OCULAR SARCOIDOSIS

Eye Learn

All about the Eye

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SARCOIDOSIS

1. Describe clinical picture, management and squeal of sarcoid uveitis. J2009
2. Ocular manifestations of sarcoidosis. D2009
3. Clinical features, investigations and management of ocular sarcoidosis. 3+3+4 D2017

Introduction

- Sarcoidosis is a multisystem granulomatous disorder of unknown etiology with protean systemic and ocular manifestations.
- Although intrathoracic manifestations are most common (90%), other sites frequently involved include the lymph nodes, skin, eyes, CNS, bones and joints, liver, and heart.
- Ocular involvement may be present in up to 50% of patients with systemic disease, and uveitis is the most frequent manifestation.
- In most large series, sarcoidosis accounts for up to 10% of all cases of uveitis.

Epidemiology

1. Sarcoidosis has a worldwide distribution and affects all ethnic groups; the highest prevalence is in the northern European countries (40 cases per 100,000 people).
2. In US the disease is up to 20 times more prevalent among African Americans than whites.
3. Both sexes are affected, albeit with a slight female predominance.
4. Onset occurs between the ages of 20 and 50 years, sarcoidosis is also an important diagnostic consideration in older patients.
5. In a recent review, sarcoidosis was a common cause of newly diagnosed uveitis among patients ages 60 years and older.
6. Patients with late-onset sarcoidosis may be more likely to have uveitis and less likely to have asymptomatic chest radiograph abnormalities than younger patients with the disease.
7. Pediatric involvement is uncommon, and the clinical course is atypical.
8. Children with early-onset sarcoidosis (younger than 5 years) are less likely than adults to manifest pulmonary disease and far more likely to have cutaneous and articular involvement; the disease course in older children (8–15 years) approximates that in adults.

Pathogenesis

1. The basic lesion of sarcoidosis is a non-caseating granuloma without histologic evidence of infection or foreign body
2. Although numerous environmental, infectious, and genetic factors have been implicated in causing the disease, no single etiologic agent or genetic locus has been clearly identified in the pathogenesis of sarcoidosis.
3. For instance, the ACCESS (A Case Control Etiologic Study of Sarcoidosis) project suggests that exposure to microbe-rich environments may modestly increase the risk of developing sarcoidosis; however, no dominant factor could be determined.
4. Molecular studies of tissue specimens provide evidence suggesting that mycobacterial and, less convincingly, propionibacterial organisms may be important etiologic factors.
5. A genetic predisposition for the disease is suggested by familial clustering; siblings of patients have a fivefold increased risk of developing the disease.

Syndromes associated with sarcoidosis

1. **Löfgren syndrome**, consists of erythema nodosum, febrile arthropathy, bilateral hilar adenopathy, and is quite responsive to systemic corticosteroids; it has a good long-term prognosis.
2. **Heerfordt syndrome** (uveoparotid fever), is characterized by uveitis, parotitis, fever, and facial nerve palsy.

Systemic disease

1. Systemic sarcoidosis may present acutely, frequently with associated anterior uveitis in young patients, and spontaneously remit within 2 years of onset.
2. Chronic sarcoidosis presents insidiously and is characterized by persistent disease of more than 2 years' duration, frequently with interpulmonary involvement and chronic uveitis. Extended corticosteroid therapy may be required.
3. Pulmonary disease is the major cause of morbidity; overall mortality from sarcoidosis approaches 5% but may be as high as 10% with neurosarcoidosis.

Ocular disease

- Symptoms of uveal involvement are variable and frequently include mild to moderate blurring of vision and aching around the eyes.

Orbit, lid and adnexa

1. Sarcoidosis can affect any ocular tissue, including the orbit and adnexa.
2. Cutaneous involvement is frequent, and orbital and eyelid granulomas are common
3. Palpebral and bulbar conjunctival nodules may also be observed and provide a readily accessible site for tissue biopsy
4. Lacrimal gland infiltration may cause keratoconjunctivitis sicca

Anterior segment

1. Anterior uveitis, presenting either acutely or as a chronic granulomatous uveitis, is the most common ocular lesion, occurring in approximately two-thirds of patients with ocular sarcoidosis.
2. Typical biomicroscopic findings include mutton-fat KPs, including those involving the anterior chamber angle
3. Koeppe and Busacca iris nodules
4. Large iris granulomas may also be noted.
5. Cornea is infrequently involved, nummular corneal infiltrates and inferior corneal endothelial opacification may be present.
6. Band keratopathy may develop as a result of either chronic uveitis or hypercalcemia.
7. Extensive posterior synechiae may lead to iris bombé and angle-closure glaucoma.
8. Peripheral anterior synechiae may also be extensive, encompassing the entire angle for 360° in advanced cases.
9. Secondary glaucoma, together with sarcoid uveitis, may be severe and portends a poor prognosis with associated severe vision loss.

Posterior segment

1. Posterior segment lesions occur in up to 20% of patients with ocular sarcoidosis.
2. Vitreous involvement is common and often presents as White clumps of cells ("snowballs") in the inferior anterior vitreous with or without diffuse cellular infiltration.
3. Vitreous cells may also form linear strands known as "string of pearls."
4. Nodular granulomas measuring ¼–1 disc diameter may be present on the optic nerve, in both the retina and the choroid, either posteriorly or peripherally.
5. Perivascular sheathing is also common, appearing most often as either a linear or segmental periphlebitis
6. Irregular nodular granulomas along venules have been termed candle-wax drippings, or taches de bougie.
7. Occlusive retinal vascular disease BRVO and, less commonly, CRVO, together with peripheral retinal capillary nonperfusion, may lead to retinal neovascularization and vitreous hemorrhage.
8. CME is frequently present.
9. Optic disc edema without granulomatous invasion of the optic nerve may be observed in patients with papilledema and neurosarcoidosis.

Differential diagnosis in children

1. Early onset sarcoidosis in children (5 years of age or younger) must be differentiated from JIA-associated anterior uveitis and from familial juvenile systemic granulomatosis (Blau syndrome), given the overlap of ocular and articular involvement.
2. Familial juvenile systemic granulomatosis, an autosomal dominantly inherited syndrome with 100% phenotypic correspondence to mutations in the NOD2 gene (also known as CARD15), may produce ocular disease that is virtually identical to sarcoidosis and should be suspected in patients with a family history of granulomatous disease.

Investigations

1. **Chest X-ray**	Abnormalities are present at some point in up to 90% of sarcoid patients, but these abnormalities do not persist throughout the disease course and thus may be absent at the time of workup.
2. **HRCT**	1. It is a more sensitive imaging modality and may be valuable in patients with a normal appearance on chest X-ray but a high clinical index of suspicion remains. 2. The risk of increased radiation must be weighed against the clinical utility of the information gained in such cases.
3. **Serum ACE and lysozyme levels**	1. They may be abnormally elevated, neither result is diagnostic nor specific; rather, they are reflective of total-body granuloma content and, as such, may be useful in tracking active disease. 2. ACE levels may be low in patients taking ACE- inhibitor medications, high in exercise
4. **serum & urinary Ca , LFT**	These assessments are not specific for sarcoidosis, but they may suggest more widespread involvement in patients likely to have the disease.
5. **Gallium scanning**	It has been used to check for occult disease activity, but it has limited sensitivity.
6. **FDG-PET Scan**	It is considered more accurate in pulmonary and extrapulmonary sarcoidosis, but its utility in ophthalmic sarcoidosis is not well defined

7. **Bronchoalveolar lavage**	The finding of mononuclear alveolitis with increased CD4+ lymphocytes
8. **Biopsy-**	1. Diagnosis of sarcoidosis is made histologically from tissue obtained from the lungs, mediastinal lymph nodes, skin, peripheral lymph nodes, liver, conjunctiva, minor salivary glands, or lacrimal glands. 2. Readily accessible and clinically evident lesions (such as those on the skin, palpable lymph nodes, and nodules on the conjunctiva) should be sought for biopsy, because they are associated with a high yield and low morbidity and may obviate the need for more invasive transbronchial biopsy.

- Some experts recommend repeating the tests annually in patients with negative results but for whom a strong suspicion for the disease exists
- Diagnostic criteria for ocular sarcoidosis were proposed in an international workshop of ophthalmologists but have yet to be validated. These criteria consist of diagnostic grades ranging from "definitive" (based on tissue biopsy), to "presumed" (based on typical ocular findings with bilateral hilar adenopathy), to "probable" or "possible" disease (with supporting ancillary evidence).

Treatment

1. **Topical, periocular, and systemic corticosteroids are the mainstays of therapy for ocular sarcoidosis.**
2. **Cycloplegia** is useful for comfort and prevention of synechiae.
3. Vision-threatening posterior segment lesions generally require, and are responsive to, **systemic corticosteroids** (prednisone, 40–80 mg/day).
4. **Intravitreal corticosteroids**, including the fluocinolone acetonide implant, are potential treatment options for patients intolerant of systemic therapy, but they leave the systemic disease untreated.
5. **Systemic IMT with methotrexate, azathioprine, mycophenolate mofetil, or cyclosporine** can provide good control of the disease while minimizing the risks of long-term corticosteroid therapy.
6. Recently, the TNF-α inhibitors **infliximab and adalimumab** have been shown to be effective in the treatment of sarcoidosis-associated uveitis. (Paradoxically, the TNF-α inhibitor etanercept has been reported to cause a sarcoid like syndrome in some patients.)
7. The likelihood of significant involvement significant visual improvement is substantially increased with systemic therapy.
8. Patients with chronic vision-threatening sarcoidosis seem to respond better to IMT than to management that simply treats flare-ups with intermittent local or systemic corticosteroids.

Prognosis

- **Prognostic factors associated with vision loss** in patients with ocular sarcoidosis include the
  - **Presence of chronic posterior uveitis,**
  - **Glaucoma,**
  - **A delay in presentation to a uveitis specialist of more than 1 year,**
  - **And the presence of intermediate or posterior uveitis.**
- Poor patient adherence also leads to vision loss, so patients should be educated about the importance of careful monitoring, even if they are asymptomatic.