

# INTERDISCIPLINARY COLLABORATION IN MANAGING PATIENTS WITH ANTERIOR UVEITIS AND SPONDYLOARTHRITIS

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## Abstract

Anterior acute uveitis is the most frequent extraarticular involvement in patients with rheumatologic diseases such as spondyloarthritis and it can often be the first clinical feature. In many cases, a prompt recognition and an early referral by the ophthalmologist to the rheumatologist can be crucial for the accurate diagnosis of these disorders. On the other hand, recognition of the signs and symptoms of ocular inflammation by the rheumatologist can facilitate prompt referral to an ophthalmologist and improve patient outcomes. Comprehensive care through collaboration between ophthalmologists and rheumatologists can help with optimal diagnostic and therapeutic decisions tailored to the individual patient.

**Keywords:** interdisciplinary collaboration, anterior uveitis, spondyloarthropathy

## BACKGROUND

Spondyloarthritis (SpA) is a heterogeneous group of diseases which include ankylosing spondylitis, psoriatic arthritis, reactive arthritis (formerly Reiter's syndrome), arthritis associated with inflammatory bowel disease (Crohn's disease, ulcerative colitis) and undifferentiated SpA [1]. Ocular inflammation is common in these rheumatologic diseases but with variable prevalence, and the major types include uveitis, conjunctivitis, scleritis, retinal vasculitis, dry eye syndrome, orbital inflammation, and neuro-ophthalmic lesions. Amongst the associated extraarticular features, the most frequent symptomatic association is with acute anterior uveitis (AAU) [2,3]. The estimated prevalence of uveitis in SpA varies in up to one third of patients depending on the disease duration and SpA type [4].

Uveitis refers to the inflammation of the uvea which is composed by the iris, ciliary body, and cho-

roid and is richly supplied with blood. The uvea is divided into anterior, intermediate, and posterior segments, and uveitis is classified by the location of inflammatory process into the following: anterior uveitis refers to the inflammation of the iris (iritis) or the ciliary body (cyclitis) or, more frequently, both the iris and the ciliary body in which case the term "iridocyclitis" is used; intermediate uveitis involving the vitreous humor and/or peripheral retina, which is known as the pars plana (pars planitis); posterior uveitis is the inflammation of the choroid or, by extension, the retina: choroiditis or retinochoroiditis; panuveitis refers to an involvement of all three segments [1,5-7].

Furthermore, uveitis subsets are recognized by such variables as onset (sudden versus insidious), duration (limited versus persistent), and course (acute, recurrent, or chronic) [7]. Acute uveitis is defined as uveitis of abrupt onset and short duration;

recurrent uveitis requires repeated episodes of uveitis separated by remissions of at least 3 months after treatment discontinuation and chronic uveitis requires a relapse within 3 months after treatment discontinuation [8].

Most cases of SpA are usually diagnosed in rheumatology units on the basis of other clinical findings such as arthritis or low back pain. However, there could be patients presenting acute anterior uveitis with an undiagnosed SpA, therefore, an early recognition of a possible SpA in patients with uveitis attending an ophthalmology unit is essential to improve these patients' management [2,9].

## EPIDEMIOLOGY

Acute anterior uveitis is rare, with an annual incidence of 12 per 100,000 in the general population. Although 60% to 80% of the acute anterior uveitis remain idiopathic [10], a systematic literature review shows a high prevalence of uveitis in SpA of 32.7% for a mean disease duration of 17.7 years, varying with the type of SpA. The highest incidence, 36.9%, was reported in patients with arthritis associated with inflammatory bowel disease and the lowest, 13.2%, in undifferentiated SpA. The prevalence of AAU was 33.2% in ankylosing spondylitis, 25.6% in reactive arthritis and 25.1% in psoriatic arthritis. The incidence of AAU increases with disease duration. Besides the highest incidence, arthritis associated with inflammatory bowel disease has the longest disease duration of about 22 years, followed by psoriatic arthritis (17.4 years) and ankylosing spondylitis (17.0 years). Reactive and undifferentiated arthritis have the shortest disease duration of 5.8 years [11].

An important characteristic of uveitis in SpA is the important rate of recurrence as in 50.6% of the cases presented more than one flare. Epidemiological data suggests that there may be a mean of 5 attacks of uveitis during the course of the disease [9,11].

## CHARACTERISTIC FEATURES OF THE AAU

Although AU affects the physical aspects of quality of life in all affected patients, especially in those with pre-existing, undiagnosed SpA [12], studies have shown that the pattern of uveitis tends to differ according to the underlying pathology. Uveitis in association with ankylosing spondylitis has a sudden onset, usually preceded by pain 1-2 days before the

appearance of clinical signs. The inflammation is usually anterior although some cells might appear in the vitreous humor. It usually remains unilateral in over half of the cases with the possibility of recurrence in a "flip-flop" pattern (alternation between the eyes) in 42% of the cases. Although this inflammation can be intense and result in fibrin exudation, hypopyon and posterior synechiae, the prognosis is excellent with most patients recovering full vision within 2 months. Ankylosing spondylitis associated uveitis has a slight predominance for the male gender [3,6].

The pattern often seen with either psoriatic arthritis or inflammatory bowel disease differs from the one seen in ankylosing spondylitis, although a small percentage of these individuals will have sudden, recurrent, unilateral, anterior uveitis. But about half of individuals with either psoriatic arthritis or inflammatory bowel disease who develop uveitis have disease which is bilateral, reaching to 63% of the cases and only in a smaller percentage of cases it is unilateral or in a "flip-flop" pattern. The onset is more often insidious and sometimes intermediate uveitis can be present in a form of vitritis. These individuals are sometimes B27 positive. Their disease tends to be much more persistent. 88% of AAU SpA patients with inflammatory bowel disease are females. Females who develop uveitis may have less classic HLA-B27-associated uveitis (i.e., insidious rather than abrupt onset) as well as atypical SpA [3,6].

## WHEN SHOULD AN OPHTHALMOLOGIST REFER A PATIENT TO THE RHEUMATOLOGIST?

Recent studies show that approximately 40% of patients presenting with idiopathic AAU have undiagnosed SpA [13]. The DUET study included 101 consecutive patients presenting with AAU at the emergency department, but without a known diagnosis of SpA prior to presentation and showed after undergoing a rheumatologic evaluation, 41.5% of the patients had undiagnosed SpA according to the ASAS classification criteria. The mean age of these newly diagnosed SpA patients was 40.8±13 years [14].

The SENTINEL study included 798 consecutive adult patients with a mean age of 45 years who presented anterior, noninfectious, clinically significant AU, diagnosed by an ophthalmologist. These were HLA-B27 positive patients who presented one or

more episodes of AU or HLA-B27 negative patients who presented more than 1 episode of AU with at least 3 months period between the episodes. A total of 50.2% presented axial and 17.5% of patients presented peripheral SpA according to ASAS criteria. HLA-B27 positive patients with AU were more frequently diagnosed with axial (69.8% vs. 27.3%) and peripheral SpA (21.9% vs. 11.1%) than patients with recurrent negative HLA-B27 [4].

These studies draw the attention on the fact that effective recognition of SpA among patients with uveitis is an achievable goal and requires an integrated multidisciplinary approach [13]. Thus, the following consensus on a referral recommendation was achieved as a result of the Delphi processes: “Patients with chronic back pain (duration  $\geq$  3 months) and back pain onset before the age of 45 should be referred to a rheumatologist if at least one of the following criteria is present: inflammatory back pain; peripheral manifestations (arthritis, dactylitis, enthesitis); extra-articular manifestations (uveitis, psoriasis, inflammatory bowel disease); presence of human leucocyte antigen-B27; sacroiliitis on imaging (X-rays or magnetic resonance imaging); positive family history for spondyloarthritis; good response to non-steroidal antiinflammatory drugs; elevated acute phase reactant” [14].

Furthermore, another study standardized red flags for referral to rheumatologists from ophthalmologists for patients suffering from acute anterior non-granulomatous non-infectious uveitis or patients suffering from intermediate, posterior, non-infectious uveitis, or panuveitis. One or more of the following statements should determine the ophthalmologist to refer the patient in a rheumatological unit: chronic low back pain  $\geq$  3 months (only for patients suffering from acute anterior non-granulomatous non-infectious uveitis); family or personal history of psoriasis involving the skin and/or nails, and/or of SpA and/or IBD and/or Behçet’s disease; genital and/or oralaphthae; children (any diagnosis) with suspect joint involvement; erythema nodosum; retinal vasculitis (only patients suffering from intermediate, posterior noninfectious uveitis, or panuveitis); disorders of the central nervous system (only patients suffering from intermediate, posterior non-infectious uveitis, or panuveitis); child with suspect joint involvement, in whom Fuchs’ uveitis has been excluded (patients suffering from chronic anterior non-infectious uveitis) [15].

## WHEN SHOULD A RHEUMATOLOGIST REFER A PATIENT TO THE OPHTHALMOLOGIST?

Since some patients seen in the rheumatology clinic present with unclear signs and symptoms, and ocular manifestations may be the only clue to aid a difficult diagnosis, understanding the ocular manifestations of rheumatic diseases is of great importance for the rheumatologist. On the other hand, some patients may present with well-documented rheumatic diseases, and eye findings may add and confirm the severity of their condition [16].

Some components of the ophthalmologic evaluation can be performed without the aid of specialized equipment. These include observation of the external appearance of the eye, visual acuity, pupillary responses, color perception, testing of ocular motility and alignment and confrontation visual field examination. For patients with suspected orbital and ocular inflammation, additional ophthalmic techniques are often utilized in more specialized evaluations of the eye in an ophthalmology unit [17].

Symptoms of acute anterior uveitis include generally an acute onset of eye redness and pain, intense photophobia, myosis and blepharospasm. There may be a reduction of visual acuity when there are medium opacities or cystoid macular oedema. Pain is caused by spasm of the ciliary muscle secondary to anterior chamber inflammation and can irradiate all around the distribution area of the first branch of the trigeminal nerve, including the periorbital area. The initial episode classically tends to subside in 2-4 months without treatment [11].

Other visible signs include ciliary flush (a violaceous ring around the cornea indicates intraocular inflammation), anterior/posterior synechiae (adhesions of the iris to the cornea or lens, respectively), hypopyon (a layering of inflammatory cells in the inferior angle), keratic precipitates (inflammatory deposit on the posterior cornea), corneal edema or band keratopathy (calcium deposits beneath the corneal epithelium) [7].

The CORE study managed to identify a series of “red flags” for patients with established rheumatic disease and suspected ocular disease to be referred from rheumatologist to ophthalmologist. One or more of the following statements should determine the referral for patients suffering from SpA, JIA or Behçet’s disease: red eye; ocular pain; photophobia; blurred vision and/or reduction in visual acuity; his-

tory of ocular inflammation; children diagnosed with JIA; patients diagnosed with Behçet's disease [15].

## CONCLUSIONS

Ophthalmic involvement, especially anterior uveitis, can be the first clinical feature of rheumatologic diseases such as SpA. In many cases, a prompt recognition and an early referral by the ophthalmologist to the rheumatologist can be crucial for the accurate diagnosis of these disorders. Also, rheumatologists can facilitate prompt referral to an ophthalmologist and improve patient outcomes by

recognition of the signs and symptoms of ocular inflammation.

Comprehensive care through collaboration between ophthalmologists and rheumatologists can help with optimal diagnostic and therapeutic decisions tailored to the individual patient.

## Acknowledgement

Cristina Stan, Anca Maria Rednik, Simona Rednic and Cristina Stan were contributors in collecting data, writing the manuscript, contributed to its design and coordination. All authors have read and approved the final manuscript.

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