

Sarcoid Uveitis: A prospective follow up experience from a tertiary care hospital in Pakistan

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Abstract

Objectives: The Primary objective was to find the frequency of Sarcoid Uveitis among the patients presented with Uveitis. The secondary objective was to follow the patients of sarcoid uveitis over treatment.

Methods: We did an observational prospective study, after acquiring ethical review letter from IRB Medicine department outpatient services of Jinnah Medical College Hospital Korangi was used where patients with Uveitis were referred for evaluation of systemic disease during Jan 2019 to Dec 2020. These patients underwent history, examination and biochemical and radiological investigations and were followed over a period of 1 year to see response to treatment.

Results: A total of 372 patients presented with established uveitis out of which 36 patients i.e. 66 eyes presented to our eye clinic with decrease in vision with a mean age of 42±2 years. Among 36 patients, 89% presented with redness of eye and 72% presented with eye pain where as 8 % presented with photophobia and floaters. Biochemically >10mg/dl calcium was observed in 18(50%) patients and ACE level was found to be more than 40nmol/ml/min in 30(83.3%) patients. Among them 32 (88.9%) patients showed resolved inflammation whereas 2(5.56%) showed a change in inflammation and 2(5.56%) showed no change.

Conclusion: We found sarcoid uveitis as fairly common cause of uveitis. The patients were treated with the standard treatment of steroids and immunosuppressants i.e. Azathioprine and we concluded that use of steroids and immunosuppressant improved the outcome in our patients. The patients responded fairly well to the designed treatment.

Keywords: Sarcoidosis, Uveitis, Sun Classification, Visual Acuity, Systemic Disease.

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Introduction

Sarcoidosis is a multi-systemic disorder of unknown etiology which forms granulomatous inflammation which is non caseous in nature. It is closely related to tuberculosis but is infrequent and rare. It affects young to middle aged individuals with female predominance¹. The primary impact is on the lung and lymphatic system, although nearly

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every organ can be influenced². About 10–25% of cases show involvement in the skin, eyes, peripheral lymph nodes, and liver. The regions with the highest yearly incidence are northern European countries, where the observed rate ranges from 5 to 40 cases per 100,000 people annually³. Pakistan as a country doesn't have much prevalence of Sarcoid and so much work isn't done in this regard as well.

Symptoms of sarcoidosis include fever, cough, dyspnea, fatigue, erythema nodosum, acute polymyositis, arthritis, and skin nodules. Symptoms are very similar to presentation of Tuberculosis hence these patients are often recognised wrong and in turn treated wrong for months. Ocular symptoms in

clude blurred vision, photophobia, floaters, redness, and pain. Diagnostic workup of sarcoidosis includes testing for an elevated angiotensin-converting enzyme (ACE) level and chest x-ray to assess for the presence of hilar lymphadenopathy. However, definitive diagnosis of sarcoidosis requires a positive biopsy of involved organ. The patients are usually mistreated as tuberculosis for months when they present with decrease in vision and photophobia.

Uveitis, characterized by inflammation of the uvea comprising the iris, ciliary body, and choroid, can have various etiologies^{2,4}. This term denotes inflammatory processes impacting the uvea, and the anatomical classification distinguishes anterior, intermediate, posterior, and pan uveitis based on the specific location of inflammation within the eye. In anterior uveitis, the inflammation primarily occurs in the anterior segment. Intermediate uveitis involves inflammation of the vitreous cavity and pars plana, while posterior uveitis affects the retina and choroid. Pan uveitis encompasses inflammation across all layers of the uvea². Conditions with autoimmune origins, such as Ankylosing Spondylitis, Behcet's disease, Psoriatic arthritis, and Sarcoidosis, are often associated with anterior uveitis, whereas infectious agents predominantly contribute to posterior uveitis.

As far as Sarcoid is concerned it can present variably as Panuveitis, Intermediate Uveitis, and Anterior Uveitis. All auto immune entities presents less common as Posterior Uveitis. The presentation also varies according to the structure involved. Patients present with decrease in vision which is progressive with the progression of disease or they may present with Photophobia or floaters. The disease if left untreated can damage the eye and can result in lost eye.

In cases of systemic sarcoidosis, the occurrence of ocular engagement varies widely across different studies, ranging from 13% in the Turkish population to 79% in Japanese patients⁵⁻⁷. Ocular involvement serves as the initial symptom in approximately 20-30% of cases^{8,9}. Uveitis has been documented in 30-70% of instances, and conjunctival nodules were identified in 40% of cases. A stu-

dy involving 121 patients with biopsy-proven ocular sarcoidosis indicated that females (56%) are more prone to developing ocular involvement compared to males (23%)⁹.

Sarcoidosis is a diagnostic challenge in countries where tuberculosis is endemic like Pakistan so there is a difficulty in diagnosing the disease which presents in a similar way. Sarcoidosis is treated with corticosteroids and immunosuppressant. This study was designed to see the prevalence of sarcoidosis in patients with uveitis in a TB endemic country and the patients were started on a standard regimen of steroid and immunosuppressive in order to see the response if it variates from other parts of the world.

The rationale of the study is to observe the prevalence of Sarcoidosis in Tuberculosis endemic area. Not much work is done on Sarcoid Uveitis in our part of country, so there was a gap to study a similar disease but with a different course and treatment regimen altogether. The signs and symptoms of the disease is observed and the patients were started on Steroids and immunosuppressants to see the response if the disease has behaved in an expected way or the outcome is contrary.

Methodology

The study conducted from January 2019 to December 2020 in the outpatient services of Medicine department of Jinnah Medical College Hospital at Korangi. The design was an observational prospective study on patients presented with symptoms of Uveitis, ethical review committee approved study protocol JMC.ERC.1.0702.19 before the commencement of the study . The sample size was calculated using open epi statistical calculator and was found to be $Sample\ size\ n = [DEFF * Np(1-p)] / [(d^2 / Z^2_{1-\alpha/2} * (N-1) + p*(1-p))]$. All patients who presented with the symptoms of Uveitis like decrease in vision, photophobia, floaters were referred to for evaluation of systemic cause. Uveitis was diagnosed through detailed history, general and slit lamp examination. Then they were classified according to standardization of Uveitis Nomenclature

(SUN) workshop¹² classification. If Uveitis was found and it was compatible with the chest and biochemical abnormalities of uveitis then this patient was taken up in study and further worked up. All data was collected on predesigned Performa.

Certain associated symptoms like fever, weight loss, skin lesion, cough, shortness of breath were also inquired. Patients with a positive Montoux test, previous history of Tuberculosis or family history of TB contact were excluded. A general physical examination was done. All patients were investigated at baseline with chest x-ray, Serum Calcium, and ACE levels. Patients with Sarcoid Uveitis were started on Steroids and azathioprine. Usual initial doses of oral prednisone can be as high as 1–1.5 mg/kg/day and were tapered gradually to the lowest effective dose to avoid a flare-up. Azathioprine was used in the dose of 50mg OD.

Ophthalmological examination was performed through slit lamp examination anterior chamber examination and visual acuity by Snellen’s chart at 1, 3, 6 and 12 months follow-up to assess clinical response to drugs. Informed consent was obtained from all patients or the attendant next of kin. Ideally patients should undergo biopsy to achieve tissue diagnosis but as this facility was not available in our set up so we relied on clinical, biochemical, radiological and treatment response grounds.

The analyses were carried out utilizing SPSS (Release 19.0, standard version, copyright © SPSS; 1989–2002). Demographic features were subjected to descriptive analysis, with age presented as mean ± SD for quantitative variables. For qualitative variables such as gender, history, type, and outcome of uveitis (including changes in inflammation, complete resolution, and no change), numbers and percentages were used.

Results

A total of 372 patients presented with established Uveitis out of which 36 patients i.e. 66 eyes presented to our eye clinic with decrease in vision with a mean age of 42 ± 2 years. More than 50% of Uveitis was diagnosed with Tuberculosis. Tuberculosis was excluded first hand in our patients and

the study was devised around patients where more than one evidence pointed towards an alternative diagnosis to Tuberculosis. Among the 36 patients diagnosed with Sarcoidosis, 24(66.7%) were males and 12(33.3%) were females. All patients presented with blurred vision and decrease vision. 89% presented with redness of eye and 72% presented with eye pain where as 8% presented with photophobia and floaters. Biochemically >10mg/dl Calcium was observed in 18 (50%) patients and ACE level was found to be more than 40nmol/ml/min in 30 (83.3%) patients as shown in table 1.

According to ophthalmologic findings, on slit lamp the patients showed features of panuveitis in 12 (33.3%) and 16 (44.4%) showed intermediate Uveitis whereas 4 (11.1%) patients presented each with Anterior and posterior uveitis. Among them 32 (88.9%) patients showed resolves inflammation whereas 2(5.56%) showed a change in inflammation and 2(5.56%) showed no change shown in table 2. Radiologically, according to Radiological findings i.e. X-ray and Computed Tomography, 18 (50%) presented in stage 1 whereas 8 (22.2%) presented in stage 2 disease. CT Hilum showed lymphadenopathy in 26 (72.2%) patients shown in table 3. Ct in table 3 also showed the stages of Sarcoidosis done with radiological finding.

Table 1: Demographics

Demographics	Frequency
Mean age	42 ± 2 years
Gender	
Male	24(66.7%)
Female	12(33.3%)
ESR (mm)	
<60	4 (11.1%)
>60	32 (88.9%)
Symptom	
Decreased vision	36 (100%)
Blurred vision	36 (100%)
Redness of eye	32 (88.9%)
Eye pain	26 (72.2%)
Photophobia	16 (44.4%)
Dark, floating spots in field of vision (floaters)	16 (44.4%)
Serum Calcium>10mg/dl	18 (50%)
ACE LEVEL*(>40 nmol/mL/min)	30 (83.3%)
CT** Hilum	26 (72.2%)

*Angiotensin Converting Enzyme

** Computed Tomography

Table 2. Type of uveitis & outcome

Type Of Uveitis		
Pan uveitis		12(33.3%)
Intermediate uveitis		16 (44.4%)
Anterior uveitis		4 (11.1%)
Posterior uveitis		4 (11.1%)
Outcome		
Resolved		32(88.9%)
Change in inflammation		2 (5.56%)
No change		2 (5.56%)
Stages Of Sarcoidosis		
Stage 0	No abnormality	4 (11.1%)
Stage 1	Hilar lymphadenopathy	18 (50%)
Stage 2	Lymphadenopathy + Infiltrates	8 (22.2%)
Stage 3	Infiltrates	4 (11.1%)
Stage 4	Fibrosis	2 (5.56%)

Discussion

Sarcoidosis exhibits elevated prevalence rates in populations such as Swedes, Danes, and African Americans in the USA. Conversely, it is found to be scarce in countries like Spain, Portugal, India, Saudi Arabia, and South America¹⁰. Limited data is available from Pakistan, where only one small case series indicated a 43% prevalence of sarcoidosis among individuals with isolated mediastinal lymphadenopathy¹¹. The patients were under diagnosed because of TB burden. The patients with long term chronic fever, weight loss and any systemic feature is first thought to have tuberculosis rather than any other entity. This renders them to be misdiagnosed and mistreated as Tuberculosis.

In elderly White females, posterior uveitis with retinal involvement was observed most frequently, while studies with a predominantly Black patient population primarily reported anterior uveitis^{13,14}. Our patients had mean age of 42 years with male preponderance (66%) which was different from the study population in Korea which had mean age of 53 years and female preponderance¹⁵. Sarcoid in our region presents invariably as PanUveitis and intermediate Uveitis, less commonly as Anterior Uveitis. The mean age also represents that mostly Sarcoid affects the patients in ages when they are at their peak working potential as it affects multiple systems of body so the control is cardinal to achieve a good quality of life.

We found ACE levels rose in 83% patients and CT hilum demonstrated hilar lymphadenopathy in 72% patients. Another study done with international cohort showed ACE levels elevated in 62% and Ct hilum with lymphadenopathy of 56%¹⁶. In the Korean study they inquired about uveitis symptoms with biopsy proven sarcoid patient retrospectively where as we investigated the uveitis patients according to radiological and biochemical evidence¹⁵. None of the patients showed any extraocular signs apart from 11% patients with pulmonary symptoms in our study. No cutaneous manifestation was noted in our setup whereas international data shows skin lesions are found in 9%-37% of the patients¹⁷. There are other conditions in which ACE levels rise but we gather evidence on the combined presentation of history ,biochemical and radiological markers.

Takayama indicated that the diagnostic features and lab markers were more likely to be found in younger individuals rather than elderly patients¹⁸, however we did not compare two population sets. They analyzed the stage and presentation of uveitis and categorized accordingly as young age and elderly patients.

Not much international data is available on treatment options in sarcoidosis. Deuchler stated a case report with the lone use of steroid in a patient with complete recovery¹⁹. Certain studies worked in identification of ocular sarcoidosis appear to be a useful decisive clinical marker for determining the prognostic outcome of sarcoidosis patients²⁰. To the best of our knowledge this is one of initial work done in Sarcoid Uveitis in a developing country like Pakistan. In our search we did not find any research pertaining to systemic sarcoidosis rather than ocular sarcoidosis. We devised the treatment in a standard way of giving steroids and immunosuppressants.

Research in Portugal stated the use of methotrexate and had improvement²¹. Patients in our setup were diagnosed and started on Steroids and azathioprine. A dose of 1–1.5 mg/kg/day of oral prednisone was used²². The response to treatment

was assessed in terms of Visual Acuity and resolution of symptoms. We analyzed the patients post treatment at first interaction, 3rd month, 6th month and 1 year of treatment and found good results in terms of resolution of symptoms and betterment of vision. The steroids were tapered off in the follow ups of treatment and azathioprine is continued. According to recent researches if systemic control is achieved eye inflammation subsides as well^{24,25}. Our patients responded fairly well to treatment. And the treatment was taken regularly. The treatment was tailored according to patients response , effects and side effects. It was a life changing experience for patients who had lost their sight to be able to see after being mistreated as tuberculosis for months.

Our study was conducted in an under privileged part of world which is a TB endemic area. The diagnosis of Ocular sarcoid was tricky in diagnostic aspect. Our treatment response was satisfactory. There were certain limitations as our sample size was limited, we cannot project our results on a large population and with that we did not perform biopsy for our patients. It was a single center study and we could not perform ocular biopsy of our patients. Such attributes will be taken into consideration in our next study. Large multicenter study with a greater number of patients can help us better predict the diagnostic challenge and outcome with treatment.

Conclusion

In a TB endemic population, the diagnosis of other uveitis etiologies is a challenge. Timely diagnosis and management can prevent visual loss which renders the patient blind. Early diagnosis still remains as a challenge as provision of ocular biopsy gives a definitive diagnosis which was not performed in our setup. We concluded that sarcoid uveitis is an entity that is fairly prevalent in our part of region and it is underdiagnosed as it is overshadowed by tuberculosis. The response to steroids and immunosuppressants was also tolerable and acceptable in our patients.

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Conflict of Interest

Authors have no conflict of interest and no grant funding from any organization.

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