SARCOIDOSIS

EyeToday

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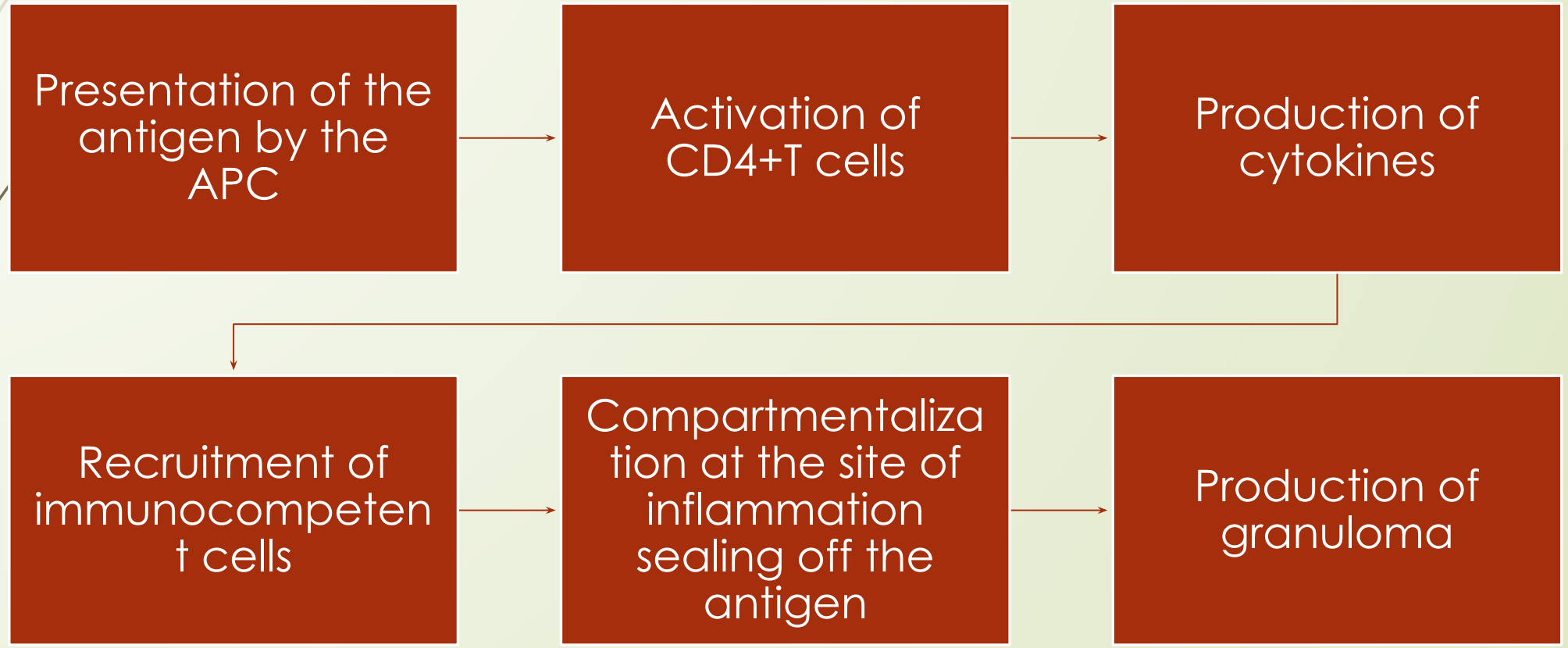
SARCOIDOSIS

It is a chronic multisystemic granulomatous disorder caused by an exaggerated cellular response to a variety of self or non self antigens in a genetically predisposed individual

It is characterized by non caseating granuloma affecting many organs including the lung,lymph nodes,skin,heart,liver,muscles and eye

PATHOGENESIS

The disorder is caused by antigenic stimulation which activates a cascade of immune response in a genetically susceptible individuals



HISTOPATHOLOGY

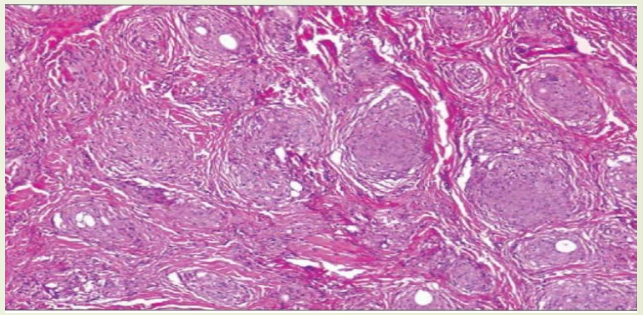
Sarcoidosis nodule- consists of non caseating epithelium cell granuloma

Granulomas- cluster of closely packed epitheloid cells,macrophages and multinucleated giant cells. It is surrounded by a thin rim of mostly CD4+ T lymphocytes, monocytes and fibroblasts

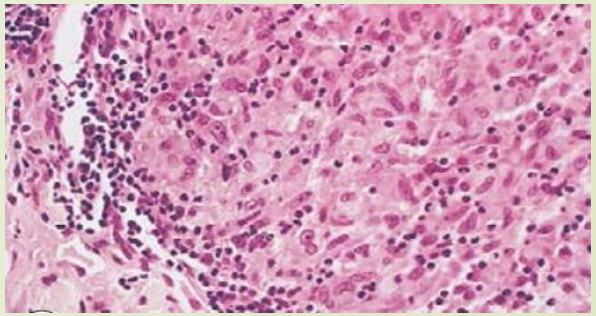
Mature granuloma- epitheloid cell fuse to form Langhan's giant cells which has eosinophilic granular cytoplasm surrounded by incomplete ring of nuclei

Inclusion bodies:

- Schaumann's bodies
- Crystalline inclusions
- Asteroid bodies



Sarcoid nodule



Epitheloid cell

ETIOLOGY

1. Infectious

- Bacterial: M. tuberculosis, Mycoplasma sp., Corynebacteria sp., Spirochetes, Atypical mycobacteria, P. acnes, B. burgdorferi
- Viral: Herpes simplex virus, Hepatitis C virus, EpsteinBarr virus, Cytomegalovirus, Coxsackievirus, Rubella virus
- Fungal: Histoplasma species, Cryptococcus species, Coccidioidomycosis, and Sporotrichosis.

2. Environmental

- Metals (e.g. zirconium, aluminum, beryllium)
- Organic dusts (e.g. pine, pollen)
- Inorganic dusts (e.g. clay, soil, talc)

3. Heat shock protein

4. Autoantigens

Systemic features

General symptoms :

Respiratory symptoms- cough,shortness of breath on exertion

Constitutional symptoms- malaise,arthralgia,weight loss

Syndromes :

- **Lofgren syndrome**- acute presentation with good prognosis

Triad of erythema nodosum,B\L hilar lymphadenopathy, polyarthralgia

- **Heerfordt's disease(Uveoparotid fever)**

  Uveitis

  Parotid gland enlargement

  Fever

  Facial nerve palsy

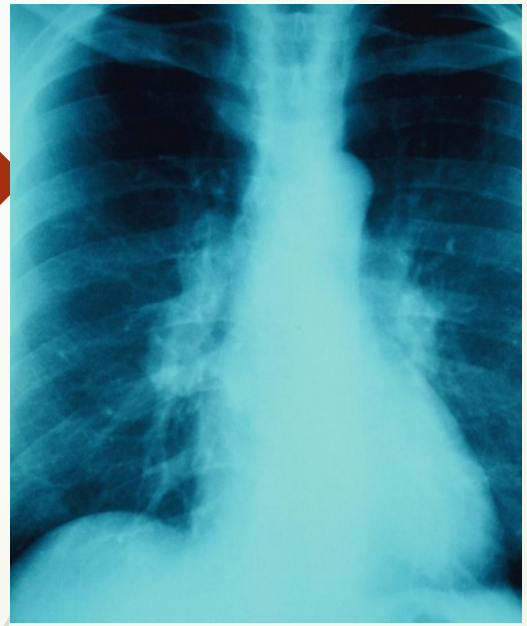
Lung manifestations

Lung disease ranges from mild parenchymal infiltration to severe pulmonary fibrosis

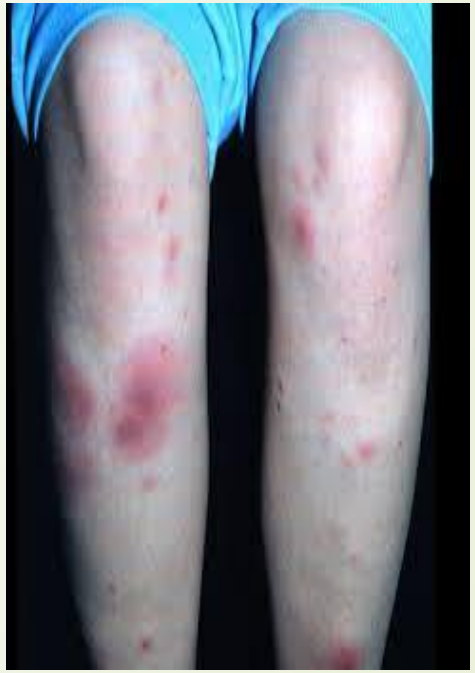
Radiological staging(Scadding scale):

- Stage 0: No abnormalities on chest X-ray; parenchymal abnormalities may be detected on CT.
- Stage I: Bilateral hilar and mediastinal adenopathy; the most common stage at presentation.
- Stage II: Hilar adenopathy plus parenchymal involvement (nodular and reticular opacities).
- Stage III: Parenchymal disease alone.
- Stage IV: Advanced disease with fibrosis.

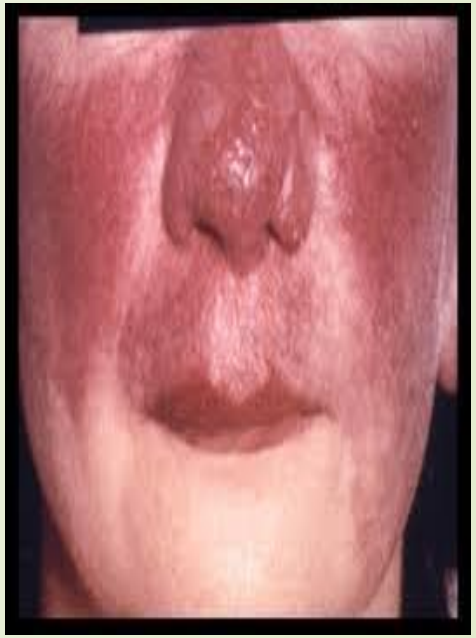
- **Cutaneous manifestation** - Erythema nodosum (common manifestation but is not diagnostic),Lupus pernio (indurated, violaceous plaque usually seen on the face), subcutaneous granulomas and nodules, maculopapular lesions, hyper- or hypo-pigmented plaques, and necrotizing cutaneous vasculitis.
- **Lymph node** enlargement could be generalized or localized to the thoracic region.
- **Hepatic involvement** is usually subclinical with an occasional increase in liver enzymes.
- **Hypercalcemia and/or hypercalcuria** occur secondary to increased production of 1,25 dihydroxyvitamin D by activated macrophages and increase the risk for nephrocalcinosis and nephrolithiasis.
- **Renal involvement** - interstitial nephritis, calculus formation, and renal failure.



B/L hilar lyphadenopathy



Erythema nodosum

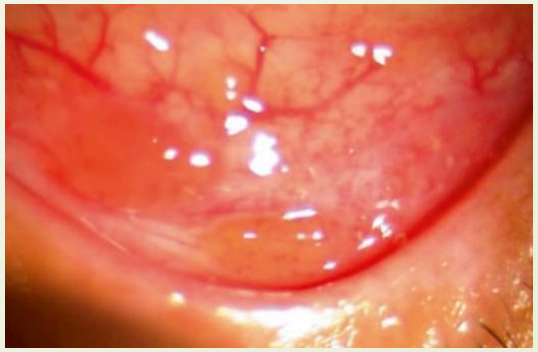


Lupus Pernio

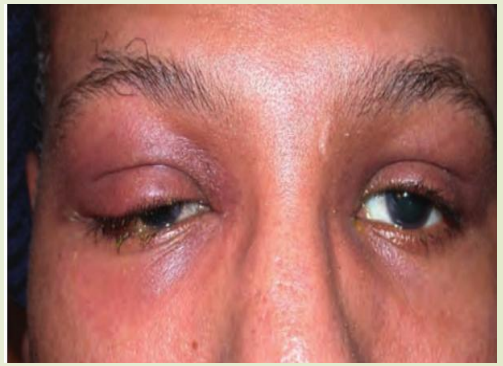
- **Cardiac sarcoidosis** - seen in less than 5 %. It may be in the form of **generalized myocardial involvement with heart failure, conduction abnormalities including paroxysmal ventricular arrhythmia or complete heart block**, and sometimes sudden cardiac death.
- **Arthropathy** is seen in about of 20 % of patients.
- **Neurological involvement** is seen in 5–26 % of patients. They include cranial nerve palsies, encephalopathy, and disorders of the hypothalamus and pituitary gland**. Chiasmal syndromes, motility disorders, facial nerve palsy, and optic nerve involvement** either due to direct sarcoid tissue infiltration or compression by cerebral mass leading to optic nerve atrophy.
- **In children** (less than 4 years of age), sarcoidosis usually manifests as a **triad of rash, uveitis, and arthritis**. In older children, it could be associated with generalized lymphadenopathy and eyes, skin, liver, and lung involvement.

Ocular features -External and anterior segment manifestations

- Dacryoadenopathy is part of the spectrum of orbital sarcoid and is its most common expression
- Lacrimal gland involvement -Dry eye, Severe keratoconjunctivitis sicca ,Sarcoid-induced myositis and Sarcoidosis coexisting with Grave's disease
- Eyelid granulomas are also seen in sarcoidosis.
- Conjunctival granulomas are millet-shaped to large cream to brown nodular lesions.

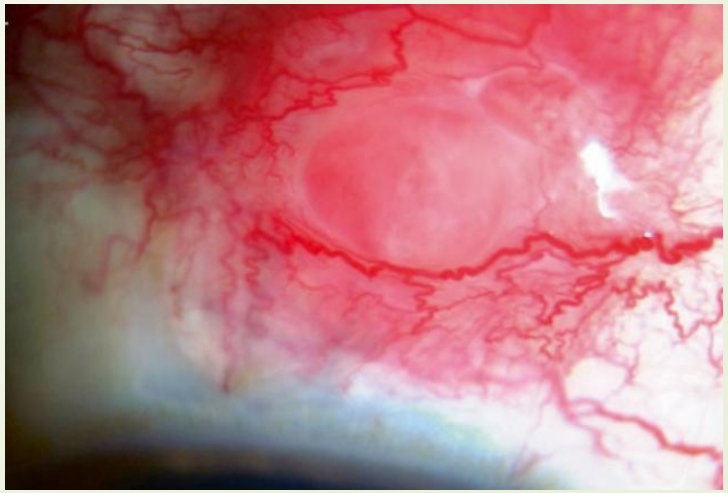


Conjunctival granuloma



Lacrimal gland enlargement

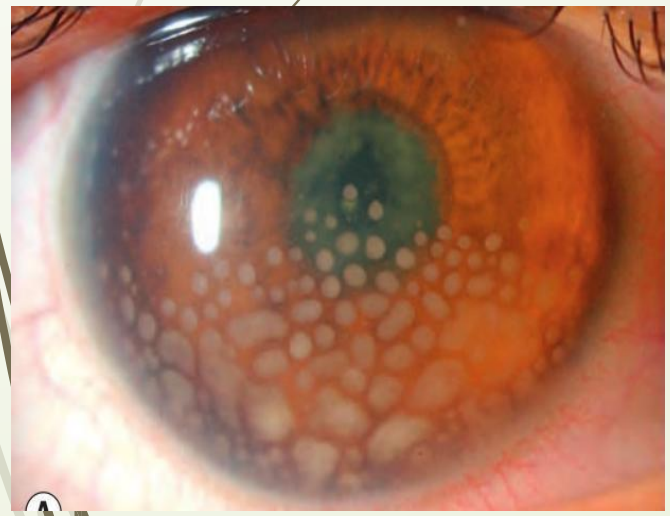
- Anterior and posterior scleral nodules – not typically associated with severe pain or necrosis.
- A nonspecific conjunctivitis, episcleritis, interstitial keratitis
- Long-standing uveitis may lead to corneal band degeneration especially in children
- Diffuse or multifocal gray infiltrates are seen with sarcoid keratitis and may leave faint superficial opacities with resolution.



Scleral nodule

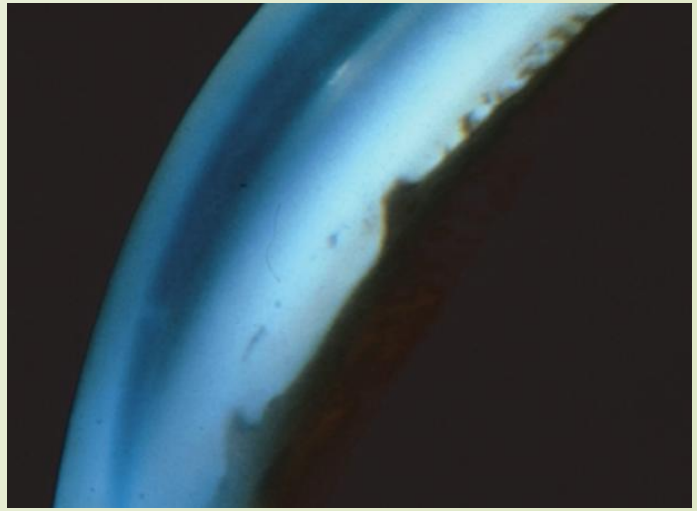
Uveitis

Uveitis- chronic bilateral uveitis and characterized by granulomatous inflammatory reaction in the anterior segment which includes mutton fat keratic precipitates, iris nodules, trabecular meshwork nodules, and tent-shaped peripheral anterior synechiae.



Mutton fat KP's

Iris nodules

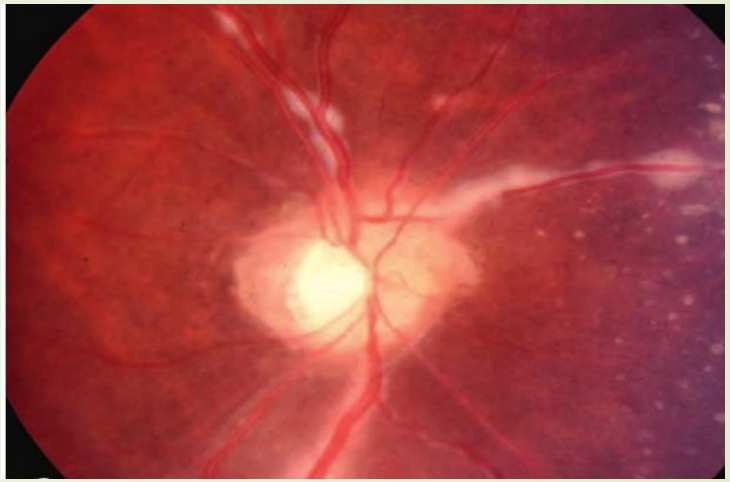


Tent shaped PAS

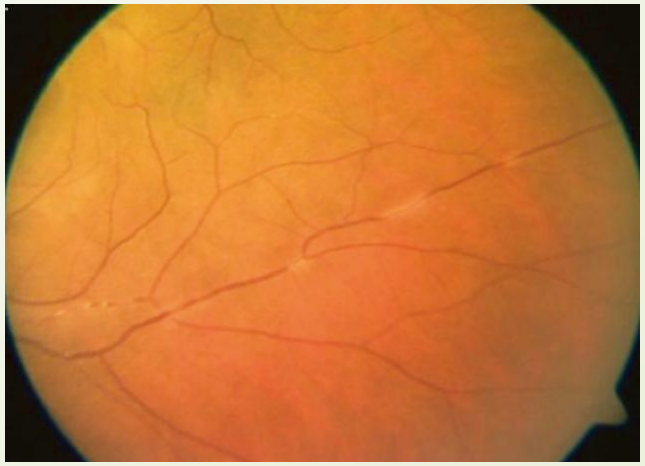
Posterior segment manifestations

- Periphlebitis and vitritis are the most common manifestations
- Periphlebitis frequently involves the midperipheral or peripheral retina, but any venous segment can be involved. When severe, the involved venous segments may demonstrate extensive perivascular exudation that has been likened to candle wax drippings (en taches de bougie).
- Vitritis- Diffuse loss of media clarity or characterized by discrete gray–white opacities that can be scattered throughout the vitreous or primarily involve the inferior vitreous. These "snowball"opacities can occur singly, in clusters, or in a linear array or strand, like a "string of pearls."
- Multiple peripheral active or atrophic chorioretinal lesions, optic disk nodules/granuloma, and choroidal nodules.

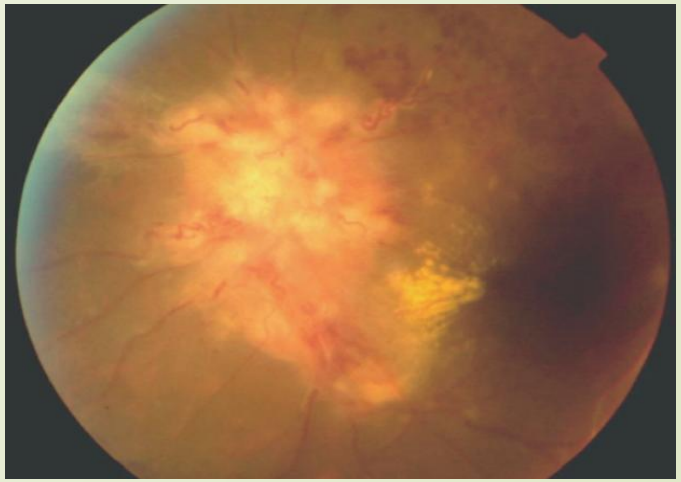
Snow ball opacities



Candle wax dripping



Perivasculitis



Optic disc granuloma

COMPLICATIONS

1. Cystoid macular edema
2. Cataract
3. Glaucoma
4. Retinal ischemia and neovascularizations
5. Corneal bandshaped keratopathy
6. Posterior and peripheral anterior synechiae
7. Epiretinal membrane,
8. Inflammatory choroidal neovascular membranes
9. Retinal detachment and phthisis.

The International Workshop on Ocular Sarcoidosis (IWOS), identified seven key signs in the diagnosis of intraocular sarcoidosis.They are:

1. Mutton fat keratic precipitates and/or iris nodules at papillary margin or on stroma
2. Trabecular meshwork nodules and/or tent-shaped peripheral anterior synechiae
3. Snowballs/strings of pearls vitreous opacities
4. Multifocal peripheral chorioretinal lesions (active and atrophic)
5. Nodular and/or segmental periphlebitis (with or without candle wax exudate) and/or macroaneurysm
6. Optic disk nodules/granuloma and/or solitary choroidal nodule
7. Bilateral inflammation

Laboratory investigations

1. Negative tuberculin test in a patient who either had BCG vaccination or previously had a positive tuberculin test
2. Elevated serum angiotensin-converting enzyme and/or elevated serum lysozyme
3. Chest X-ray: bilateral hilar lymphadenopathy
4. Abnormal liver enzyme tests (any 2: of alkaline phosphatase, aspartate transaminase, alanine transaminase)
5. Chest CT scan in patients with normal chest X-ray

Diagnostic criteria

1. Biopsy supported diagnosis with compatible uveitis - Definite ocular sarcoidosis
2. Biopsy not done; bilateral hilar lymphadenopathy with compatible uveitis - Presumed ocular sarcoidosis
3. Biopsy not done; chest X-ray normal; 3 suggestive ocular signs and 2 positive investigational tests- Probable ocular sarcoidosis
4. Biopsy negative; 4 suggestive ocular signs and 2 positive investigations -Possible ocular sarcoidosis

Other investigations:

- Fibreoptic bronchoscopy with biopsy- lung is a common site.
- Thoracic endosonography (endobronchial or oesophageal) with needle aspiration
- Miscellaneous biopsy sites- superficial lymph nodes or skin lesions, conjunctival nodules and lacrimal glands .
- Vitreous biopsy
- MRI cardiac and CNS imaging
- PET scanning and occasionally whole-body gallium scanning.
- Calcium and vitamin D levels
- Pulmonary function test
- Bronchoalveolar lavage fluid (BALF) -CD4/CD8 T cell ratios are a key indicator
- Induced sputum analysis

DIFFERENTIAL DIAGNOSIS

DD for Granulomatous uveitis

Tuberculosis

Syphilis

Vogt-Koyanagi-Harada syndrome

Toxoplasmosis

Herpetic uveitis

Multiple sclerosis

DD for Chorioretinal granulomas

Tuberculosis

Syphilis

Vogt-Koyanagi-Harada syndrome

Birdshot retinochoroidopathy

Primary intraocular lymphoma.

TREATMENT

- **Uveitis**- Corticosteroids(topical, periocular, intravitreal and systemic routes)
- **Indication for systemic steroids**- optic nerve involvement (pulse intravenous route) and severe or resistant posterior uveitis.
- **Corticosteroid resistant or steroid-intolerant cases**- steroid-sparing immunosuppressive agents like methotrexate, mycophenolate mofetil, azathioprine, and cyclosporine.
- **Resistant cases of sarcoidosis**- TNF-a-blocking drugs
- **Peripheral retinal neovascularization**- systemic antiinflammatory treatment and in some cases may require laser treatment(scatter photocoagulation to ischaemic areas).
- **Inflammatory choroidal neovascular membranes and neovascularization**- intravitreal injections of anti VEGF like bevacizumab and ranibizumab
- **Cystoid macular edema**- Intravitreal steroids or sustained steroid drug delivery devices like dexamethasone implants and fluocinolone acetonide implants