

Top 10 Things You Should Know About the Eye in Your Rheumatology Practice

By Vanessa Ocampo, MD, FRCPC

Rheumatology is a subspecialty that doesn't just treat diseases that affect the musculoskeletal (MSK) system. One of the most common extra-musculoskeletal (EMSK) anatomical sites involved is the eye. The following are things we should know about the intersection of these two subspecialties, that you may find helpful.

1. Knowledge about basic ocular anatomy and the structures that can be affected by inflammatory conditions will help us to recognize them more easily, perform an appropriate evaluation, and prompt referral to the ophthalmology team. (see Figure 1).¹

The outer layer of the eye is composed of the cornea and the sclera. The inner layer consists of the retina. In conditions such as uveitis, dividing the eye anatomically by segments can help to classify the disease more easily (see Figure 2):

- Anterior: iris
- Intermediate: ciliary body, anterior vitreous, pars plana
- Posterior: choroid, retina and optic nerve

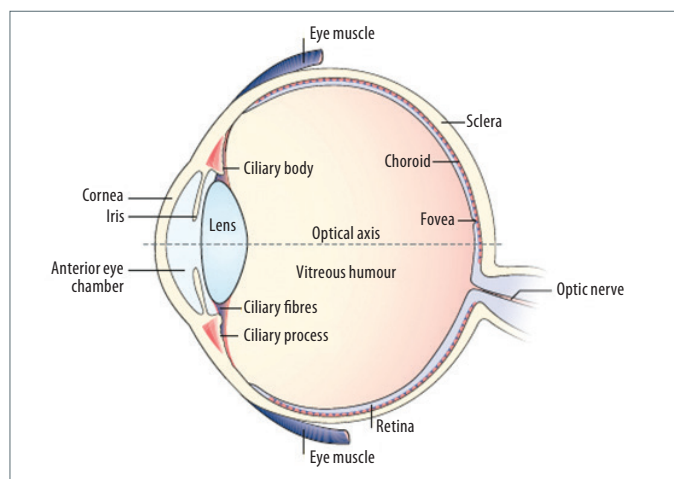


Figure 1: Overview of the Eye

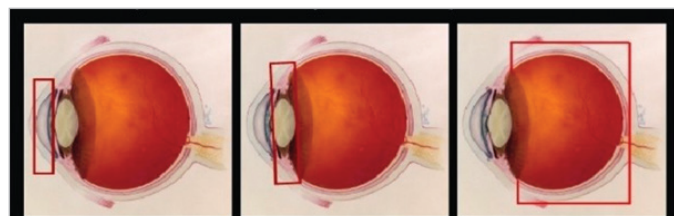


Figure 2: Classification of Uveitis

2. The most common ocular manifestations of rheumatic diseases include keratoconjunctivitis sicca, anterior uveitis (AU) and scleritis among others.^{2,3}

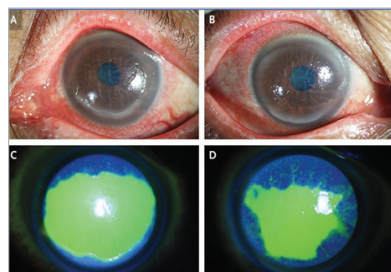


Figure 3: Keratoconjunctivitis Sicca in Sjogren's⁴

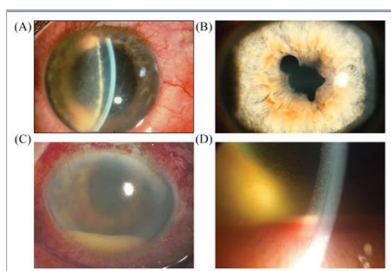


Figure 4: Acute Anterior Uveitis (AAU): A) Ciliary injection; B) Synechia; C) Hypopyon; D) Fibrin coating at the front of the lens⁵

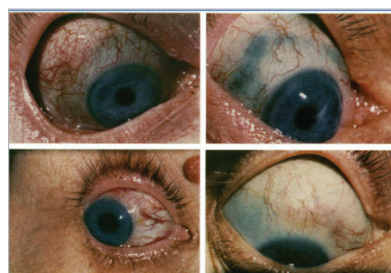


Figure 5: Scleritis in Rheumatoid Arthritis⁶

3. As rheumatologists we should recall that there are multiple eye manifestations of rheumatologic conditions such as the ones listed in Table 1.^{7,3,8,9,2}
4. Approximately 40% of patients with SpA experience ≥ 1 EMSK manifestation during the course of the disease:^{10,11,12,13}
 - Acute anterior uveitis (AAU) is one of the common EMSK manifestations of the SpA spectrum of diseases.
 - The prevalence of AAU is 22-40% in AS, with lower presentation in the rest of the entities (psoriatic arthritis or reactive arthritis).
 - HLA-B27 is present in 50% of AAU patients.

Table 1: Ophthalmologic and Rheumatologic Associations

Ophthalmologic diagnosis	Rheumatologic association
Orbital inflammatory disease	GPA*, sarcoidosis, IgG4-related disease, Sjogren's syndrome, IBD*, Behcet's disease, RA*, adult-onset still's disease, amyloidosis, histiocytic disorders
Keratoconjunctivitis sicca	RA*, SLE*, scleroderma, Sjogren's syndrome, graft vs host disease, RPC*
Episcleritis	RA*, vasculitis, IBD*, RPC*
Scleritis	RA*, GPA*, SpA*, Behcet's disease, IBD*, PMR*,
Scleritis associated with ulcerative keratitis	RA*, GPA*, RPC*, SLE*, Sjogren's, Behcet's disease, PsA, sarcoidosis
Necrotizing scleritis without inflammation (scleromalacia perforans)	Almost exclusively in RA
Uveitis	Behcet's disease & sarcoidosis can present in any form of uveitis
Anterior	RA/JIA, SpA, HLA-B27* non-specific arthropathy, reactive arthritis, PsA*, GPA*, IBD*, JIA*, Kawasaki disease
Intermediate	Multiple sclerosis
Posterior	PsA*, IBD*, SLE*, GCA*, PAN*, GPA*
Panuveitis	SLE*, VKH*, HLA-B27* associated, RPC*, PAN*, dermatomyositis
Retinal vasculitis	Most commonly Behcet's disease, sarcoidosis, multiple sclerosis Less frequently: ANCA associated vasculitis, large and medium vessel vasculitis, APS* Other: HLA-B27* associated uveitis dermatomyositis, Takayasu's, polymyositis, RPC*, RA*
Optic neuropathy	GCA*, SLE*, APS*

*GPA: Granulomatosis with polyangiitis; IBD: Inflammatory bowel disease; RA: Rheumatoid arthritis; SLE: Systemic lupus erythematosus; RPC: Relapsing polychondritis; SpA: spondyloarthritis; PMR: Polymyalgia rheumatica; JIA: Juvenile idiopathic arthritis; PsA: Psoriatic arthritis; PAN: polyarteritis nodosa; VKH: Vogt-Koyanagi-Harada; APS: Antiphospholipid syndrome

- Uveitis, when left untreated, is an important cause of blindness¹⁴ after under-corrected refractive errors, cataracts, glaucoma, and diabetic retinopathy.¹⁵
 - It is estimated to cause 10-15% of blindness in the U.S.
- Always remind yourself about the possible eye-gut connection.^{16,17}
 - The prevalence of IBD in AS is about 5-10%.
 - The prevalence of ophthalmic inflammatory disorders in IBD is variable, according to the population studied, ranging from 0.3% to 13.0% among all IBD patients.
- AAU therapy includes topical cycloplegics (i.e., topical atropine), nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids (topical, ocular injections, systemic). In recalcitrant cases, agents such as disease-modifying antirheumatic drugs (DMARDs) (i.e., methotrexate), mycophenolic acid, or adalimumab can be highly effective.
- The most significant side effects of some of the drugs used to treat rheumatic disease are maculopathy associated with anti-malarial agents, and cataracts and glaucoma associated with corticosteroid use.²
- When referring a patient to ophthalmology or when getting a referral from an ophthalmologist asking to rule out a rheumatologic condition in a patient with an inflammatory eye disease, be mindful of the investigations sent. Not every single condition in rheumatology causes eye involvement, such as uveitis.^{9,18-20}

For example, a diagnostic workup of value in a patient with unclassified uveitis includes routine complete blood count (CBC), comprehensive metabolic panel, urinalysis (UA), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Based on these results and the medi-

cal history, infectious disease studies, imaging and autoantibodies may be ordered.

- All patients should have a chest X-Ray, venereal disease research laboratory test (VDRL) and the fluorescent treponemal antibody absorption (FTA-ABS).
 - Purified protein derivative (PPD) test and QuantiFERON: if there is suspicion of exposure to tuberculosis, CXR findings or pre-immunomodulatory therapy (IMT) assessment.
 - ANA: only in pediatric patients with pauciarticular JIA and uveitis (prognosis). In adults, only consider if there are other features of SLE, anti-C1q disease or another ANA-associated disease.
 - HLA-B27 is appropriate for patients with AAU, even in the absence of demonstrable SpA (prognostic implications).
- With multiple crossover patients among these two subspecialties, rheumatologists should not ignore ocular symptoms and ophthalmologists should be specific in their referral regarding the ocular diagnosis and the possible systemic diseases they are suspecting in their patients. Ideally the two specialties should hold a clinic together to follow-up and manage these complex patients together. If a combined clinic is not possible, there should be a communication tool that allows for clear communication of patients' progress and management between the two of them.

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