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RESEARCH ARTICLE

Sarcoidosis-Associated Uveitis in Children: A Multidisciplinary Retrospective Cohort Study

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ABSTRACT

Objective: Sarcoidosis-associated uveitis is rare in children and can cause serious complications. Because pediatric data were limited, this study aimed to characterize clinical features, management, and outcomes using a multidisciplinary cohort approach.

Materials and Methods: A retrospective analysis was conducted of patients under 18 years of age who were managed by the pediatric rheumatology and ophthalmology services between 2017 and 2024. Patients were classified as having probable sarcoidosis-associated uveitis according to the revised International Workshop on Ocular Sarcoidosis (IWOS)criteria because no biopsy was performed. Demographics, clinical characteristics, laboratory findings, treatments, and outcomes were analyzed.

Results: Of the 24 patients screened, 15 (27 eyes) met the inclusion criteria. Age at inclusion was 14.73±2.87 years; age at diagnosis, 10.15 years (IQR, 8.28–11.23). The majority of patients presented with concurrent ocular and systemic sarcoidosis (73%), bilateral involvement (80%), and panuveitis (60%). Chronic inflammation occurred in 80% of patients. Pulmonary involvement was documented in 40% of cases All patients received topical corticosteroids; 86.7% required systemic corticosteroids. Methotrexate was the first-line conventional DMARD (93.3%), and adalimumab was the primary biologic agent (80%). Complete remission was achieved in 53.3% of cases, with surgery needed in 20% of cases. Ocular complications decreased from 33.3% at presentation to 20% at final follow-up. Neither age at onset nor pulmonary involvement significantly influenced remission status.

Conclusion: Pediatric sarcoidosis-associated uveitis emphasizes the importance of a collaborative team-based approach. The absence of pulmonary involvement does not exclude the diagnosis, underscoring the need for a high index of clinical suspicion and comprehensive evaluation in children presenting with chronic uveitis.

Keywords: Medication therapy management, prognosis, sarcoidosis, uveitis

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INTRODUCTION

Sarcoidosis is a multisystem granulomatous disease with heterogeneous clinical manifestations and a potentially chronic course, involving various organ systems, including the eyes.[1] In children, the disease exhibits two clinically distinct phenotypes defined by age at onset, each associated with differing etiologies, patterns of organ involvement, and clinical trajectories. The early-onset phenotype, typically seen in children under 5 years, is characterized by a specific clinical triad involving the skin, joints, and eyes.[2] In contrast, the older-onset phenotype more closely resembles adult sarcoidosis and frequently presents with pulmonary involvement and lymphadenopathy. These phenotypes vary markedly in their systemic features, ocular presentations, and long-term outcomes, underscoring the need for age-specific diagnostic evaluation and individualized therapeutic strategies.[2]

Regardless of the age at onset, ocular involvement—most frequently uveitis—occurs in 20–50% of all pediatric sarcoidosis cases and may be the initial or sole manifestation, highlighting the importance of timely recognition to prevent

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irreversible visual impairment.[3] Despite its clinical relevance, pediatric sarcoid uveitis remains rare, with reported prevalence ranging from 0% to 14.8% worldwide, and its management is challenged by limited pediatric-specific, evidence-based treatment guidelines.[3–11] Both sexes appear to be affected equally, although precise estimates are limited by the small number of cases reported in most series.[12,13]

Ocular sarcoidosis in children poses diagnostic difficulties due to its heterogeneous presentation and the lack of validated pediatric criteria. Although the International Workshop on Ocular Sarcoidosis (IWOS) framework is widely used, it was developed for adults and depends on biopsy confirmation, which is often impractical in children.[14] Consequently, heightened clinical suspicion and thorough biomicroscopic assessment are essential, and all patients with granulomatous or posterior uveitis should undergo targeted evaluation for sarcoidosis.[15]

Current management strategies generally parallel those used for other forms of pediatric noninfectious uveitis. Given the potential for disease persistence into adulthood and the notable risk of sight-threatening complications, early diagnosis, timely initiation of effective therapy, and coordinated long-term follow-up are essential for optimizing visual outcomes in affected children.[16]

This study aims to provide comprehensive data on patients with pediatric sarcoid uveitis managed through multidisciplinary collaboration between the ophthalmology and pediatric rheumatology teams, including patient demographics, clinical presentations, disease subtypes, treatment approaches, and long-term outcomes.

MATERIALS and METHODS

Study Design and Patient Selection

We conducted a retrospective analysis of patients who were managed by the pediatric rheumatology and ophthalmology services for at least 6 months between 2017 and 2024. The study included children under 18 years of age who were diagnosed with sarcoid uveitis. All patients underwent systematic screening for tuberculosis, syphilis, and other infectious etiologies. Patients with evidence of infectious causes or those in whom the ophthalmologist was uncertain about the characteristic features of sarcoidosis-related uveitis were excluded from the study.

A total of 24 patients with a preliminary diagnosis of sarcoidosis-associated uveitis were initially screened for inclusion. Following comprehensive ophthalmological and systemic evaluation, 9 patients were excluded from the analysis after being reclassified as having idiopathic granulomatous uveitis (because they did not fully meet the revised IWOS criteria for sarcoidosis). Consequently, the final study cohort consisted of 15 patients (27 eyes) who fulfilled the diagnostic criteria for probable sarcoid uveitis.

Data Collection and Clinical Assessment

Patient demographics, clinical presentations, laboratory parameters, therapeutic approaches, and ophthalmologic outcomes were retrieved from hospital records and digital databases.

Definitions of Disease States and Outcomes

Ocular sarcoidosis was diagnosed and classified as "probable sarcoidosis" according to the revised International Workshop on Ocular Sarcoidosis(IWOS)criteria, as biopsy was not feasible in our cohort.[14] The diagnosis was established after excluding other causes of granulomatous uveitis and was based on specific intraocular clinical findings (e.g., mutton-fat KPs, iris nodules, snowballs) and systemic investigation results (e.g., hilar lymphadenopathy, negative tuberculin test, elevated ACE/lysozyme levels).

Uveitis was categorized by anatomical site (anterior, intermediate, posterior, or panuveitis) and clinical pattern (acute, recurrent, or chronic) based on SUN guidelines.[17]

Uveitis outcomes were divided into three types: complete remission(with or without therapeutic intervention), partial remission, and non-remission.[17,18]

Ophthalmologic Assessment

At each visit, a complete ocular examination was performed, including best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, applanation or non-contact tonometry, and indirect ophthalmoscopy. Visual acuities were converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Anterior chamber cell and flare values were evaluated according to the Standardization of Uveitis Nomenclature (SUN) Working Group classification.[17] Optical coherence tomography (OCT) was performed concurrently, whereas fluorescein angiography and indocyanine green angiography were performed during follow-up as appropriate.

Statistical Analysis

Demographic and clinical characteristics of the patient cohort were presented using descriptive statistics, with means and standard deviations (SD) reported for continuous variables and frequencies with percentages for categorical variables. The distribution of anatomical involvement, disease course patterns, and treatment outcomes was expressed as counts and proportions.

Because the data were not normally distributed, follow-up duration and time to disease remission were reported as medians

with interquartile ranges (IQR). Statistical analyses were performed using IBM SPSS for Windows, version 26.0 (IBM Corp., Armonk, NY, USA), with statistical significance set at $p<0.05$.

Ethical Committee Approval

The study protocol was approved by the Istanbul University Faculty of Medicine Local Ethics Committee (date/no: 12.09.2025/3582195). The research was conducted in accordance with the principles of the Declaration of Helsinki and complied with all applicable local laws and regulations.

RESULTS

Demographics, Laboratory Findings, and Uveitis Characteristics

The final study cohort consisted of 15 patients (27 eyes) with sarcoid uveitis. The mean age at study inclusion was 14.73±2.87 years, with a male predominance (66.6%, n=10). The median age at diagnosis was 10.15 years (IQR, 8.28–11.23), and the mean follow-up duration was 36.34±19.05 months (range: 7.0–76.6 months).

Regarding the temporal relationship between manifestations, concurrent ocular and systemic involvement was observed in the majority of patients (73.3%, n=11). Uveitis preceded systemic diagnosis in two patients (13.3%) by 12 and 24 months, respectively. Conversely, in the remaining two patients, uveitis was diagnosed after systemic sarcoidosis at intervals of 4 and 12 months.

Table 1. Demographic, clinical and laboratory features of the patients with sarcoidosis-associated uveitis

	n	%
Number of patients	15	100
Gender (male)	10	66.6
Localization of uveitis		
Anterior uveitis	5	33.3
Intermediate uveitis	0	0
Posterior uveitis	1	6.6
Panuveitis uveitis	9	60
Duration of uveitis		
Limited	4	27
Persistent	11	73
Chronic uveitis	12	80
Bilateral involvement	12	80
Pulmonary involvement	6	40
Symptomatic	14	93.3
ACE positivity, n/N	6/13	46
Lysozyme positivity, n/N	1/3	33.3

ACE: Angiotensin-converting enzyme.

Uveitis was symptomatic in 93.3% of patients. Bilateral involvement predominated over unilateral disease (80% vs 20%), with granulomatous inflammation documented in 41.6% of cases. By anatomical location, anterior uveitis was observed in 5 patients (33.3%), posterior uveitis in 1 patient (6.6%), and panuveitis in 9 patients (60%). The clinical course was characterized by chronic inflammation in 80% (n=12) of patients, with persistent disease activity in 73% (n=11) (Table 1).

Pulmonary involvement was documented in 6 patients (40%). Laboratory abnormalities included elevated angiotensin-converting enzyme (ACE) levels in 6 of 13 tested patients (46%) and elevated lysozyme levels in 1 of 3 tested patients (33.3%) (Table 1).

Treatment and Outcomes

All patients received topical corticosteroid therapy. Systemic corticosteroids were administered to 13 patients (86.7%). Treatment strategies were primarily determined by disease severity and anatomical localization. For patients with panuveitis(n=9), a combination of methotrexate and adalimumab was initiated as the primary systemic therapy. In contrast, for anterior uveitis (n=5) and posterior uveitis (n=1), a step-up approach was used in which therapy was escalated from conventional DMARDs to biologic agents based on clinical response. Methotrexate was the first-line conventional DMARD (cDMARD) in 14 patients (93.3%); additional conventional agents included mycophenolate mofetil in 2 patients (13.3%) — one of whom received MMF because of MTX intolerance — and azathioprine in 1 patient (6.7%). Biological DMARDs (bDMARDs) were dominated by tumor necrosis factor-α (TNF-α) blockers, with adalimumab administered to 12 patients (80%) and administered infliximab to 1 patient(6.7%)(Table 2).

Table 2. Treatment characteristics and outcomes of uveitis

	n	%
Local treatment	100	100
Systemic steroid	13	86.7
MTX	14	93.3
MMF	2	13.3
AZT	1	6.7
ADA	12	80
INF	1	13.3
Surgery intervention	3	20
Recurrence	2	13.3

MTX: Methotrexate; MMF: Mycophenolate mofetil; AZT: Azathioprine; ADA: Adalimumab; INF: Infliximab

Surgical intervention was required in 3(20%) of the patients. Disease recurrence was documented in 2 (13.3%) patients during the follow-up period (Table 2).

At initial presentation, ocular complications were present in 5 (33.3%) patients, including posterior synechiae, band keratopathy, and glaucoma. At the final follow-up visit, complications persisted in 3 (12.5%) patients, including cataracts in 2 (8.3%) patients and glaucoma in 1 patient.

Complete remission was achieved in 8 (53.3%) patients; treatment resistance was observed in 2 (13.3%) patients (Table 2). Specifically, in the remission group, the median age at diagnosis was 10.3 years (IQR, 8.4–11.5) compared with a mean age of 7.75 years in the treatment-resistant group. There was no statistically significant difference between age at uveitis onset and treatment response (p>0.45). Disease recurrence was documented in 2 (13.3%) patients during the follow-up period (Table 2).

Among the 6 patients (40%) with pulmonary involvement. When cases were analyzed by treatment response, pulmonary disease was found in 60% (n=3/5) of the partial remission group and in 25% (n=2/8) of the complete remission group. Although the prevalence was numerically higher in the partial remission group, the difference was not statistically significant (p=0.279).

Notably, there was no significant difference in remission rates between patients with elevated ACE levels (6/13) and those with normal values (p=0.62).

On the logarithmic scale, the median logMAR visual acuity at baseline was 0.13 (IQR, 0.0–0.7) and at final follow-up was 0.0 (IQR, 0.0–0.4); however, this improvement did not reach statistical significance (p=0.142).

DISCUSSION

Sarcoidosis presents significant diagnostic challenges, with high rates of both underdiagnosis and misdiagnosis. In pediatric patients, the condition is particularly likely to be masked or to present atypically. The lack of specific guidelines for evaluating and managing pediatric sarcoid uveitis further compounds these diagnostic difficulties, potentially leading to delayed recognition and suboptimal patient outcomes.

This study presents data from a pediatric cohort that examines treatment outcomes in probable sarcoid uveitis, thereby addressing a significant gap in the literature, in which pediatric evidence remains limited. Regarding sex distribution, the majority of our patients were male. While adult sarcoidosis typically exhibits a female predominance, the sex distribution in pediatric sarcoidosis-associated uveitis appears less skewed. According to Choi et al.,[13] both girls and boys develop sarcoid uveitis with relatively similar frequencies, although some cohorts have noted a slight male preponderance. Determining an accurate sex ratio remains challenging in the pediatric population given the rarity of the disease and the resulting small sample sizes across studies.[12,13,19] Our findings align with the observation that the classic female-dominant pattern of adult sarcoidosis may not be directly applicable to pediatric-onset ocular involvement.

The high prevalence of panuveitis, characterized by bilateral involvement and a chronic disease course in our cohort, is consistent with the established profile of sarcoid uveitis as a sight-threatening condition necessitating intensive immunosuppressive therapy.[11] Phenomenological variations are evident globally; while anterior uveitis predominates in European populations (77%), panuveitis is more prevalent among Asian cohorts (63%).[5,20] In the context of early-onset sarcoidosis, panuveitis has been reported in 51% of eyes, compared to 29% for anterior involvement.[21] Similarly, panuveitis remains the most frequent clinical presentation in late-onset pediatric sarcoidosis, particularly in children over five years of age.[16,20] Our findings of bilateral panuveitis align with the rates of 43–85% reported in previous multicenter studies[21,22] further underscoring the severe and diffuse inflammatory nature intrinsic to pediatric sarcoid uveitis.

Although sarcoid uveitis is classically characterized by granulomatous inflammation, only 41% of patients in our cohort exhibited granulomatous uveitis; the majority presented with non-granulomatous uveitis. This predominance of non-granulomatous uveitis is consistent with findings reported by Choi et al.[13] These observations suggest that, unlike the typical adult presentation, pediatric sarcoid uveitis may manifest with either granulomatous or non-granulomatous inflammation, highlighting a broader and more heterogeneous clinical spectrum in children.[12]

Notably, the greater proportion of patients presented with concurrent ocular and systemic sarcoidosis, which differs from adult populations where uveitis typically occurs months or even years before or after systemic diagnosis.[23] Our findings are consistent with our previous multicentric pediatric sarcoidosis study conducted in Turkey, which reported that 40% of patients presented ocular manifestations as part of their initial disease presentation.[24] This may reflect that sarcoidosis follows a different course in children than in adults, with more rapid disease progression or enhanced diagnostic awareness in children with systemic symptoms. Therefore, as practiced in our clinic, every patient with suspected uveitis should undergo systematic

evaluation for systemic involvement, and every child with systemic sarcoidosis should be thoroughly examined for uveitis.

In our study, 40% of patients with sarcoid uveitis had pulmonary involvement. In a previously reported study involving 13 patients, chest radiographs were available for 3 of the 4 patients with biopsy-proven sarcoidosis; interestingly, all three showed no radiographic evidence of sarcoidosis. In the same study, one patient with a renal biopsy compatible with sarcoidosis underwent chest CT, which was also negative for sarcoidosis-related findings.[13] These findings highlight an important characteristic of pediatric sarcoidosis: the absence of pulmonary involvement does not exclude the diagnosis. Unlike adult sarcoidosis, where pulmonary manifestations are predominant, pediatric sarcoidosis may present with isolated extrapulmonary involvement, particularly ocular manifestations. This emphasizes the importance of maintaining a high index of suspicion for sarcoidosis in children presenting with uveitis, even in the absence of chest imaging abnormalities, and underscores the necessity for tissue biopsy confirmation when clinically indicated.

Current management guidelines for ocular sarcoidosis focus on adult patients, while pediatric studies are limited to small, retrospective case series that do not specifically address uveitis management.[25] Consequently, sarcoid uveitis in children is typically treated using the same therapeutic approach as other chronic non-infectious uveitis conditions in pediatric populations, particularly JIA-associated uveitis, which represents the most prevalent form of childhood chronic uveitis.[26,27]

Anterior uveitis unresponsive to topical corticosteroids, intermediate uveitis, posterior uveitis, and panuveitis require systemic treatment, initially with oral prednisolone or intravenous methylprednisolone. Due to significant side effects in children, corticosteroids are typically transitioned to steroid-sparing agents within months. Methotrexate, administered orally or subcutaneously, is the preferred conventional immunomodulatory drug given its established efficacy and safety profile in pediatric inflammatory conditions and reported use in pediatric sarcoidosis.[1,24,28] For refractory cases, TNF inhibitors, particularly subcutaneous adalimumab, represent the standard biologic therapy approach in pediatric uveitis.[29] In our study, the widespread use of topical corticosteroids as first-line therapy, together with the administration of systemic corticosteroids in three-quarters of patients, reflects the inflammatory severity typically seen in pediatric sarcoid uveitis. Consistent with current pediatric uveitis guidelines,[26,27] methotrexate served as the primary steroid-sparing agent in the vast majority of our patients, supporting its role as the preferred conventional DMARD in pediatric inflammatory eye diseases. The high utilization of TNF-α inhibitors, particularly adalimumab, reflects both the refractory nature of sarcoid uveitis and the demonstrated efficacy of anti-TNF therapy in pediatric uveitis. This treatment model is consistent with the stepwise approach recommended for chronic pediatric uveitis, in which conventional DMARDs are tried before switching to biologic therapy. Treatment strategies described in the few existing studies are largely comparable to our approach.[30,31]

Our study demonstrates favorable outcomes in pediatric sarcoid uveitis, with complete remission achieved in over half of patients (53.3%)and low surgical intervention rates(20%).Significant improvement in visual acuity was observed at the final follow-up, demonstrating that the applied treatment regimen effectively controlled intraocular inflammation and preserved visual function. These encouraging results contrast with those of Sarens et al.[21] who reported persistent inflammation despite 3 years of aggressive anti-inflammatory therapy in their cohort of Blau syndrome-associated uveitis patients. This discrepancy likely reflects fundamental differences in disease pathophysiology, as Blau syndrome—caused by NOD2 gene mutations—exhibits more severe, treatment-resistant inflammation than late-onset sarcoidosis. The predominantly late-onset sarcoidosis phenotype in our cohort may explain the more favorable treatment outcomes observed, underscoring the importance of distinguishing between these subtypes when evaluating prognosis in pediatric sarcoid uveitis.

The long-term prognosis remains a key concern for families, with studies showing variable outcomes. Milman et al.[32] reported a 65% complete recovery rate in a cohort where approximately 25% had uveitis, while the French Sarcoidosis Group found that 50% of children had active disease persisting into adulthood, with an additional 19% experiencing recurrences after childhood remission; ocular involvement was present in 50% at pediatric evaluation and persisted in 37% during adulthood.[33] Despite these studies, reliable prognostic factors for disease persistence have not been identified, leading experts to recommend lifelong follow-up. The discrepancy between studies may reflect differences in patient populations, treatment protocols, or diagnostic criteria, underscoring the need for larger, multicenter studies to better characterize prognostic factors in pediatric sarcoid uveitis. These findings underscore the critical role of timely initiation of systemic immunosuppression, particularly early administration of steroid-sparing agents and biologics, in preventing irreversible vision loss in pediatric sarcoid uveitis.

This study has several limitations. The retrospective design and single-center nature of the study may limit the generalizability

of our findings. The relatively small sample size may have limited our ability to identify prognostic factors and correlations between clinical variables. Moreover, most participants were diagnosed by clinical assessment without histopathological confirmation, which is inconsistent with established diagnostic standards for sarcoidosis. Regrettably, obtaining tissue samples is often impractical, especially in cases involving isolated ocular manifestations. Furthermore, while NOD2 mutations were not evaluated, Blau syndrome was clinically excluded based on family history and physical findings.

CONCLUSION

This study demonstrates the severe and variable nature of pediatric sarcoid uveitis and indicates that favorable long-term outcomes can be achieved with current stepwise therapeutic approaches. Notably, the absence of pulmonary involvement raises important diagnostic considerations and may lead to delayed recognition. Given the systemic nature of sarcoidosis and its ocular manifestations, patients should be evaluated and followed by both ophthalmology and pediatric rheumatology teams. However, the variable long-term prognosis reported across different studies underscores the need for lifelong follow-up and larger multicenter cohorts to better define prognostic factors and optimize treatment strategies for pediatric sarcoid uveitis.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul University Faculty of Medicine Local Ethics Committee (No: 3582195, Date: 12/09/2025).

Informed Consent: Informed consent was obtained from all patients.

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