentation, diagnosis and treatment, demonstrating the need for a close collaboration between rheumatologists and ophthalmologists in the management of the disease and its manifestations. The authors used the PubMed (MEDLINE), LILACS and Library of the Center for Ophthalmology Studies databases. Behcet's diseases, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, reactive arthritis, enteropathic arthritis, juvenile spondyloarthritis, undifferentiated spondylarteritis. Anterior uveitis is characterized by preponderant inflammation of the anterior segment of the eye. Conjunctival hyperemia, anterior chamber reaction with cells and flare, keratic precipitates and posterior synechiae are signs that make up the inflammatory process.

Keywords: Uveitis/classification; Anterior uveitis/etiology; Anterior uveitis/diagnosis; Rheumatic diseases; HLA-B27

Introduction and Classification

Uveitis is the term used to define inflammation of the iris, choroid and ciliary body. The optic nerve and the retina may also be affected. It is an important cause of eye morbidity and blindness in several countries.

The elaboration of an international classification by the International Uveitis Study Group (IUSG) (1987) [1], had an important role in the standardization of the nomenclature and in the understanding of factors related to the natural history of the different types of uveitis. Anterior uveitis includes terms anteriorly known as: iritis (iris-related inflammation, with inflammatory cells in the anterior chamber and without anterior vitreous involvement), iridocyclitis (primary inflammation of the iris, with secondary inflammation of the ciliary body, inflammatory cells will be present both in the anterior chamber and in the anterior vitreous) and cyclite (inflammation present mainly in the ciliary body).

Another classification of uveitis is related to a term used for anatomopathology, which can be used to aid in the diagnosis and classification of uveitis: granulomatous and non-granulomatous. Granulomatous uveitis is characterized by the tendency of iris nodules (Koeppe or Bussaca) and "mutton fat" precipitates. Non-granulomatous uveitis has little or no tendency to form both nodules and certian precipitates [2].

Uveitis whose inflammation lasts weeks or months, and when the crisis ends, are called acute uveitis. In chronic uveitis the inflammation lasts for months or years, without its complete disappearance between periods of exacerbation. The above classifications have been useful in developing new laboratory tests and adjuvant ophthalmic tests.

The diagnosis of anterior uveitis is based on the patient's complete anamnesis, bilateral ocular examination, and relevant systemic and laboratory evaluation. Anamnesis and physical examination provide information on systemic diseases such as arthritis, gastrointestinal diseases, sexually transmitted diseases, dermatological and central nervous system diseases. Important personal data regarding sex, age, origin, can also be obtained through anamnesis. Some diseases occur in childhood and others in more advanced age groups. The clinical evaluation of the ophthalmologist is of paramount importance in establishing the diagnosis of the patient with uveitis. Laboratory tests should be ordered only after clinical findings and ocular and physical examination directed to certain differential diagnoses among the many possible.

Anterior Uveitis in Rheumatological Diseases

Behçet's disease

It is a systemic vasculitis generalized and chronic, classified as autoimmune, which presents varied clinical features. It has preference for vessels of small caliber (mainly venous), and can cause changes in practically all the organs. Its most frequent signs are oral and genital ulcers, occurring also ocular, dermal, neural, pulmonary and other manifestations. The etiology of Behçet's disease remains unknown, and several factors have been implicated in its appearance, such as: viruses (Herpes simplex, adenovirus), exposure to streptococcal antigens, heredity (HLA B51). Ocular involvement is frequent in Behçet's disease, ranging from acute non-granulomatous iridocyclitis to hypopyon (one third of cases) or retinal vasculitis [3]. There is no specific diagnostic test for Behçet's disease. The clinical picture is composed of signs considered major and minor in the formulation of the criteria used in the diagnostic hypothesis of Behçet's disease. Non-specific data include cutaneous hypersensitivity reaction (patergia), increased chemotactic activity of neutrophils and cellular immunity, elevated serum levels of C9 and others [4].

Rheumatoid arthritis (RA)

RA is a chronic and progressive disease characterized by

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polyarticular synovitis, which affects approximately 1% of all people around the world. Ocular impairment includes dry keratoconjunctivitis, anterior scleritis, episcleritis, keratopathy and anterior uveitis [5]. Rheumatoid factor (RF) in uveitis may be useful in some conditions.

Most patients with RA, Systemic Lupus Erythematosus (SLE), Sjögren's syndrome, connective tissue diseases and chronic infections have FR-positive. Patients with juvenile rheumatoid arthritis (JRA), psoriatic arthritis, arthritis associated with ulcerative colitis, enteritis, reactive arthritis and ankylosing spondylitis have negative RF.

Juvenile rheumatoid arthritis

JRA is the most common rheumatic disease in childhood, affecting people under 16 years of age, usually starting at two to four years. Iridocyclitis is the most frequent ocular finding and when undiagnosed or untreated, may lead to blindness in these patients.

Intraocular inflammation in JRA is characterized by non-granulomatous anterior uveitis. The inflammation is chronic and mild and the patient never presents the "red eye". Sometimes uveitis is noticed when some of its complications occur (visual loss, cataract, keratopathy in band) [6]. Unlike RA, RF is rarely positive in patients with JRA. The fluorescence test, with nuclear factors (ANF), is not specific for all antinuclear antibodies found in serum. Serum ANF levels may be elevated in many diseases such as JRA, SLE, polyarteriris nodosa, dermatomyositis, scleroderma, Raynaud's disease and Sjögren's syndrome. This test is important in the diagnosis of uveitis because it remains permanently positive in 80% of patients with iridocyclitis associated with JRA. It should be emphasized that according to some authors, a single negative test is not conclusive; must be negative in three or four samples to be conclusive [7].

Spondylarthritis

Ankylosing spondylitis (AS) represents the prototype of a group of inflammatory diseases once known as spondyloarthropathies and now called spondylarteritis, which have epidemiological, clinical, anatomopathological, radiological and immunogenetic peculiarities (HLA - Human leukocyte antigen) HLA B27, of which it does part to AS, reactive arthritis formerly called Reiter's syndrome, psoriatic arthritis, spondyloarthritis related to inflammatory bowel disease and undifferentiated spondyloarthritis. They represent 52% of all cases of anterior uveitis [8].

Diagnostic criteria have been undergoing updating since the mid-1990s. This new epidemiological concept includes the importance of peripheral joint involvement, such as enteritis, arthritis and dactylitis, as well as a new criterion for the measurement of inflammatory activity for spondyloarthritis, in which laboratorial tests of inflammatory activity of disease, erythrocyte sedimentation rate and C-reactive protein were valued. These new concepts were proposed by the Assessment on SpondyloArthritis International Society (ASAS) group that reside in the differentiation of axial and peripheral spondylarteritis.

In relation to axial spondyloarthritis, the new criteria emphasize the inflammatory lumbar pain clinic of more than three months of evolution in individuals younger than 45 years associated with the diagnosis of sacroiliitis by imaging (X-ray or RM) and the presence of HLA- B27. In the peripheral spondyloarthritis, a greater sensitivity and specificity for the early diagnosis of the disease was evidenced [9].

Ankylosing spondylitis

AS is an inflammatory, chronic and progressive disease that primarily affects the sacroiliac joints and the axial skeleton (vertebral column), and less frequently the peripheral joints. It usually begins in the second to third decades of life, male, white and HLA-B27 positive [10].

Its etiology and pathogenesis are not fully understood, but the prevalent hypothesis involves immune mediators as the main mechanism, including various cytokines such as tumor necrosis factor (TNF), interaction between T cell response, genetic factors, environmental factors and bacterial antigens. There is a strong association of this disease with HLA-B27 [11].

As for extra-articular manifestations, the most frequent is acute anterior uveitis (AAU), observed in up to 40% of patients in a prolonged follow-up, usually associated with positive HLA-B27 and seldom courses with sequelae.

Anterior uveitis includes terms known as: iritis, and cyclite.

In the chronic, recurrent forms, alterations in the posterior segment, such as vitreitis, macula edema and edema of the optic disc can be found [12].

There is a peculiar behavior of HLA-B27-related uveitis that are characterized as acute unilateral iridocyclitis with sudden onset, recurrent (affects one eye at a time), fibrin and cells in the moderate to severe anterior chamber. They generally respond well to topical corticosteroid treatment and use of mydriatics prescribed in the prevention of posterior synechiae [12].

Reactive arthritis

Currently restricted to cases characterized by the triad urethritis, arthritis and conjunctivitis, which occurs after genitourinary or gastrointestinal infection; is included in the group of reactive arthritis. The modern concept of reactive arthritis within the spondyloarthropathies group requires the presence of oligoarthritis associated with the evidence of anterior infection [13].

The infectious agent represents, in the genetically predisposed individual, the "trigger factor" for the development of the disease.

Clinical symptoms usually begin one to four weeks after infection (in the enteric etiology, it is common to have a self-limiting, sometimes dysenteric, diarrhea, while urethritis with mild symptomatology occurs in the genitourinary etiology). Within the characteristic triad of the disease, the first manifestation is usually urethritis, often serous, with morning discharge, oligosymptomatic; their diagnosis is difficult in women, and may progress with prostatitis (often asymptomatic) in affected men. The conjunctivitis usually is light, of spontaneous resolution, lasting seven to ten days, without leaving sequels. The joint condition is usually characterized by recurrent asymmetric oligoarthritis, predominant in large joints of the lower limbs, and the presence of massive recurrent joint effusions in the knees in patients with active disease is common.

The HLA-B27 study, which is positive in 50% to 80% of the

cases, is important not as a diagnosis, but as a determinant of disease prognosis [11].

Enteropathic arthritis

Classically, we can observe joint manifestations associated with ulcerative colitis and Crohn's disease, and, to a lesser extent, with Whipple's disease, celiac disease and bypass-surgery [14].

Joint involvement may be subdivided into peripheral oligoarthritis, peripheral polyarthritis, and enteropathic spondylitis. Peripheral oligoarthritis mainly affects large lower limb joints, associated with peripheral enthesopathies (notably insertion of Achilles tendon and plantar fascia); has no sex predominance or specific histocompatibility antigen, and its evolution is invariably associated with the activity of the intestinal disease; cutaneous lesions, such as erythema nodosum, may occur in 10% to 25% of these patients. A peripheral polyarthritis, usually non-deforming, may occur in Whipple's disease and after intestinal bypass surgery; A similar but potentially more aggressive and deforming picture may occur in patients with Crohn's disease; also have no association with specific HLA, and their evolution is usually independent of intestinal involvement. Enteropathic arthritis can affect 2% to 12% of patients with ulcerative colitis and Crohn's disease; predominates in males, and 50% to 75% of these patients present HLA-B27 positive; the clinical and radiological features of enteropathic arthritisare similar to those observed in ankylosing spondylitis, and their evolution is usually independent of the intestinal tract [15].

Juvenile spondyloarthritis

Juvenile spondyloarthritis (which begin in individuals younger than 16 years) usually have clinical characteristics that allow them to differentiate them from the disease that starts in the adult. Primordially, it presents a clear predominance of peripheral joint involvement, usually as an oligoarthritis of lower limb joints, associated with peripheral enthesopathy; axial involvement is usually late, often already in adulthood [16]. Diagnosis of undifferentiated spondyloarthropathy, such as syndrome of seronegative enthesopathy and arthropathy (SEA), is characterized by an arthritis with peripheral enthesopathy, which is seronegative for ANA and RF, which in a significant number of cases usually develops into spodilitis [17].

Undifferentiated spondyloarthritis

Undifferentiated spondyloarthritis encompasses a group of patients presenting clinical and / or radiological features suggestive of spondyloarthritis but not fulfilling the diagnostic criteria for any of the diseases defined within the group. It often represents a provisional diagnosis, encompassing a very heterogeneous set of patients, which may vary from an early stage or an abortive or frustrated form of defined spondyloarthritis [18]. Long-term controlled studies have indicated that a patient with inflammatory pain in the sacrum iliac may take up to 14 years to develop a radiologic sacroiliitis, allowing the diagnosis of spondylitis to be made [19]. The presence of HLA-B27 represents a prognostic factor of evolution for a defined disease [20]. In patients who meet the spondyloarthritis classification criteria of the European Spondyloarthropathies Study Group [21] and do not meet the diagnostic criteria for a defined disease, it may be considered undifferentiated.

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