UVEITIS IN SARCOIDOSIS

Dr. NURCHALIZA H. SIREGAR

Bagian Ilmu Penyakit Mata
Fakultas Kedokteran
Universitas Sumatera Utara

UVEITIS IN SARCOIDOSIS

Sarcoidosis, first recognised as a dermatological rarity in later related to a widely disseminated involvment of the reticulo-endothelial system (benign lymphogranulomatosis), is an affection, or perhaps a group of affection of unknown aetiology which may involve almost every organ in the body. (1)

Sarcoidosis is a common, idiopathic, multistem disorder characterized by the presence of non-caseating granulomata wich may affec virtually any single or combination of organs in the body (2,3,4,6)

Histologically, the lesion consist of non-caseating tubercle comprised of accumulation of epitheloid cell with giant cells. Clinically it may be symptomless but usually it tends to pursue an indolent course for many years, often with exacerbations and remissions, sometimes show spontaneous recovery but occasionally to be progressive with a fatal termination. (1)

Uveitis is the most frequent ocular inflammation in sarcoidosis. Between 25% and 50% of patients with systemic sarcoidosis exhibit ocular inflammatory disease. Sarcoidosis ia 10 times more frequent among American blacks than among White. Person of all age can be affected, although occurrence is most common between the age 20 and 50 years.(3,4,5,6)

PATHOGENESIS

Granulomatous disease is mediated by antigen-stimulated activated T-helper cells, which secrete lymphokines that attract, arrest, and activate monocytes and cause them to differentiate into epitheloid and multi nucleated giant cells. Sarcoidosis seems to reflect an immune response to a still unidentified antigen (or antigens), probably air-borne because of the high frequency of hilar lymphadenopathy involvement at the on set.

In Sarcoidosis the immunoglobulin levels and the absolute and relative amounts of T-cells and activated T-cells are increased at the site of active lesions, as in bronchopulmonary lavage fluid. In active sarcoidosis humoral immunity is heightened, causing increased levels of all major classes of immunoglobulins in the plasma, and common antigens evoke an exaggereated antibody response. Some of the antibodies in the serum react with the patien’s own tissues. Such autoantibodies include rheumatoid factor an antibodies against nuclei and T-lymphocytes. T. Cells activation is manifested by the presence of an increased number of circulating activated lymphocytes and aspontaneous increase in DNA synthesis and lymphokine production by these cells in vitro. Paradoxically, T-cells have a diminished capacity to proliferate with phytohemagglutinin and concanavalin A or to ubiquitous antigens to which they have previously been exposed. This T-cells suppressions affects mainly helper T-cells, hence the ratio of suppressor to helper T-cells becomes elevated. T.cells suppressions is due partly to inhibitory factors, which are also lymphocytotoxuc in the presence of complement. Most person with sarcoidosis are unable to be sensitized to dinitrochlorobenzene or to develop delayed skin rections to
tuberculin and other ubiquitous antigens, or they lose their positive reactivity if they develop sarcoidosis. This anergy is restored after the sarcoidosis resolves. However, persons with sarcoidosis do not manifest impaired rejections of homografts or increased susceptibility to malignant neoplasms or infection (provided that they are not receiving long-term high-dose corticosteroid therapy). A peripheral blood T-cells lymphopenia occurs in sarcoidosis, apparently due to the extravascular pooling of T-lymphocytes in tissue rather than because of immune deficiency.(4) The lungs are affected in about 90% of cases. The initial presentation may vary dramatically, and the clinical course may be acute, subacute or chronic.

1. **Acute disease** usually affects patients during the third decade. It develops over a few and present in one of the following ways:
   a. Lofgren syndrome, which is characterized by fever, erythema nodosum, bilateral hilar lymphadenopathy and frequently arthralgia.
   b. Heerfordt syndrome (unveoparotid fever) which is characterized by fever, parotid enlargement and uveitis.
   c. Seventh nerve palsy with other neurological involvement may be present.

2. **Insidious-onset disease** typically presents during the fifth decade with fatigue, dyspnoea and arthralgia.

**CLINICAL FEATURES (1,2,3,4,5,6)**

1. Lung involvement is the hallmark of these diseases, and staging is based on radiological assessment of both parenchymal and lymphatic involvement as follows:
   a. Stage 1: Bilateral hilar lymphadenopathy
   b. Stage 2: Bilateral hilar lymphadenopathy and reticulonodular parenchymal infiltrates.
   c. Stage 3: Reticulonodular infiltrates alone
   d. Stage 4: Progressive pulmonary fibrosis with bullae formation and bronchiectasis

3. **Skin lesions**
   a. Erythema nodosum is by far the most common. It is characterized by red, tender nodules on the anterior surface of the both legs and occasionally on the buttocks and arms.
   b. Cutaneous granulomata, which may be maculopapular, raised or nodular, may be seen on the face, buttocks and extremities.
   c. Lupus pernio (purple lupus) is the classical cutaneous granulomaous manifestation which is characterized by chronic, indurated, purple-blue lesions

4. **CNS lesions** occur in 5% patients and are associated with significant morbidity and mortality.
   a. Cranial nerve palsies, which may affect any cranial nerve, are the most common CNS manifestation. The facial nerve is most frequently affected
   b. Other lesions include meningeal infiltration, seizures and personality disturbance.
   c. Other lesions may involve the reticuloendothelial system, the liver, kidney, bones and heart.
OCULAR FEATURES
The eye is involved in about 30% of patients with sarcoidosis. Ocular involvement may occur in patients with few, if any, constitutional symptoms, as well as in those with inactive systemic disease.

The posterior segment is involved in about 25% of patients with ocular sarcoidosis and is usually associated with anterior uveitis.

1. Anterior segment lesions may involve the conjunctive, episleraa and rarely, the sclera.
2. Keratoconjunctivities sicca may occur as a result of lacrimal gland involvement.
3. Anterior uveitis is usually bilateral and may be either acute or chronic.
   a. Acute iridocyclitis typically young patients with acute sarcoidosis.
   b. Chronic granulomatous iridocyclitis usually affects older patients with chronic lung fibrosis in whom the systemic disease may be inactive.

The intraocular inflammation, may be difficult to control the complications such as band keratophaty, complicated cataract. Koepppe and Busacca iris nodules and white clups of cells (snowballs) in the inferior anterior vitreous are typical findings. Nummular corneal infiltrates, inferior corneal endothelial opacification, and large iris granulomas also occur. Posterior synechiae can be extensive and may lead to iris bombe and large angle-closure glaucoma. Peripheral anterior synechiae may be extensive, encompassing the entire angle, 360° in advanced cases. Secondary glaucoma may be severe, particularly when aggressive steroid theraphy reverses ciliary body hyposcretion. The iridocyclitis may vary and at time can be indistinguishable from acute nongranulomatous disease.

4. Vitreous changes are either in the form of diffuse vitritis or, less frequently, “cotton ball” opacities.
5. Periphlebitis is the most common feature of posterior segment sarcoidosis. It is most frequently mild, although rarely advanced peprphlebitis gives rise to the characteristic perivascular “candle-wax drippings”. Although acute lesions may resolve spontaneously or with the use of systemic steroids, vascular sheating, once established, usually persists.
6. Retinal and preretinal granulomata are uncommon. The letter are typically discrete, grey-white and located inferior and anterior to equator (Lander sign).
7. Choroidal granulomata are common and characterized by bilateral, multiple, small, pale-yellow elevated lesion, usually most numerous inferiorly. Rarely a choroidalgranuloma may be solitary and large and may be mistaken for an amelanotic melanoma.
8. Acute sarcoid retinopathy is characterized by combination of vitreous haze, “candlewax drippings”, retinal and preretinal granulomata and retinal haemorrhages.
9. Periperal retina neovascularatization may occur in association with capillary drop-out on fluorescein angiography. In black patients it may be a confused with sickle-cell retinopathy.
10. Optic nerve lesions may be of the following types:
   a. Focal granulomata may involve the optic nerve but do not usually affect visual acuity.
   b. Papilloedema is usually secondary to CNS involement and may occur in the absence of the other ocular lesions.
   c. Disc neovascularization is an occasional complication of retinal branch vein occlusion, secondary to reserve periphlebitis or rarely, it may be associated with an optic nerve head granuloma.
d. Persistent disc oedema of unknown cause is frequent finding in patients with retinal or vitreous involvement.

**DIAGNOSTIC TEST (2,3,4,5,6)**

Although the diagnostic is often easy, in some patients of features are missing and the following special investigation may be useful:

1. Chest radiographs are abnormal in over 90% of patients.
2. Biopsy
   a. Lung biopsy is accurate in diagnosing sarcoidosis in about 90% of patients.
   b. Conjunctival biopsy is positive in about 90% patients irrespective of the presence of eye involvement.
   c. Lacrimal gland biopsy by transjunctival route may be considered in patients with suspected sarcoidosis, particularly if the lacrimal glands are enlarged or if they demonstrated increased gallium uptake. Biopsies are positive in 25% of patients non-enlarged and in 75% enlarged glands.
3. The Kveim Silzbach test is positive in 85-90% in patients with early or active systematic disease but sensitive decreases with chronicity.
4. Serum angiotensin-converting enzyme (ACE) is usually elevated in patients with active sarcoidosis and normal during remission. In patients with suspected neutosarcoid, ACE should be measured in the cerebrospinal fluid.
5. Calcium assays show abnormal metabolism. Hypercalciuria is common but hypercalcaemia is unusual.
6. Gallium-67 scan of the head, neck and thorax frequently shows increased uptake in patients with active sarcoidosis.
7. Bronchoalveolar lavage shows a raised proportion of activated T-helper lymphocytes.

**TREATMENT (2,3,5)**

Topical periocular, and systematic corticosteroids are variable necessary. Cycloplegia is required for comfort and for prevention of synechiae. When systematic disease is present, cooperation between the ophthalmologist and internist is required to device an optimal therapeutic plan.

Patients diagnosed and treated early have a favorable outcome and are left with little residual ocular disability. Topical steroids are not always adequate, and periocular steroid injection of 20-40 mg of depomethylprednisolone may be needed to supplement drops for anterior nodular iritis and glaucoma. Systemic corticosteroids in high initial doses are often necessary as well as, e.g. prednisone 40-60 mg PO qd with taper over several weeks. Cycloplegics (atropine, homotropine) are continued throughout the steroid course. Cyclosporine A has been used successfully in recalcitrant cases, but no regimen has been established. Cytotoxic agents such as azathioprine or cyclophosphamide offer no advantage.

**REFERENCES**