Cohort Study

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The pattern of sarcoid uveitis at a tertiary care center in Nepal

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Introduction: Sarcoidosis is an idiopathic, multisystemic granulomatous disorder involving the eye with various ocular presentations, the most common being sarcoid uveitis. The diagnosis was based on typical clinical features, chest radiography, laboratory findings and biopsy based on revised International Workshop on Ocular Sarcoidosis criteria. Here in, the authors aim to present the first report on the trend of cases of sarcoid uveitis in Nepal.

Materials and Methods: A retrospective quantitative cross-sectional study was conducted at the uveitis clinic of the Institute of Medicine by obtaining medical data from the medical record section on sarcoid uveitis cases visiting from March 2018 to March 2021. Demographic profile, ocular findings, laboratory findings and treatment details were documented and statistical analysis was done via Statistical Program for Social Science (SPSS) version 23.

Results: Out of 50 eyes of 30 patients included in the study; 66.6% patients ($n = 20$) had bilateral and 33.3% ($n = 10$) had unilateral ocular involvement. Anterior with intermediate uveitis (26.7%) was the most common type of uveitis among the cases. Serum angiotensin converting enzyme was raised in 66.7%, Chest X-ray showed hilar changes in 63.33%, and high-resolution computed tomography showed mediastinal, hilar lymphadenopathy with or without the involvement of the lung in 63.33% of patients.

Conclusion: Sarcoid uveitis may have varied ocular presentations, the commonest being anterior and intermediate uveitis. The commonest complications are cataract and cystoid macular oedema, which are associated with vision loss. Steroids and immunomodulators are the mainstays of treatment.

Keywords: angiotensin converting enzyme, lymphadenopathy, Nepal, sarcoid uveitis, steroid

Introduction

Sarcoidosis is a chronic multisystem granulomatous disorder caused by the exaggerated cellular immune response to a variety of self and non-self-antigen in genetically predisposed individuals[1]. Ocular involvement in systemic sarcoidosis varies worldwide from 12.9 to 79%[2–4]. Ocular sarcoidosis can involve any part of the eye and can present in the form of conjunctival granuloma, episcleritis, scleritis, uveitis, optic neuropathy and adnexal tissues leading to lacrimal gland enlargement and orbital inflammation[5]. Sarcoid uveitis constitute 1.22% of all uveitis cases in the tertiary eye centre in Nepal[6].

HIGHLIGHTS

- It is the first report on the trend of cases of sarcoid uveitis in Nepal.
- The majority of the patients of sarcoid uveitis are between 31 and 45 years of age with the mean age at presentation of 37.4 ± 12.75 years.
- Sarcoid uveitis may have varied presentations, of which anterior and intermediate are the most common and can present with vision-threatening complications.
- Sarcoid uveitis are more common in Stage I systemic sarcoidosis (89.5%).

Majority of sarcoid uveitis are bilateral and chronic. Granulomatous uveitis with keratic precipitates, iris nodules, and vitritis and retinal vasculitis are typical of sarcoid uveitis[7,8]. Vitreous opacity and cystoid macular oedema can cause decreased vision[8]. Systemic involvement includes lungs, thoracic lymph nodes, skin and central nervous system features[8,9]. Diagnosis is made with typical clinical features, positive chest radiography, laboratory findings and biopsy based on International Workshop on Ocular Sarcoidosis (IWOS) criteria[10–12]. Recently, Standardization Of Uveitis Nomenclature (SUN) working group has come up a newer classification criteria where the exclusion criteria's are included[13,14].

This study aims to highlight the pattern of sarcoid uveitis presenting at the tertiary eye hospital of Nepal. To the best of our knowledge, this is the first report from Nepal dedicated to sarcoid uveitis.

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Table 1

Laboratory and radiological parameters in patients with sarcoid uveitis.

Laboratory parameters	Frequency (*n*)	Percentage (%)
Raised serum angiotensin converting enzyme	20	66.7
Negative mantoux reading (< 5 mm)	20	66.7
Hilar and mediastinal lymph node enlargement in HRCT chest	19	63.33
Hilar lymphadenopathy in chest X-ray	19	63.33
Lymphopenia	19	30
High serum calcium	4	13.3
Lymph node biopsy with non-caseating necrosis	2	6.6
Altered liver function test	1	3.3

Few patients have more than one deranged parameters.
HRCT, high-resolution computer tomography.

Materials and methods

A retrospective quantitative study was done in the uveitis clinic of a tertiary eye care centre of Nepal from March 2018 to March 2021. The record of diagnosed cases of sarcoid uveitis meeting the IWOS diagnosis criteria was collected from the hospital medical record section. The demographic analysis, ocular manifestations, ocular complications, and laboratory findings were recorded. Special attention was paid to rule out ocular tuberculosis and ocular syphilis cases based on the exclusion criteria of SUN new classification criteria for sarcoidosis-associated uveitis[15]. The data was tabulated and interpreted in terms of percentage, mean, and standard deviation in the computer using Statistical Program for Social Science (SPSS) version 23. Quantitative parameter was expressed as mean ± SD. Categorical parameter was expressed as number and frequency. The Ethical clearance was obtained from the Institutional Review Committee. The study adhered to the tenets of the Helsinki declarations. And the work has been reported in line with the Strengthening the Reporting of Cohort, Cross Sectional and Case Control Studies in Surgery (STROCSS) criteria[16].

Results

Total 50 eyes of 30 cases of sarcoid uveitis meeting the inclusion criteria were analyzed. The majority of the patients (43.33%) were between 31 and 45 years of age. The mean age at presentation was 37.4 ± 12.75 years (range 9–62 years). Among them 60% ($n = 18$) were female. Around 66.6% ($n = 20$) cases presented with bilateral uveitis.

The diagnosis of sarcoid uveitis was based upon the IWOS clinical and laboratory criteria. The finding of the investigation is tabulated in Table 1.

High-resolution computer tomography chest scan showed mediastinal and hilar lymphadenopathy in 63.3% (*n*-19 cases). Stage I chest involvement was present in 89.5% (*n*-17/19) and rest had Stage II (1/19) and Stage III (1/19) involvement (Fig. 1).

Diagnostic transbronchial bronchoalveolar lavage) was done in 4% of cases, which confirmed the predominance of lymphocytes in the lavage suggestive of pulmonary sarcoidosis. In addition cervical and mandibular lymph node biopsy confirmed the presence of non-caseating granuloma in 6.6% of cases.

Diminution of vision was the most common presenting symptom (57.6%) followed by red eye (26.7%), floaters (16.7%) and ocular pain (16.7%). Anterior uveitis combined with intermediate uveitis was the most common (26.7%) anatomical site of involvement. Next to it was the posterior uveitis (23.3%) (Fig. 2).

Non-granulomatous uveitis was present in 66% (n-33 eyes) and granulomatous uveitis in 34% (*n*–17 eyes). Mutton fat keratic precipitates were present in 22% eyes. There was presence of other signs of granulomatous uveitis in the form of broad-based posterior synechiae (6%) peripheral anterior synechiae (2%) and Koeppe nodule (2%) as shown in Figure 3 A.

Vitritis was present in 24% and snowballs detected in 12% of eyes. Around 26% had multifocal choroiditis and 2% had sclerouveitis (Fig. 3B).

One eye presented with superior-temporal branch venous occlusion, which was managed with focal laser and oral anti-inflammatory agents (Fig. 3C).

Posterior sub-capsular cataract (32%), cystoid macular oedema (16%) eyes and steroid induced ocular hypertension (16%) were the common ocular complications. Corticosteroid as topical eyedrop and oral route (1 mg/kg) was the commonest mode of treatment used for all patients. Around 30% (*n*-9 cases) were under immunosuppressant like oral methotrexate (10–20 mg/week) and azathioprine (1–2 mg/kg). Intravitreal steroid (triamcinolone acetonide (0.1 ml/40 mg) was injected in 4% of eyes ($n = 2$) with cystoid macular oedema.

Discussion

This is the first report on sarcoid uveitis with the aim to contribute to the existing literature from various geographical regions in

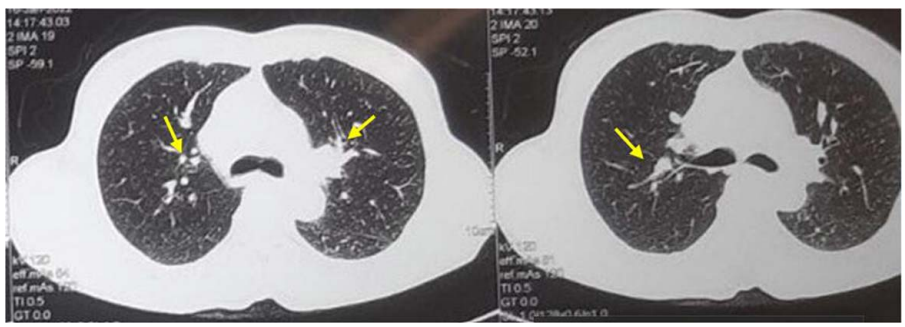

Figure 1. HRCT chest showing miliary nodules predominantly in bilateral upper lung fields with patchy fibrotic changes (yellow arrows) in the right middle lobe, suggestive of sarcoidosis in one of our patient. HRCT, high-resolution computer tomography.

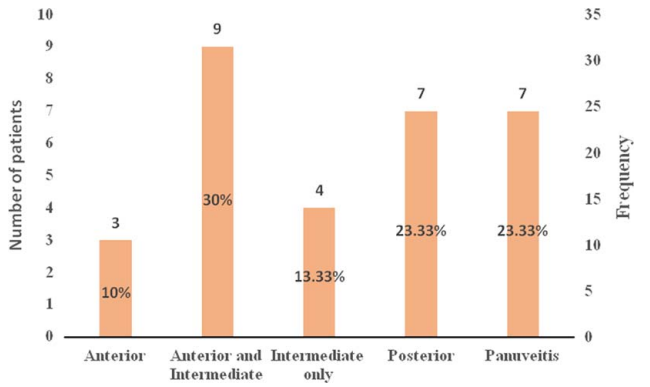

Figure 2. Anatomical distribution of different types of sarcoid uveitis.

Nepal. The vividness in the clinical manifestations of sarcoid uveitis has imparted diagnostic challenges to ascertain the true prevalence of the disease[8,17].

About 30–60% of patients with sarcoidosis develop ophthalmic changes at some point in life[18]. Uveitis is the most common clinical feature of ocular sarcoidosis[1] and is termed as sarcoid uveitis in addition, it can lead to significant visual morbidity in lack of inappropriate diagnosis[19].

Sarcoid uveitis usually affects young adults. The majority of the cases were older than 40 years which is similar to the age pattern from our neighbouring country India[4]. Slightly different from the western studies, where peak ages have been noted between 20–35 years and 50–60 years[10,11]. This difference could be due to a lack of awareness and self-ignorance leading to delayed diagnosis among some geographic regions of the world. Usually among biopsy-proven systemic sarcoidosis cases, females are more likely to develop ocular involvement compared with males[8]. Dana *et al.*[21] reported a prevalence of granulomatous infammation in 81% of those with sarcoid uveitis.

The visual symptoms present among our sarcoid uveitis cases are comparable to the studies from other terrains[4,22,23]. Anterior with intermediate uveitis was the most common uveitis followed by posterior uveitis and panuveitis in this study. It is similar to the Lee and Salmon's studies[24,25]. Panuveitis are common presentation among sarcoid uveitis probably due to delayed presentation to the hospitals in India[4]. In USA too, after anterior uveitis, any anatomic class of uveitis have been reported with sarcoidosis, including intermediate, a mixed anterior and intermediate type, posterior and panuveitis[26].

Vision-threatening complications like cataract, cystoid macular oedema, glaucoma and other macular complications are common in sarcoid uveitis[27].

Babu and colleagues reported deranged serum Angiotensin converting enzyme (ACE) levels and hilar lymphadenopathy in chest computed tomography scan in Indian population; which is similar with our series too[4,28]. But SUN data have not given any definite answer if chest computed tomography scanning should replace chest radiography as a screening tool[26]. Hence, for screening purposes in developing country like ours, the more conventional approach with X-ray chest may be adequate to establish sarcoid or exclude tuberculosis. In endemic regions like ours, as both sarcoid and tuberculosis can produce a similar picture on chest imaging[26,28].

Sarcoid uveitis responds well to steroids, applied locally to the eye or systemically. In some refractory cases, the therapeutic options might be expanded to conventional or biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs)[29]. Sarcoidosis is associated with an overreaction of the immune system. The use of immunomodulators can help to suppress the part or all of the immune response to reduce the symptoms and prevent permanent damage. Hydroxychloroquines and anti-metabolites are in common practice[8,21,28,30].

There have been advances in the classification criteria for sarcoidosis-associated uveitis. Machine learning using multinomial logistic regression and recommendations for the management of ocular sarcoidosis has recently been introduced[14]. This shall establish a wider universal criteria for classification and shall set a universal management protocol for the sarcoid uveitides[14].

Conclusion

Sarcoid uveitis may have varied presentations. Early diagnosis and intervention can be crucial in preventing severe vision-related complications. The commonest complications are cataract and cystoid macular oedema. Hilar and mediastinal lymph nodes are predominantly affected. Steroids (including topical, systemic, and periocular) and immunomodulators (Methotrexate and Azathioprine) are the mainstays of treatment.

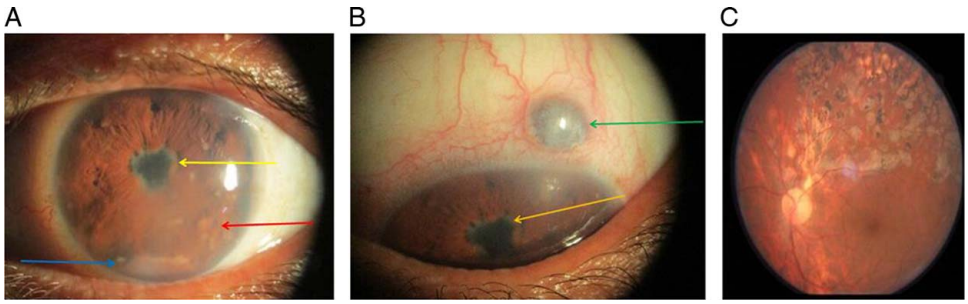

Figure 3. (A) Clinical picture of Sarcoid uveitis showing broad-based synechiae (yellow arrow), multiple iris nodules (red arrow) and peripheral anterior synechiae (blue arrow); (B) Clinical picture of sarcoid sclera-uveitis showing congestion, ciliary staphyloma (green arrow) and broad-based synechiae (yellow arrow) and (C) Fundus photograph of superior-temporal branch venous occlusion in a sarcoid patient treated with focal retinal photocoagulation.

Ethics approval and consent to participate

The study was approved by institutional ethics committee.

Consent

Written informed consent was obtained from the patient for the publication.

Source of funding

No funding was received for the study.

Author contribution

R.K.S., A.P. and S.S. were involved in concept and designing of the study. R.K.S., A.P. and S.S. were involved in data acquisition, data analysis, data interpretation and literature search. R.K. and S.J. were involved in treatment of the patients selected for the study. R.K.S. were involved in manuscript preparation, manuscript editing and manuscript review. A.P. and S.S. were involved in statistical analysis. R.K.S., A.P., S.S. and S.J. worked for editing and revising the manuscript. All authors have read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no competing interests.

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All the required information is in manuscript itself.

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