Ocular Sarcoidosis

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KEYWORDS

• Sarcoidosis • Eye • Uveitis • Dry eye • Optic neuropathy • Orbital inflammation

KEY POINTS

- Ocular sarcoidosis can involve any part of the eye and its adnexal tissues.
- The most common ocular manifestations are uveitis, dry eye, and conjunctival nodules.
- Ocular involvement is the presenting symptom in approximately 20% to 30% of patients with sarcoidosis.
- Multidisciplinary approaches are required to achieve the best treatment outcomes for both ocular and systemic manifestations.
- With appropriate treatment, visual prognosis is generally good.

Sarcoidosis can involve almost any structure within or around the eye. In addition, the first recognized clinical manifestation of sarcoidosis often is eye disease. Both ophthalmologists and nonophthalmologists need to be aware of the protean ocular manifestations of sarcoidosis.

EPIDEMIOLOGY

Ocular involvement of sarcoidosis has been known since the early 1900s and has become more recognized since the mid-1900s.[1] Variability in the diagnostic criteria has made epidemiologic studies of ocular sarcoidosis challenging.

The prevalence of ocular involvement in different series ranges widely from 13% (Turkish study) to 79% (Japanese study) in patients with systemic sarcoidosis.[2–4] Ocular involvement is the presenting symptom in approximately 20% to 30%.[5,6] Uveitis was reported in 30% to 70%, and conjunctival nodules were found in 40%.[2] In patients with systemic sarcoidosis, females (56%) were more likely to develop ocular involvement compared with males (23%) in a study of 121 patients with biopsy-proven sarcoidosis.[6]

Sarcoidosis reportedly may affect children, and most of these cases begin between the ages of 8 and 15 years.[7] Many patients, however, previously diagnosed as having early-onset sarcoidosis are now recognized as having Blau syndrome with de novo mutations.[8] Age distributions of ocular sarcoidosis in adults are bimodal. Two peaks of incidence are 20 to 30 years and 50 to 60 years.[2] The mean age at presentation of uveitis is 42 years (range, 4–82 years).[9] African Americans with biopsy-proven sarcoidosis have a higher likelihood of developing ocular involvement compared with Caucasians.[10] Race may also influence the age of onset of uveitis. Blacks tend to develop uveitis at a mean age of 35 to 44 years, whereas whites are more likely to have uveitis at a mean age of 43 to 52 years.[9,11]

Sarcoidosis accounted for approximately 1% to 3% of pediatric uveitis in referral centers,[12,13] whereas approximately 10% of adult uveitis was found to be associated with sarcoidosis.[14,15] An epidemiologic study in the southeastern United States showed that sarcoidosis was the cause of uveitis in 11% of the studied population (385 patients: 67% Caucasian and 31% African

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American). Subgroup analysis demonstrated that sarcoidosis accounted for 25% of uveitis among the African American patients.[15]

Most sarcoid uveitis is bilateral, and approximately 90% are chronic.[9] The prevalence of uveitis subtype based on anatomic location varies among different studies, partly because of the different terminologies used. Dana and colleagues[9] reported that of 112 eyes with sarcoid uveitis, 28% were anterior, 38% were intermediate, 12% were posterior, and 22% were panuveitis. A Turkish study reported 46% as intermediate, 15% as anterior, and 38% as panuveitis.[16] Another study from Japan described 75% eyes with iritis and 67% eyes with retinal vasculitis.[4]

The rate of sarcoidosis in patients with multifocal chorioretinitis is variable because of the different diagnostic criteria and the extent of investigations among different studies. A study by Abad and colleagues[17] of 37 patients with multifocal chorioretinitis demonstrated a prevalence (68%) of biopsy-proven and presumed sarcoidosis, while Ossewaarde-Van Norel and colleagues[18] reported a 39% rate. Of note, 62% of patients in the former study received a chest computed tomographic (CT) scan,[17] but only 26% did in the latter.[18]

A Case-Control Etiologic Study of Sarcoidosis (ACCESS) presented evidence for the allelic variation at the HLA-DRB1 locus as a significant contributing factor for sarcoidosis. HLA-DRB1*0401 allele was associated with ocular involvement in both blacks and whites (odds ratio 3.49).[19]

CLINICAL MANIFESTATIONS OF OCULAR SARCOIDOSIS

Ocular disease may be the initial manifestation in patients with sarcoidosis and may cause severe visual impairment. The involvement may be characterized by granulomatous inflammation, which can affect any part of the eye and its adnexa. Examples of the clinical presentations of ocular sarcoidosis are listed in **Table 1**. The most common ocular manifestations are uveitis, dry eye, and conjunctival nodules.

Uveitis and Fundoscopic Abnormalities

Uveitis is the term used to describe an inflammation of the uveal tissues, which are composed of the iris, ciliary body, and choroid. Uveitis commonly affects tissue or space adjacent to the

Table 1
Examples of clinical manifestations of ocular sarcoidosis

Ocular Structures	Ophthalmic Manifestations
Eyelids	Eyelid granuloma, madarosis (loss of eyelashes), poliosis (whitening of lashes), entropion, trichiasis, lagoghthalmos (if associated with facial palsy)
Conjunctiva	Conjunctival nodules or granuloma, conjunctivitis, symblepharon, conjunctival cicatrization
Episclera/sclera	Episcleritis, scleritis
Cornea	Peripheral ulcerative keratitis, interstitial keratitis, exposure keratopathy, band keratopathy
Trabecular meshwork and anterior chamber angle	Trabecular granuloma, peripheral anterior synechiae, ocular hypertension, glaucoma
Iris	Anterior uveitis (iritis), iris nodules/granuloma, posterior synechiae, pupillary abnormalities
Lens	Cataract
Pars plana/vitreous	Intermediate uveitis
Retina	Retinitis, retinal vasculitis, macular edema
Choroid	Choroiditis, granuloma
Optic nerve	Papillitis, papilledema (increased intracranial pressure due to neurosarcoid), granuloma, optic neuropathy (compressive or infiltrative), optic atrophy
Lacrimal gland	Granuloma, dacryoadenitis, keratoconjunctivitis sicca (dry eye)
Nasolacrimal drainage system	Nasolacrimal duct obstruction
Extraocular muscles and other orbital tissues	Granuloma, strabismus, proptosis, optic nerve compression
Intracranial lesions involving visual pathway	Decreased vision, visual field defects, abnormal pupillary response, abnormal eye movement