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ORIGINAL RESEARCH

Sarcoid Uveitis with Choroidal Involvement

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Purpose: To investigate characteristics of choroidal involvement in sarcoid uveitis.

Patients and Methods: Included were patients with confirmed sarcoidosis and uveitis with an eye examination at the Tays Eye Center at Tampere University Hospital between January 2014 and January 2021.

Results: Choroidal involvement was found in 31 of 97 sarcoid uveitis patients (32%), and 5 of them were detected only after reviewing the ocular images for this study. None of our patients presented with vasculitis. Choroidal nodules were found in 10%, multifocal choroiditis in 90% and serpiginous choroiditis in 3% of patients with choroidal involvement. They had a higher rate of chronic course of uveitis (71% vs 29%, $p < 0.001$), bilateral uveitis (90% vs 58%, $p = 0.001$), vitreal snowballs (65% vs 15%, $p < 0.001$), and macular edema (36% vs 9%, $p = 0.001$).

Conclusion: Choroidal involvement is common and may be underdiagnosed in sarcoid uveitis. Therefore, we recommend carefully looking for choroidal involvement not only with slit-lamp but also with ocular imaging in patients with uveitis.

Keywords: sarcoidosis, uveitis, sarcoid uveitis, choroidal involvement

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Introduction

Sarcoidosis is a multiorgan granulomatous inflammatory disease of unknown origin.[1] Ocular manifestations of sarcoidosis occur in 2–80% of patients, results varying depending on the study setting, included ocular diseases and study population.[2–5] Asymptomatic ocular sarcoidosis requiring treatment is rare, 0.8%.[3] Lymphopenia, lower serum lysozyme (LZM) levels, neurosarcoidosis, older age, skin lesions and smoking seem to associate with the risk of ocular sarcoidosis.[6–9]

The most common ocular disease associated with sarcoidosis is uveitis, inflammation of the uveal tract, affecting 19–41% of sarcoidosis patients.[2,10,11] Uveitis is classified based on the anatomical site of inflammation as anterior, intermediate, posterior or panuveitis.[12] Typical sarcoidosis-associated uveitis is bilateral anterior uveitis, but intermediate and panuveitis have also been shown to be prevailing clinical presentations.[13–16] Other studies have shown panuveitis to be a rare form of uveitis in sarcoidosis patients (2–4%) in addition to posterior uveitis (5–11%).[2,14,17] Exclusion criteria for sarcoidosis-associated uveitis are evidence of syphilis or tuberculosis infection.[18] Exclusion of tuberculosis should be performed in endemic areas and on tuberculosis-exposed patients. Testing is not routinely performed in Finland because of a low risk for tuberculosis.[19]

Clinical findings related to sarcoidosis-associated choroidal involvement include multifocal choroiditis (MFC) and choroidal nodules, their proportions of sarcoid posterior uveitis patients being 92% and 17%, respectively.[18] In addition, there are documented cases of serpiginous choroiditis in sarcoidosis patients without evidence of tuberculosis.[20] Presence of posterior uveitis has been shown to correlate with lower visual acuity in sarcoidosis-associated uveitis.[21] In MFC patients, cystoid macular edema, glaucoma, epiretinal membrane and poor visual outcome are common complications.[22] Hadjadj et al have found an association between sarcoidosis and MFC, as in 24% of uveitis patients with MFC, chest CT confirms sarcoidosis. Also, the presence of snowballs and/or MFC and blood lymphopenia in combination with serum angiotensin-converting enzyme (ACE) >1.5 ULN are highly effective in predicting sarcoidosis.[23] Ocular imaging is

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helpful for the diagnosis and management of choroidal involvement as it makes the followup reproducible. In addition to traditional fundus photographs, widefield imaging, optical coherence tomography (OCT) and its angiographic form (OCTA), fundus autofluorescence imaging, fluorescein angiography (FAG) and indocyanine green angiography (ICGA) increase understanding of the inflammatory process in uveitis.[24]

To study the characteristics of sarcoidosis-associated uveitis with choroidal involvement, we compared sarcoid uveitis patients with choroidal nodules, MFC and serpiginous choroiditis to those without these findings.

Patients and Methods

Sarcoidosis patients with an eye exam from January 2014 to January 2021 at Tays Eye Centre, Tampere University Hospital, Tampere, Finland, were included in this retrospective registry study. The population of Pirkanmaa hospital district area is 0.5M.

All entries from the Pirkanmaa Hospital District database of patients with an ICD-10 (International statistical classification of diseases and related health problems, 10th revision) code for sarcoidosis and a visit to Tays Eye Centre after diagnosis of sarcoidosis were reviewed from January 2014 to December 2021. The records of patients with an ICD-10 code D86 for any sarcoidosis were reviewed. The patient was included if 1) there was a histopathological report confirming the diagnosis or 2) the clinical diagnosis was clearly stated by the sarcoid specialist in the patient charts. Date of sarcoidosis diagnosis was determined as the date of the histopathological diagnosis and if not available, as the date when an ICD-10 code for sarcoidosis was first recorded in the patient registry. If a confirmation for the sarcoid diagnosis was found, patient's ophthalmological records were reviewed. A senior uveitis consultant (SL) reviewed the records and ocular images to confirm or rule out uveitis and determine the classification of uveitis. We followed the Standardization of Uveitis Nomenclature criteria.[25] In the analysis, we included all patients with a comprehensive ocular examination who had 1) confirmation of sarcoidosis and 2) confirmed uveitis. Excluded patients are presented in our previous study on the risk factors for sarcoidosis-related uveitis.[7]

We recorded date of and age at sarcoidosis/uveitis diagnosis, years between diagnoses, sex and followup time. Sarcoidosis-related data included histopathological test results (biopsy or bronchoalveolar lavage, BAL) and clinical presentation of sarcoidosis (intrathoracic with or without bilateral hilar lymphadenopathy, extrathoracic sarcoidosis excluding ocular sarcoidosis, or both).

Ophthalmological data included clinical presentation of uveitis (anterior, intermediate, posterior or panuveitis, uni- or bilateral, duration), ocular symptoms and findings, complications, medication (topical, intravitreal or systemic corticosteroid treatment, synthetic disease-modifying antirheumatics, or biologic medication), confirmed glaucoma diagnosis, and best corrected visual acuity in decimal notation measured with an autorefractor (ARK-1, NIDEK CO., LTD, Gamagori, Japan) and if not applicable, with a Snellen chart. FAG and ICGA images were collected, if they were taken. Enhanced depth imaging OCT (EDI-OCT) was unavailable.

Included laboratory tests were serum ACE in patients without ACE inhibitor treatment, lymphocyte count and serum LZM when measured. Lymphopenia was determined as lymphocyte count $<1.2\times10^9$/L following the laboratory guidelines of Tampere University Hospital. High ACE was determined as >97U/L (>1.5xULN). Laboratory tests were taken before initiation of systemic immunosuppressive medication for sarcoidosis.

Statistical analysis was performed using SPSS (IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.2.0 Armonk, NY: IBM Corp). To study the choroidal involvement in sarcoid uveitis, we formed two patient groups 1) with choroidal involvement and 2) without choroidal involvement in either eye. Choroidal involvement included choroidal nodules, multifocal choroiditis and serpiginous choroiditis. We present our results for sarcoidosis patients with 1) any uveitis 2) uveitis with choroidal involvement compared with patients without choroidal involvement 3) uveitis following the IWOS criteria.[26] Results are presented using rates and means with standard deviation (SD). Median and range were used if the data was skewed or had outliers. The relationship between categorial variables was assessed by using the Chi-square test. If the expected frequencies were low, Fisher's exact test was applied. Mean scores were compared by using the independent-samples *t*-test, 95% confidence intervals (CI) are presented. Median scores were compared by the Mann–Whitney *U*-test. Differences were considered statistically significant if $p \leq 0.05$.

The ethics committee of the Pirkanmaa Hospital District approved this study (R21508/2021), and its design complies with the Declaration of Helsinki.

Results

Ninety-seven sarcoid patients were diagnosed with or had history of uveitis at Tays Eye Centre from January 2014 to January 2021.

Anterior uveitis was the most frequent type of sarcoid uveitis (56%), while sole intermediate (3%) or posterior uveitis (3%) were rare. Panuveitis was diagnosed in 37 patients (38%), of whom 28 (29%) had choroidal involvement and 9 (9%) had anterior and intermediate uveitis without choroidal involvement. None of our sarcoid uveitis patients presented with vasculitis.

Of all uveitis patients, 31 (32%) had uveitis including choroidal involvement, and 66 (68%) had anterior and/or intermediate uveitis without choroidal involvement. Choroidal involvement included multifocal choroiditis (Figure 1) in 28 (90%), choroidal nodules (Figure 2) in 3 participants (10%) and serpiginous choroiditis (Figure 3) in one participant (3%). One participant had MFC in one eye and a nodule in the other eye. Five (16%) out of 31 patients with choroidal involvement were found to have choroidal involvement only after reviewing the ocular images for this study. Patients with choroidal involvement had a higher rate of bilateral uveitis (90% vs 58%, $p = 0.001$), vitreal snowballs (65% vs 15%, $p < 0.001$) and chronic course of uveitis (71% vs 29%, $p < 0.001$). Patients with choroidal involvement had a higher

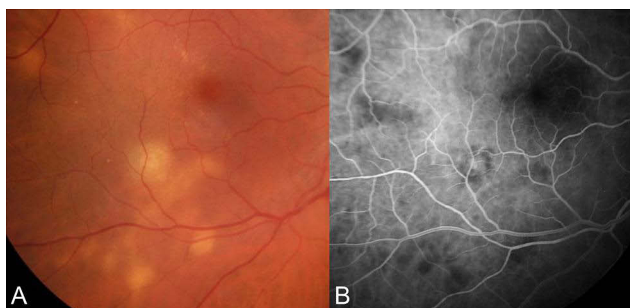

Figure 1 Multifocal choroiditis in sarcoid uveitis, 20 years after sarcoidosis diagnosis. (**A**) Color fundus image. (**B**) Fluorescein angiography at 1 minute.

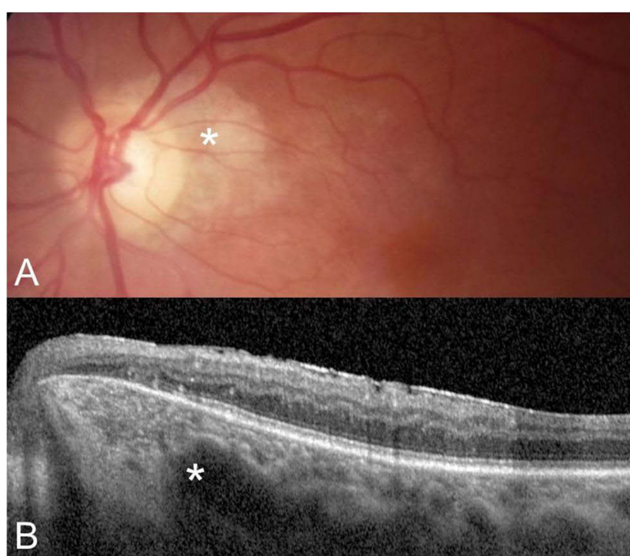

Figure 2 Choroidal nodule in sarcoid uveitis, 4 years after sarcoidosis diagnosis. (**A**) Color fundus image, * marks the nodule. (**B**) Optical coherence tomography, * marks the nodule.

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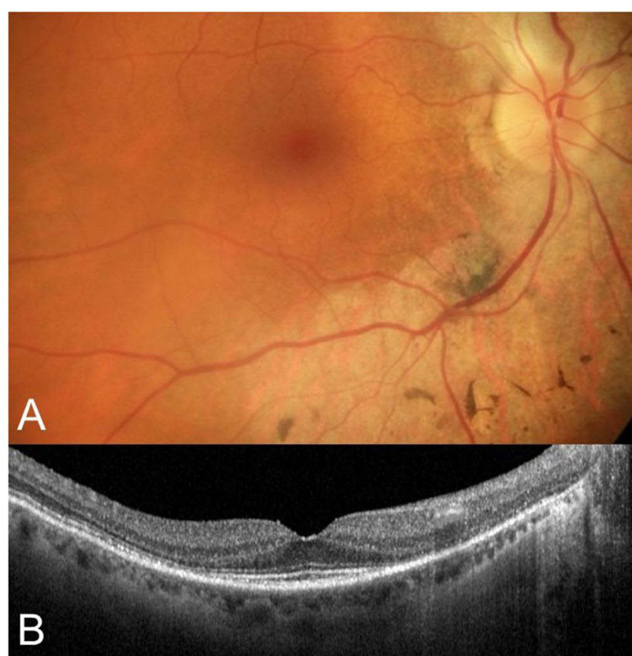

Figure 3 Rare serpiginous choroiditis in sarcoid uveitis, 7 years after sarcoidosis diagnosis. (**A**) Color fundus image. (**B**) Optical coherence tomography.

rate of synthetic disease-modifying antirheumatic (DMARD, 48% vs 27%, p = 0.041) treatment. Also, their rate of macular edema was higher (36% vs 9%, p = 0.001). As expected, the rate of fundus (94% vs 52%, p < 0.001) and OCT (84% vs 38%, p < 0.001) imaging during the follow-up was higher in patients with choroidal involvement. Of all patients, 10 (10%) had FAG and 2 (2%) had ICGA taken. Patients without choroidal involvement had a higher rate of recurrent uveitis (44% vs 13%, p = 0.003), and lower rate of oral steroid (41% vs 77%, p < 0.001) and DMARD use (Table 1).

Table 1 Patient Characteristics and Statistical Testing Between Sarcoid Uveitis Patients with and without Choroidal Involvement

	All Sarcoid Uveitis Patients	With Choroidal Involvement	Without Choroidal Involvement	Comparison of Patients with and without Choroidal Involvement, p-Value
n (% of total)	97 (100%)	31 (32%)	66 (68%)	
Age at 1st diagnosis, years, mean (SD)	49 (14)	52 (13)	47 (14)	0.146, 95% CI (−1.563; 10.381)
Woman, n (%)	59 (61%)	18 (58%)	41 (62%)	0.703
Followup duration, years, mean (SD)	7.3 (6.8)	7.0 (6.7)	7.5 (6.9)	0.736, 95% CI (−3.501; 2.481)
Uveitis first, n (%)	53 (61%)	14 (45%)	39 (59%)	0.257
Years between diagnoses, mean (SD)	4.0 (5.6)	2.6 (3.8)	4.3 (6.2)	0.109, 95% CI (−3.768; 0.383)
Median (range)	0.9 (0–26)	1.2 (0–19)	0.8 (0–26)	0.390
PAD pos, n (%)	61 (63%)	19 (61%)	42 (64%)	0.752
BAL pos, n (%)	8 (8%)	2 (7%)	6 (9%)	1.000[a]
PAD or BAL pos, n (%)	64 (66%)	19 (61%)	45 (68%)	0.504
Definite sarcoid uveitis, n (%)	60 (62%)	18 (58%)	42 (64%)	0.598
Presumed sarcoid uveitis, n (%)	23 (24%)	12 (39%)	11 (17%)	0.017

(*Continued*)

Table 1 (Continued).

	All Sarcoid Uveitis Patients	With Choroidal Involvement	Without Choroidal Involvement	Comparison of Patients with and without Choroidal Involvement, p-Value
Probable sarcoid uveitis, n (%)	1 (1%)	0	1 (2%)	1.000[a]
IWOS pos, n (%)	84 (87%)	30 (97%)	54 (82%)	0.056[a]
IWOS neg, n (%)	13 (13%)	1 (3%)	12 (18%)	0.056[a]
Thoracic sarcoidosis, n (%)	88 (91%)	28 (90%)	60 (91%)	1.000[a]
Extrathoracic (excl. ocular) sarcoidosis, n (%)	41 (42%)	14 (45%)	27 (41%)	0.693
Thoracic and extrathoracic (excl. ocular) sarcoidosis, n (%)	32 (33%)	11 (36%)	21 (32%)	0.720
Neurosarcoidosis, n (%)	4 (4%)	3 (10%)	1 (2%)	0.095[a]
BHL, n (%)	78 (80%)	28 (90%)	50 (76%)	0.092
Thorax CT, n (%)	83 (86%)	29 (94%)	54 (82%)	0.326[a]
BHL in CT, n (%)	63 (65%)	24 (77%)	39 (59%)	0.285
Thorax imaging +-6kk from sarcoidosis dg, n (%)	85 (88%)	28 (90%)	57 (86%)	1.000[a]
BHL +-6kk from dg, n (%)	63 (65%)	22 (71%)	41 (62%)	0.439
Thorax CT +-6kk from dg, n (%)	58 (60%)	19 (61%)	39 (59%)	0.773
BHL in CT +-6kk from dg, n (%)	42 (43%)	16 (52%)	26 (39%)	0.161
Fundus image, n (%)	63 (65%)	29 (94%)	34 (52%)	<0.001
OCT, n (%)	51 (53%)	26 (84%)	25 (38%)	<0.001
FAG, n (%)	10 (10%)	6 (19%)	4 (6%)	0.074[a]
ICGA, n (%)	2 (2%)	1 (3%)	1 (2%)	0.548
Bilateral, n (%)	66 (68%)	28 (90%)	38 (58%)	0.001
PPT, n (%)	39 (40%)	13 (42%)	26 (39%)	0.812
Snowballs, n (%)	30 (31%)	20 (65%)	10 (15%)	<0.001
Choroidal nodules, n (%)	3 (3%)	3 (10%)	0	0.030[a]
MFC, n (%)	28 (29%)	28 (90%)	0	<0.001
Periphlebitis, n (%)	5 (5%)	1 (3%)	4 (6%)	1.000[a]
Serpiginous choroiditis, n (%)	1 (1%)	1 (3%)	0	0.320[a]
Vasculitis, n (%)	0	0	0	
Ocular symptoms, n (%)	83 (86%)	26 (84%)	57 (86%)	1.000[a]
Ocular symptoms unknown at the diagnosis, n (%)	4 (4%)	3 (10%)	1 (2%)	0.095[a]
Acute, n (%)	19 (20%)	4 (13%)	15 (23%)	0.256
Relapsing, n (%)	33 (34%)	4 (13%)	29 (44%)	0.003
Chronic, n (%)	41 (42%)	22 (71%)	19 (29%)	<0.001
Topical steroid, n (%)	91 (94%)	27 (87%)	64 (97%)	0.080[a]
Oral steroid, n (%)	51 (53%)	24 (77%)	27 (41%)	<0.001

(*Continued*)

Table 1 (Continued).

	All Sarcoid Uveitis Patients	With Choroidal Involvement	Without Choroidal Involvement	Comparison of Patients with and without Choroidal Involvement, p-Value
Intravitreal steroid, n (%)	7 (7%)	3 (10%)	4 (6%)	0.679[a]
DMARD, n (%)	33 (34%)	15 (48%)	18 (27%)	0.041
AZA	4 (4%)	2 (7%)	2 (3%)	
Mercapto	1 (1%)	1 (3%)	0	
MMF	3 (3%)	2 (7%)	1 (2%)	
MTX	23 (24%)	10 (32%)	13 (20%)	
MTX, CyA	1 (1%)	0	1 (2%)	
OXI	2 (2%)	0	2 (3%)	
BIOL, n (%)	11 (11%)	6 (19%)	5 (8%)	0.166[a]
ADA	4 (4%)	2 (7%)	2 (3%)	
IFX	6 (6%)	4 (13%)	2 (3%)	
IFX, ADA	1 (1%)	0	1 (2%)	
Immunosuppressive medication, n (%)	96 (99%)	30 (97%)	66 (100%)	0.320[a]
VA o.dx, mean (SD)	0.9 (0.3)	0.9 (0.3)	0.9 (0.3)	0.753, 95% CI (−0.108; 0.149)
VA o.sin, mean (SD)	0.8 (0.3)	0.8 (0.3)	0.9 (0.3)	0.354, 95% CI (−0.208; 0.075)
VA of all uveitis eyes, mean (SD)	0.9 (0.3)	0.9 (0.2)	0.9 (0.3)	0.957, 95% CI (−0.123; 0.116)
VA <0.3, n (%)	10 (10%)	4 (13%)	6 (9%)	0.722[a]
Complication, n (%)	58 (60%)	21 (68%)	37 (56%)	0.274
Synechiae, n (%)	9 (9%)	2 (7%)	7 (11%)	0.714[a]
Cataract, n (%)	33 (34%)	13 (42%)	20 (30%)	0.259
Glaucoma, n (%)	16 (17%)	6 (19%)	10 (15%)	0.603
Macular edema, n (%)	17 (18%)	11 (36%)	6 (9%)	0.001
Epiretinal membrane, n (%)	5 (5%)	3 (10%)	2 (3%)	0.323[a]

Note: [a]Fisher's exact test.

Abbreviations: AU, anterior uveitis; IU, intermediate uveitis; PU, posterior uveitis; PAN, panuveitis; PAD, pathological anatomical diagnosis; BAL, bronchoalveolar lavage; IWOS, International Workshop on Ocular Sarcoidosis; BHL, bilateral hilar lymphadenopathy; CT, computed tomography; OCT, optical coherence tomography; FAG, fluorescein angiography; ICGA, indocyanine green angiography; PPT, precipitates; MFC, multifocal choroiditis; DMARD, disease-modifying antirheumatic drugs; AZA, azathioprine; Mercapto, mercaptopurine; MMF, mycophenolate mofetil; MTX, methotrexate; CyA, cyclosporin A; OXI, hydroxychloroquine; BIOL, biologic medication; ADA, Adalimumab; IFX, Infliximab; VA, visual acuity.

No other statistically significant differences among the studied factors were found. Among the studied factors were age, female sex, followup duration, time between diagnoses, laboratory testing and results (ACE, LZM and lymphocyte count), biopsy and BAL positivity, intra- and/or extrathoracic sarcoidosis excluding ocular sarcoidosis, bilateral hilar lymphadenopathy (BHL) in chest x-ray or computed tomography (CT), corneal precipitates, iris nodules, ocular symptoms, visual acuity, complications, cataract, glaucoma and epiretinal membrane (Tables 1 and 2).

Of the studied uveitis patients, 84 (87%) met the IWOS criteria for sarcoidosis-related uveitis.[26] Thirteen (13%) did not meet the criteria (Table 3).

Considering bilateral course of uveitis and vitreal snowballs, statistical testing between patients with and without choroidal involvement was reworked for patients meeting the IWOS criteria for sarcoidosis-related uveitis.[26] The rates of

Table 2 Laboratory Results and Statistical Testing Between Sarcoid Uveitis Patients with and without Choroidal Involvement

	All Sarcoid Uveitis Patients	With Choroidal Involvement	Without Choroidal Involvement	Comparison of Patients with and without Choroidal Involvement, p-Value
n (% of total)	97 (100%)	31 (32%)	66 (68%)	
ACE measured, n (%)	82 (85%)	26 (84%)	56 (85%)	1.000[a]
ACE at diagnosis, U/L, mean (SD)	61 (27)	66 (22)	59 (30)	0.277, 95% CI (−5.822; 20.064)
ACE>1.5ULN, n (%)	11 (11%)	3 (10%)	8 (12%)	1.000[a]
LZM measured, n (%)	76 (78%)	23 (74%)	53 (80%)	0.496
LZM at diagnosis, mg/L, mean (SD)	2.0 (0.8)	1.9 (0.6)	2.0 (0.9)	0.421, 95% CI (−0.548; 0.231)
Lymphocytes measured, n (%)	66 (68%)	21 (68%)	45 (68%)	0.965
Lymphocytes at diagnosis, x10^9/L, mean (SD)	1.4 (0.6)	1.4 (0.6)	1.4 (0.6)	0.866, 95% CI (−0.346; 0.292)
Lymphopenia, n (%)	29 (30%)	11 (36%)	18 (27%)	0.397

Note: [a]Fisher's exact test.
Abbreviations: ACE, angiotensin-converting enzyme; ULN, upper limit of normal; LZM, lysozyme.

Table 3 Patient Characteristics of Uveitis Patients Grouped by the Criteria Formed by the International Workshop on Ocular Sarcoidosis

	IWOS pos	IWOS neg
n (% of total)	84 (87%)	13 (13%)
Age at 1st diagnosis, years, mean (SD)	49 (14)	44 (11)
Woman, n (%)	54 (64%)	5 (39%)
Followup duration, years, mean (SD)	7.2 (7.0)	8.1 (5.6)
Uveitis first, n (%)	45 (54%)	8 (62%)
Years between diagnoses, median (range)	0.8 (0–26)	5.3 (0.06–20)
PAD pos, n (%)	61 (73%)	0
BAL pos, n (%)	5 (6%)	3 (23%)
PAD or BAL pos, n (%)	61 (73%)	3 (23%)
Definite sarcoid uveitis, n (%)	60 (71%)	0
Presumed sarcoid uveitis, n (%)	23 (27%)	0
Probable sarcoid uveitis, n (%)	1 (1%)	0
Thoracic sarcoidosis, n (%)	75 (89%)	13 (100%)
Extrathoracic (excl. ocular) sarcoidosis, n (%)	38 (45%)	3 (23%)
Thoracic and extrathoracic (excl. ocular) sarcoidosis, n (%)	29 (35%)	3 (23%)
Neurosarcoidosis, n (%)	4 (5%)	0
BHL, n (%)	67 (80%)	11 (85%)
Thorax CT, n (%)	72 (86%)	11 (85%)
BHL in CT, n (%)	54 (64%)	9 (69%)

(*Continued*)

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Table 3 (Continued).

	IWOS pos	IWOS neg
Thorax imaging +-6kk from sarcoidosis dg, n (%)	74 (88%)	11 (85%)
BHL +-6kk from dg, n (%)	52 (62%)	11 (85%)
Thorax CT +-6kk from dg, n (%)	51 (61%)	7 (54%)
BHL in CT +-6kk from dg, n (%)	36 (43%)	6 (46%)
ACE measured, n (%)	71 (85%)	11 (85%)
ACE at diagnosis, U/L, mean (SD)	62 (29)	58 (19)
ACE>1.5ULN, n (%)	11 (13%)	0
LZM measured, n (%)	66 (79%)	10 (77%)
LZM at diagnosis, mg/L, mean (SD)	2.0 (0.8)	2.0 (0.5)
Lymphocytes measured, n (%)	56 (67%)	10 (77%)
Lymphocytes at diagnosis, x10^9/L mean (SD)	1.4 (0.6)	1.4 (0.8)
Lymphopenia, n (%)	24 (29%)	5 (39%)
Fundus image, n (%)	59 (70%)	4 (31%)
OCT, n (%)	47 (56%)	4 (31%)
FAG, n (%)	10 (12%)	0
ICGA, n (%)	2 (2%)	0
Bilateral, n (%)	60 (71%)	6 (46%)
PPT, n (%)	38 (45%)	1 (8%)
Snowballs, n (%)	30 (36%)	0
Choroidal nodules, n (%)	3 (4%)	0
MFC, n (%)	27 (32%)	1 (8%)
Periphlebitis, n (%)	5 (6%)	0
Serpiginous choroiditis, n (%)	1 (1%)	0
Vasculitis, n (%)	0	0
Ocular symptoms, n (%)	73 (87%)	10 (77%)
Ocular symptoms unknown at the diagnosis, n (%)	4 (5%)	0
Acute, n (%)	16 (19%)	3 (23%)
Relapsing, n (%)	27 (32%)	6 (46%)
Chronic, n (%)	39 (46%)	2 (15%)
Topical steroid, n (%)	78 (93%)	13 (100%)
Oral steroid, n (%)	47 (56%)	4 (31%)
Intravitreal steroid, n (%)	6 (7%)	1 (8%)
DMARD, n (%)	32 (38%)	1 (8%)

(*Continued*)

Table 3 (Continued).

	IWOS pos	IWOS neg
• AZA	4 (5%)	0
• Mercapto	1 (1%)	0
• MMF	3 (4%)	0
• MTX	22 (26%)	1 (8%)
• MTX, CyA	1 (1%)	0
• OXI	2 (2%)	0
BIOL, n (%)	11 (13%)	0
• ADA	4 (5%)	
• IFX	6 (7%)	
• IFX, ADA	1 (1%)	
Immunosuppressive medication, n (%)	83 (99%)	13 (100%)
VA o.dx, mean (SD)	0.9 (0.3)	0.9 (0.3)
VA o.sin, mean (SD)	0.8 (0.3)	0.8 (0.2)
VA of all uveitis eyes, mean (SD)	0.9 (0.3)	0.8 (0.3)
VA <0.3, n (%)	9 (11%)	1 (8%)
Complication, n (%)	52 (62%)	6 (46%)
Synechiae, n (%)	6 (7%)	3 (23%)
Cataract, n (%)	30 (36%)	3 (23%)
Glaucoma, n (%)	16 (19%)	0
Macular edema, n (%)	15 (18%)	2 (15%)
Epiretinal membrane, n (%)	5 (6%)	0

Abbreviations: AU, anterior uveitis; IU, intermediate uveitis; PU, posterior uveitis; PAN, panuveitis; PAD, pathological anatomical diagnosis; BAL, bronchoalveolar lavage; IWOS, International Workshop on Ocular Sarcoidosis; BHL, bilateral hilar lymphadenopathy; CT, computed tomography; ACE, angiotensin-converting enzyme; ULN, upper limit of normal; LZM, lysozyme; OCT, optical coherence tomography; FAG, fluorescein angiography; ICGA, indocyanine green angiography; PPT, precipitates; MFC, multifocal choroiditis; DMARD, disease-modifying antirheumatic drugs; AZA, azathioprine; Mercapto, mercaptopurine; MMF, mycophenolate mofetil; MTX, methotrexate; CyA, cyclosporin A; OXI, hydroxychloroquine; BIOL, biologic medication; ADA, Adalimumab; IFX, Infliximab; VA, visual acuity.

bilateral course of uveitis (90% vs 61%, $p = 0.005$) and snowballs (67% vs 19%, $p < 0.001$) remained higher in uveitis patients with choroidal involvement.

Discussion

In this Finnish sarcoid uveitis population, choroidal involvement in sarcoid uveitis patients was common, 32%. Choroidal involvement included choroidal nodules, multifocal, and serpiginous choroiditis. The two groups (patients with and without choroidal involvement) were formed to better study the characteristics of uveitis with choroidal involvement. We revealed that the rate of chronic uveitis was higher (71% vs 29%, $p < 0.001$) in patients with choroidal involvement and their uveitis was more often bilateral (90% vs 58%, $p = 0.001$) than in sarcoid uveitis patients without choroidal involvement. Vitreal snowballs were more common in patients with choroidal involvement (65% vs 15%, $p < 0.001$).

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Rates of bilaterality and vitreal snowballs remained higher in patients with choroidal involvement even after reworking the analysis to only include IWOS criteria positive[26] patients. Also, macular edema was more frequent (36% vs 9%, p = 0.001) in choroidal involvement group. The rate of recurrent uveitis was higher in the group without choroidal involvement (44% vs 13%, p = 0.003), and this might relate to their lower rate of oral steroid (41% vs 77%, p < 0.001) and DMARD (27% vs 48%, p = 0.041) use.

We did not find other studies on the differences between sarcoid uveitis patients where the grouping design was similar to ours. However, choroidal involvement seemed similarly common in a sarcoid uveitis study by Niederer et al where MFC was found in 43% and isolated choroidal or optic nerve nodules in 11% of 362 sarcoid uveitis patients.[27]

One (3%) patient with choroidal involvement had serpiginous choroiditis in this sarcoidosis population. Our finding may also be coincidental, as the association of serpiginous choroiditis with sarcoidosis is uncertain. The association between serpiginous choroiditis and tuberculosis has been described, but its relation to other infectious and noninfectious agents is unclear.[28]

We found that in this sarcoid uveitis population, panuveitis was frequent (38%) and sole posterior uveitis rare (3%). This is in concordance with the article by The Standardization of Uveitis Nomenclature Working Group, where the prevalences of sarcoidosis-associated panuveitis and posterior uveitis were 37% and 4%, respectively.[18] In our study population, 5 (16%) out of 31 patients with choroidal involvement were only diagnosed with choroidal involvement after reviewing the ocular images taken during their followup for this study. Thirty-four patients (35% of total) did not have any fundus images taken during followup. Posterior segment involvement like MFC may remain undetected without imaging and experience in evaluating the images which can delay initiation of systemic treatment. As presence of posterior uveitis may result in worse visual outcome, we encourage fundus and OCT imaging in addition to thorough fundus examination in patients with sarcoid uveitis.[21]

Sarcoidosis should be screened when encountering uveitis patients with choroidal involvement or other typical signs of sarcoid uveitis such as bilateral disease and snowballs.[18,26] At Tampere University Hospital, sarcoidosis is screened primarily with chest x-ray, complete blood count and ACE in patients who present with uveitis typical of sarcoidosis.[26]

There are limitations to this study. Our population represents sarcoid uveitis patients from a tertiary referral centre and thus has a bias towards more severe uveitis, as mild and limited inflammations may not require referral. As a result, patients with choroidal involvement may be overrepresented in our study. Second, the retrospective design of our study causes limitations. The data was partly different in the compared groups and could not be complemented, patients with choroidal involvement naturally had higher rates of fundus and OCT images taken. As 16% of patients with choroidal involvement were only detected after reviewing the ocular images for this study and 48% of the patients without choroidal involvement did not have fundus images to review, we recognise that some patients with choroidal involvement without ocular images may still have been undetected. In addition, only few patients in our study population had FAG (n = 10) and ICGA (n = 2) taken. At Tays Eye Center, both FAG and ICGA have been used more routinely in uveitis management since 2020. Before 2020, FAG was used in cases with inconclusive posterior findings or suspected vasculitis. EDI-OCT was unfortunately unavailable. These imaging modalities would provide more information on retinal and choroidal involvement in uveitis. Also, tuberculosis was not routinely screened. However, the incidence of tuberculosis has been low and decreased in Finland during this study period. We acknowledge that in other regions and with immigration, tuberculosis should be ruled out when diagnosing sarcoidosis.[18]

The rates of chronic course of uveitis, bilateral uveitis, and macular edema were higher among sarcoid uveitis patients with choroidal involvement, and they were treated more commonly with synthetic disease-modifying antirheumatics. We suggest diligently looking for choroidal involvement in sarcoid uveitis by ocular imaging, especially in bilateral diseases, chronic diseases, and diseases presenting with snowball formation. For future studies, we recommend systematical fundus and angiographic imaging in sarcoid uveitis to better compare and understand choroidal involvement in sarcoid uveitis.

Ethics Approval and Informed Consent

The retrospective, registry-based study was approved by the administration of the Tampere University Hospital (R21508/2021). Patient data was used under the Act on the Secondary Use of Health and Social Data, and thus informed consent was not required.[29] Patients have the right to prohibit the use of their data for secondary purposes under the EU General Data Protection Regulation (GDPR).[30] The study was conducted in accordance with the Declaration of Helsinki.

Disclosure

The authors report no conflicts of interest for this work.

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