A study of ocular sarcoidosis using international workshop for ocular sarcoidosis criteria in a south Indian population

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Abstract

Purpose: To study the clinical profile of patients with ocular sarcoidosis using the new International Workshop for Ocular Sarcoidosis (IWOS) guidelines, in a tertiary care hospital in South India.

Materials and Methods: A retrospective observational study where the records of patients diagnosed to have sarcoidosis were analyzed and regraded according to the new guidelines by the International Workshop for Ocular Sarcoidosis.

Results: Among the 36 sarcoidosis patient records evaluated in the study period, respiratory involvement was found in 80.6% whereas ocular involvement in 38.9% cases. Uveitis was the most common ocular manifestation seen in 59.1% of those who underwent ocular evaluation. Applying the IWOS guidelines in our patients with uveitis, we found, two had definite ocular sarcoidosis; seven had presumed ocular sarcoidosis; four had probable ocular sarcoidosis and none with possible ocular sarcoidosis.

Conclusion: Sarcoidosis is not uncommon in India. Ocular features are common and need to be screened in all patients diagnosed with systemic sarcoidosis. An ophthalmologist can use IWOS criteria in cases of uveitis to clinically diagnose and refer cases for systemic evaluation of sarcoidosis.

Keywords: Angiotensin converting enzyme, Sarcoidosis, Uveitis.

Introduction

Sarcoidosis is a chronic granulomatous disease involving multiple systems including the eye.[1] Ocular sarcoidosis usually presents as a chronic granulomatous uveitis involving both eyes.[2] However, it is often overlooked in favor of tuberculosis, which can also present with similar clinical features. Especially in regions endemic for tuberculosis.[3] There is a wide difference in the line of subsequent management of the two conditions.

The international workshop on ocular sarcoidosis (IWOS) laid down certain diagnostic criteria to aid the identification of ocular sarcoidosis.[4] Our study aimed to apply these revised criteria to patients presenting to our center with a diagnosis of sarcoidosis, to assess ocular involvement.

Materials and Methods

The study was conducted in the Department of Ophthalmology, at a multi-specialty tertiary care University Hospital in South India. The study was conducted according to the guidelines of the declaration of Helsinki and had received the Institutional ethics committee approval. The records of all patients diagnosed with sarcoidosis by the Pulmonologist or Physician, in whom tuberculosis had been excluded by means of a Mantoux test and/or chest x-ray, were analyzed. The period of study was restricted from 2010 to 2016 due to the availability of records. The ocular clinical features were recorded and re-graded as per the guidelines of the IWOS, and results noted. The clinical features recorded included a detailed ocular and systemic history, slit lamp biomicroscopic anterior segment evaluation, fundus evaluation with indirect ophthalmoscopy. Systemic evaluation included a general dermatological evaluation for any papulonodular lesions, chest x-ray or CT scan for hilar lymphadenopathy, serum angiotensin converting enzyme (ACE) levels, Bronchoalveolar lavage (BAL), biopsy of skin lesions or lymph nodes. The results of the systemic examination and investigations performed by other specialties including dermatology, pulmonology and internal medicine were also recorded.

Results

A total of 36 patients had been diagnosed with sarcoidosis according to the hospital database.

22 (61.1%) of these patients had undergone an ophthalmological evaluation, among whom 13 (59%) were females and 9 (41%) were males.

Table 1: Systemic involvement

System involved	Number of patients	Percentage
Respiratory	29	80.6%
Ocular	14	38.9%
Dermatological	8	22.2%
Neurological	4	11.1%

Table 2: Ocular involvement

Ocular feature	Number of patients	Percentage
Uveitis	13	59.1%
3rd cranial nerve palsy	1	4.5%
Other ocular conditions	2	9%

(Primary open angle glaucoma; refractive error)		
Normal ocular study	6	27.4 %

Table 3: Anterior segment manifestations in patients with uveitis (Total number: 13 patients)

Clinical Sign	Number of patients	Percentage
Conjunctival nodule	1	7.7%
Large keratic precipitates	11	84.61%
Iris nodules	10	76.92%
Peripheral anterior synechiae	3	23.07%
Posterior synechiae (broad based)	11	84.61%
Cataract	5	38.46%

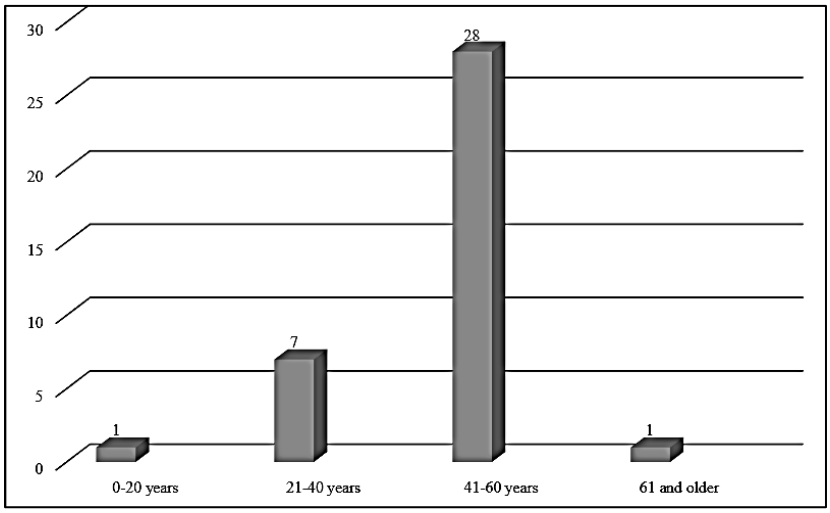
Table 4: Posterior segment manifestations in patients with uveitis (total number: 13 patients)

Clinical sign	Number of patients	Percentage
Vitritis	11	84.61%
Choroiditis	3	23.07%
Retinal vasculitis	4	30.76%
Disc edema	1	7.7%

Table 5. Investigations performed for sarcoidosis (Total number: 36 patients)

Investigation	Number of patients with positive results/ number of patients in whom test was performed	Percentage
Chest x-ray/CTscan for Hilar lymphadenopathy	32/36	88.9%
Serum Angiotensin converting enzyme	25/32	78.1%
Skin biopsy/BAL positivity for sarcoidosis	4/4	100%
Negative Mantoux test	18/18	100%

Chart 1: Age distribution



Discussion

Sarcoidosis is a chronic, immunologically mediated, multisystem disorder.[1] The etiology is not clearly known, but various infectious agents including mycobacteria, herpes group of viruses and environmental factors have been implicated.[5] The pathological characteristic of the disease is a granulomatous inflammation of various systems with the formation of non-caseating granulomas.[3] The respiratory system is most commonly involved. Other systems involved include the skin, lymph nodes, salivary glands, heart, liver and nervous system. In our study we found the respiratory system is involved in almost 80% of patients, followed by ocular involvement in 38.9%, dermatological involvement in 22.2%, and neurological involvement in 11.1%. Our prevalence rates are similar

to those reported in the literature with regards to ocular, dermatological and nervous system involvement respectively.[5,6]

The diagnosis of sarcoidosis in a tuberculosis-endemic country such as ours has been less owing to the overlap of clinical features between the two diseases. Clinicians preferred to err on the side of tuberculosis considering its wider prevalence and contagious nature. Moreover, facilities for biopsy and sample processing for the diagnosis of sarcoidosis were less. The condition was thought to be more prevalent in the socioeconomically affluent western countries. However, with improving standards of living, better control of tuberculosis, and largely due to improved diagnostic facilities, sarcoidosis is gaining recognition and being detected and treated at an earlier stage.[7] Various studies have also described a differing presentation of this condition in our ethnicity, compared to the form seen in the Caucasians, Afro-Americans and Japanese.[8]

The ocular manifestations of sarcoidosis may be seen in 25- 60% of the cases. The classical description of ocular involvement includes orbital inflammatory syndrome, lid and conjunctival granulomata, keratoconjunctivitis sicca, chronic granulomatous anterior uveitis, with large keratic precipitates, iris nodules and both anterior and posterior synechiae. Granulomata in the trabecular meshwork may also be present. Posterior segment involvement may present with intermediate uveitis with vitritis and snow balls in vitreous, multifocal choroiditis, retinal vasculitis with perivascular exudation classically described as candle wax drippings. Optic nerve head involvement may present as Opto ciliary shunts or granulomata.[5] A report from India has mentioned a 29% ocular involvement which is very similar to our result. It also failed to notice the bimodal age distribution or female preponderance in ocular sarcoidosis, a contrast to western reports and found the prevalence of posterior uveitis to be more common in our population.[9]

In our study, of the 22 patients who underwent an ophthalmological exam, 13 had uveitis, one had a third cranial nerve palsy, 6 had no features of ocular involvement and two had conditions which were probably unrelated to sarcoidosis.

Of the 13 with uveitis, keratic precipitates, vitritis, and posterior synechiae were seen in 11 patients; iris nodules in 10; retinal vasculitis in 4 and choroiditis in 3 patients. Our results indicate an increased anterior compared to posterior segment inflammation in our cohort compared to results by Khanna et al.[9]

Investigations in sarcoidosis include nonspecific indicators including serum angiotensin converting enzyme (s ACE) and lysozyme levels.[10] Hilar lymphadenopathy detected by chest radiography or high-resolution computed tomography (HRCT)scan is a more sensitive test.[11] Specific confirmation, however, can be obtained only by detecting the characteristic granulomatous features in biopsied tissue. In respiratory or mediastinal lymphadenopathy, a biopsy may be obtained using bronchoalveolar lavage, or bronchoscopy-assisted specimen retrieval. Of late, endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) of mediastinal lymph nodes with or without transbronchial lung biopsy (TBLB) has been found to have high diagnostic yield especially in early stages of pulmonary sarcoidosis.[12] The dermatological involvement of sarcoidosis may present an ease of access to the biopsy site. However, as the lesions are difficult to diagnose owing to similarity to other conditions, a thorough examination with high index of suspicion is needed to arrive at a diagnosis.[6] In our cohort of 36 sarcoidosis patients, Hilar lymphadenopathy was detected in 32 patients, sACE was elevated in 25 patients, skin biopsy in 3 patients and BAL cytology features in one patient.

The diagnosis of ocular sarcoidosis is further complicated by the fact that it may present without coexisting systemic involvement. As the focus of inflammation is small, most of the diagnostic features including hilar lymphadenopathy and elevated serum ACE levels may be absent. The presence of coexisting cutaneous or lid involvement in these cases may provide an opportunity for biopsy confirmed diagnosis. Another factor in the diagnosis of ocular sarcoidosis in endemic regions is the similarity of its clinical features with ocular tuberculosis. In the absence of coexisting systemic features, the ability to differentiate the two rests solely on certain specific investigative modalities. In such circumstances, the ruling out of Mycobacterium tuberculosis infection is preferred over investigating for sarcoidosis. Intraocular fluid analysis using real time Polymerase chain reaction (RT-PCR) can help in the identification of tuberculosis.[13] The presence of a positive Mantoux test helps to rule out sarcoidosis, which is characterized by cutaneous anergy. The role of interferon gamma assays such as Quantiferon TB Gold, is less specific as there have been some reports of positivity even in sarcoidosis. The role of Mantoux test in the diagnosis of pulmonary tuberculosis in our country is limited due to its low specificity in the presence of high prevalence of latent tuberculosis.[14] Hence it is not routinely asked in all patients with respiratory symptoms. In our study, of the 18 patients who had been administered the Mantoux test, all were negative, supporting the diagnosis of sarcoidosis.

To assist the diagnosis of ocular sarcoidosis, the international working group for ocular sarcoidosis (IWOS) framed guidelines integrating clinical features and investigations.[4] Applying these guidelines in our patients with uveitis, we found, two had definite ocular sarcoidosis; seven had presumed ocular sarcoidosis; four had probable ocular sarcoidosis and none with possible ocular sarcoidosis.

As chronic uveitis, which is relatively painless, is one of the most frequent ocular manifestation of sarcoidosis, if not diagnosed in time, may result in sight

threatening complications including band shaped keratopathy, complicated cataract, secondary glaucoma, cystoid macular edema, and retinal or optic atrophy.[5] In our cohort of 36 patients with systemic sarcoidosis, only 22(61.1%) had undergone an ophthalmological evaluation after their diagnosis. Hence the awareness of ocular involvement should be communicated to other specialties dealing with sarcoidosis, so as to ensure a holistic approach in its management and better quality of life for the patient.

Conclusion

Sarcoidosis is not uncommon in India. Ocular features are common and need to be screened in all patients diagnosed with systemic sarcoidosis. An ophthalmologist can use IWOS criteria in cases of uveitis to clinically diagnose and refer cases for systemic evaluation of sarcoidosis.

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Ethics Approval: The study was approved by the Institutional Ethical committee.

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