Are Specific Trabecular Meshwork Nodules Distinctive for Sarcoidosis? Case Report and Review of the Literature

Serão Nódulos Específicos da Malha Trabecular Característicos de Sarcoidose? Caso Clínico e Revisão da Literatura

João Romana [1], Pedro Simões [1], Maria Madeira [1], Marta Correia [1], Marta Guedes [1]

[1] Serviço de Oftalmologia, Hospital de Egas Moniz, Unidade Local de Saúde Lisboa Ocidental, Lisbon, Portugal

Recebido/Received: 2023-07-19 | **Aceite/Accepted:** 2024-02-24 | **Published online/Publicado online:** 2024-03-11 | **Published/Publicado:** 2024-06-27

DOI: https://doi.org/10.48560/rspo.32331

ABSTRACT

Uveitis is an important cause of visual loss in sarcoidosis patients. Although diagnostic approaches have changed over the past decade, clinical and laboratory findings appear to be insufficient for diagnosing ocular sarcoidosis. The authors report the case of a patient with atypical sarcoidosis-associated uveitis, highlighting the importance of specific trabecular meshwork nodules for establishing diagnosis.

KEYWORDS: Sarcoidosis/diagnosis; Trabecular Meshwork; Uveitis/diagnosis.

RESUMO

A uveíte é uma causa importante de perda de acuidade visual em doentes com sarcoidose. Apesar do progresso ao longo da última década na abordagem diagnóstica, os achados clínicos e laboratoriais atuais parecem ser insuficientes para o diagnóstico de sarcoidose ocular. Os autores descrevem o caso de uma doente com apresentação atípica de uveíte associada a sarcoidose, destacando a importância de nódulos da malha trabecular característicos, para o diagnóstico correto.

PALAVRAS-CHAVE: Malha Trabecular; Sarcoidose/diagnóstico; Uveíte/diagnóstico.

INTRODUCTION

Sarcoidosis is a multisystemic, idiopathic, chronic inflammatory disease. Ocular involvement is present in 30% to 80% of patients and is frequently manifested before a definitive diagnosis.[1,2] Although dry eye is the most common form of ocular involvement, uveitis is the leading cause of visual loss in sarcoidosis patients.[3,4]

Sarcoidosis-associated uveitis usually presents in the form of chronic, bilateral, granulomatous intraocular inflammation, manifesting as anterior, intermediate, posterior, or panuveitis.[4]

The first International Workshop on Ocular Sarcoidosis (IWOS), in 2009, proposed diagnostic criteria for sarcoidosis-associated uveitis.[5] Yet, the diagnosis of sarcoidosis remains very difficult as the gold standard for definitive diagnosis is still the biopsy of relevant tissue.

Recently, the International Ocular Sarcoidosis Working Group described the clinical characteristics and laboratory findings of patients with biopsy-confirmed sarcoidosis and estimated the sensitivity and specificity of IWOS clinical signs and laboratory tests.[6] They concluded that, apart from evidence of bilateral hilar lymphadenopathy on chest radiograph or computed tomography (CT) scan, current IWOS clinical and laboratory findings are insufficient for diagnosing ocular sarcoidosis.

Trabecular meshwork (TM) nodules, known as Berlin nodules, are an important feature of sarcoidosis-associated uveitis, present in up to 18% of the patients. However, they can also be found in malignancies and infectious causes such as syphilis and tuberculosis.[7,8]

The authors report the case of a patient with atypical sarcoidosis-associated uveitis, highlighting their pearls and pitfalls, including specific TM nodules characteristics, for establishing diagnosis.

CASE REPORT

A 57-year-old Caucasian woman, with history of thyroidectomy 10 years ago for toxic multinodular goiter, cataract surgery (phacoemulsification with intraocular lens implantation) and macular hole surgery (pars plana vitrectomy and internal limiting membrane peeling) of the right eye (RE), 3 and 2 years ago respectively, developed, over two days, painless progressive vision loss in her RE. She did not detect visual loss in the left eye (LE).

Ocular examination revealed best corrected visual acuity of 0.18 in the RE and 0 in the LE (LogMAR notation). Pupils were 3 mm bilaterally without relative afferent pupillary defect. Intraocular pressure was 17 mmHg in the RE and 16 mmHg in the LE.

Slit-lamp examination revealed a ciliary injection with multiple mutton-fat keratic precipitates and cells (2+) in the anterior chamber of the RE. Gonioscopic examination showed flocculated nodules on the surface of the TM at 3, 4 and 6 hours (Fig. 1).

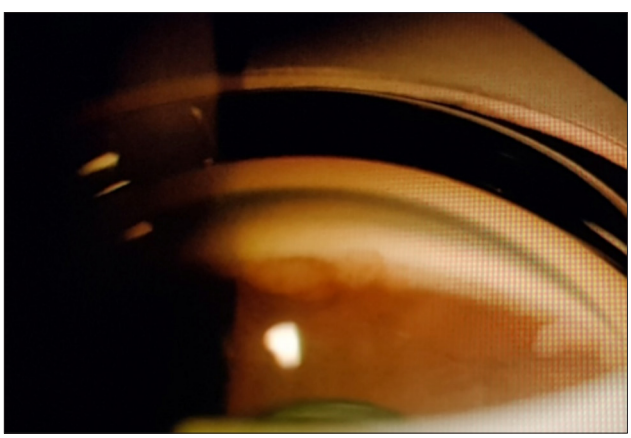

Figure 1. Flocculated trabecular meshwork nodules.

Fundus examination of the RE demonstrated moderate haze in the vitreous cavity, optic disc edema and multiple chorioretinal peripheral lesions (Fig. 2). A flocculated granulomatous lesion, similar to the trabecular meshwork nodules was identified in the inferior periphery (Fig. 3). The anterior and posterior segments of the left eye were normal.

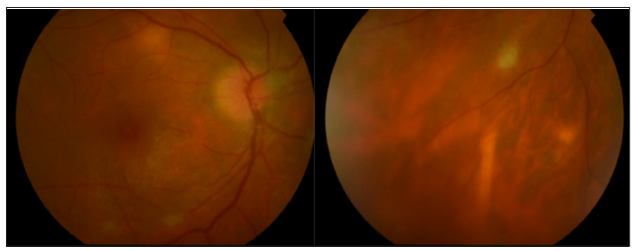

Figure 2. Optic disc edema and multiple chorioretinal lesions.

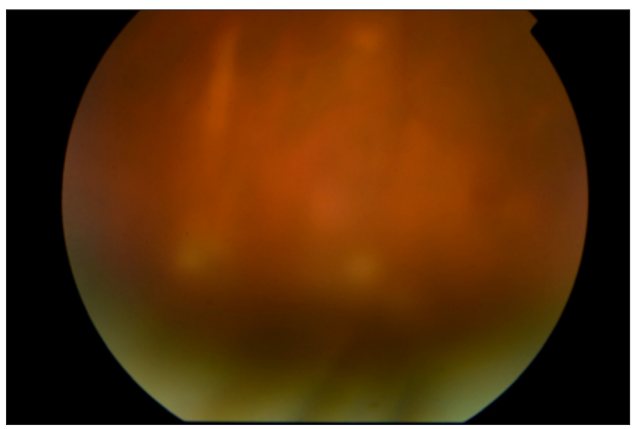

Figure 3. Flocculated granulomatous lesion, alike the trabecular meshwork nodules at the inferior periphery.

Ultrasound biomicroscopy showed a moderate number of cells in the anterior chamber and stromal oedema of the ciliary body. Spectral domain optical coherence tomography (SD-OCT) confirmed RE optic disc edema, without macular edema or macular hole recurrence. Fluorescein angiography showed papillary leakage of the RE, without signs of vasculitis.

Personal and family history were negative for autoimmune disorders. Physical examination was normal. A complete blood count and comprehensive metabolic panel were shown to be normal, except for lymphopenia (1.13 x10^9/L) and a slight elevation of liver enzyme tests, (AST 42 U/L, reference <32; ALT 51 U/L, reference <33).

Serologic test of syphilis, toxoplasmosis, human immunodeficiency virus and hepatitis B were negative, as well as tuberculin skin test and Interferon-γ release assay (IGRA).

Antinuclear antibody, anti-ds DNA antibody, rheumatoid factor and C-reactive protein were negative as well. Angiotensin-converting enzyme (ACE) was 38.0 U/L (reference 8.0 – 52.0) and lysozyme was 1.79 U/L (reference <1.71). A chest scan for hilar lymphadenopathy was unremarkable.

High resolution computed tomography (HRCT) of the lung lacked evidence of parenchymal or pleural abnormalities. Abdominal ultrasound was normal. Whole-body 67 Ga scintigraphy was negative for active inflammatory process of the RE and did not find neoplastic disease.

Two days after symptoms onset, the patient was treated with oral prednisolone 60 mg/day, topical prednisolone acetate 1.0% 2/2 hours and tropicamide 1.0% 8/8 hours.

Two weeks after starting treatment, visual acuity improved to 0 (LogMar) in both eyes. The anterior segment of the RE showed marked improvement and resolution of the TM nodules without scarring. During a follow-up appointment, the patient recalled discrete nodular involvement of the skin on the pretibial and scapular area (Fig. 4). A skin biopsy revealed non-caseating granulomas and established the diagnosis of sarcoidosis.

Prednisolone was slowly weaned off, starting at 60 mg per day, followed by reductions to 40 mg, 30 mg, 25 mg, 20 mg, 15 mg and 10 mg over the course of several months. Tapering continued with reductions of 2.5 mg per day every four weeks and was stopped after reaching a dose of 2.5 mg on alternate days. The patient started taking 10 mg per week of methotrexate as a steroid sparing agent, 2 months after starting oral steroids.

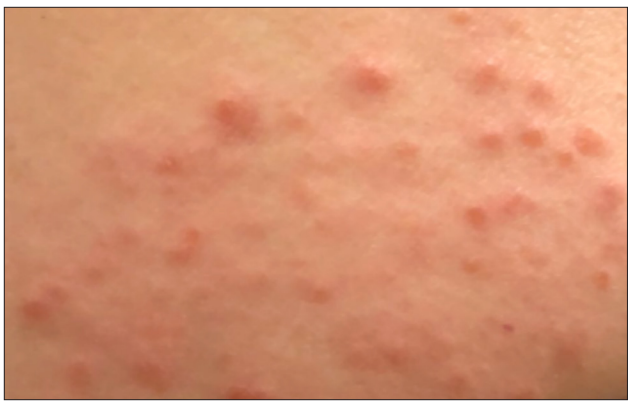

Figure 4. Skin nodular involvement at the scapula.

DISCUSSION

The diagnosis of sarcoidosis remains extremely difficult, as current IWOS clinical and laboratory findings are inadequate, and the gold standard for establishing a definitive diagnosis requires a biopsy of the affected tissue.[5]

The most common clinical signs reported by the International Ocular Sarcoidosis Working Group were bilaterality (86%), snowballs or string of pearls (50%) and mutton-fat keratic precipitates, iris nodules, or both (46%) but unfortunately these findings are highly non-specific.[6] The same Working Group found TM nodules and/or tent-shaped peripheral anterior synechiae (PAS) in 38% of the sarcoidosis-associated uveitis patients. The two signs were combined as they believed that tent-shaped PAS result from scarring of the TM nodules. This premise is logical and supported by the lower incidence reported of TM nodules (18%) when compared to tent-shaped PAS (35%).

Furthermore, in the study by Kawaguchi *et al*, TM nodules and/or tent-shaped PAS had by far the highest values for sensitivity, specificity, positive and negative predictive values in a biopsy-proven sarcoidosis group.[9]

TM nodules are not specific for sarcoidosis and can also be found in malignancies and infectious causes.[10-12] However, some nodules' features might be associated with the diagnosis of sarcoidosis, namely: (1) regression after corticosteroid treatment; (2) presence of concomitant tent-shaped PAS; (3) absence of atypia signs on Ultrasound biomicroscopy.

Regarding laboratory findings, although increased ACE levels and serum lysozyme are useful for the presumptive diagnosis of sarcoid uveitis, they lack sensitivity. Sensitivity varies from 58% to 84% for ACE and 60% to 78% for lysozyme.[13] This may explain normal ACE levels in this patient. This patient also has asymptomatic elevation of liver enzyme tests. These abnormalities are encountered in 20%-40% of patients, although clinical expression of hepatic disease is uncommon.[14]

CONCLUSION

Specific TM nodules might be distinctive for sarcoidosis. The identification of these characteristics may facilitate early diagnosis and improve clinical outcome.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

JR: Literature review, data collection, writing, revision.
PS: Literature review, writing.
MM, MC and MG: Literature review, data collection, revision.
All authors approved the final version to be published.

JR: Revisão bibliográfica, recolha de dados, redação, revisão.
PS: Revisão bibliográfica, redação.
MM, MC e MG: Revisão bibliográfica, recolha de dados, revisão.
Todos autores aprovaram a versão final a ser publicada.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento do doente para publicação obtido.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Patient Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer reviewed.

REFERENCES

1. Liu D, Birnbaum AD. Update on sarcoidosis. Curr Opin Ophthalmol. 2015;26:512-6. doi: 10.1097/ICU.0000000000000207.
2. Jabs DA, Johns CJ. Ocular involvement in chronic sarcoidosis. Am J Ophthalmol. 1986;102:297-301. doi: 10.1016/0002-9394(86)90001-2.
3. Radosavljević A, Jakšić V, Pezo L, Kovačević-Pavićević D, Ilić A, Mihailović Vučinić V. Clinical Features of Ocular Sarcoidosis in Patients with Biopsy-proven Pulmonary Sarcoidosis in Serbia. Ocul Immunol Inflamm. 2017;25:785-9. doi: 10.3109/09273948.2016.1167224.
4. Yang SJ, Salek S, Rosenbaum JT. Ocular sarcoidosis: new diagnostic modalities and treatment. Curr Opin Pulm Med. 2017;23:458-67. doi: 10.1097/MCP.0000000000000409.
5. Herbort CP, Rao NA, Mochizuki M; members of Scientific Committee of First International Workshop on Ocular Sarcoidosis. International criteria for the diagnosis of ocular sarcoidosis: results of the first International Workshop On Ocular Sarcoidosis (IWOS). Ocul Immunol Inflamm. 2009;17:160-9. doi: 10.1080/09273940902818861.
6. Acharya NR, Browne EN, Rao N, Mochizuki M; International Ocular Sarcoidosis Working Group. Distinguishing Features of Ocular Sarcoidosis in an International Cohort of Uveitis Patients. Ophthalmology. 2018;125:119-26. doi: 10.1016/j.ophtha.2017.07.006.
7. Kassa E, Elner VM, Moroi SE, Sun Y. Diffuse Berlin nodules: unusual presentation of ocular sarcoidosis. Br J Ophthalmol. 2013;97:1214, 1223-4. doi: 10.1136/bjophthalmol-2013-303112.
8. Hamanaka T, Takei A, Takemura T, Oritsu M. Pathological study of cases with secondary open-angle glaucoma due to sarcoidosis. Am J Ophthalmol. 2002;134:17-26. doi: 10.1016/s0002-9394(02)01507-6.
9. Kawaguchi T, Hanada A, Horie S, Sugamoto Y, Sugita S, Mochizuki M. Evaluation of characteristic ocular signs and systemic investigations in ocular sarcoidosis patients. Jpn J Ophthalmol. 2007;51:121-6. doi: 10.1007/s10384-006-0413-2.
10. Li Z, Li X, Song Z, Liu J, Dong M, Shi T, et al. Sarcoidosis misdiagnosed as malignant tumors: a case report. World J Surg Oncol. 2015;13:333. doi: 10.1186/s12957-015-0748-6.
11. Simeoni S, Puccetti A, Tinazzi E, Codella OM, Sorleto M, Patuzzo G, et al. Leprosy initially misdiagnosed as sarcoidosis, adult-onset still disease, or autoinflammatory disease. J Clin Rheumatol. 2011;17:432-5. doi: 10.1097/RHU.0b013e31823a55e5.
12. Berent R, Auer J, Lassnig E, von Duvillard SP, Crouse SF, Tuppy H, et al. Whipple's disease: misdiagnosed as sarcoidosis with further tricuspid valve endocarditis and pulmonary embolism - a case report. BMJ Case Rep. 2009;2009:bcr07.2008.0441. doi: 10.1136/bcr.07.2008.0441.
13. Sève P, Jamilloux Y, Tilikete C, Gerfaud-Valentin M, Kodjikian L, El Jammal T. Ocular Sarcoidosis. Semin Respir Crit Care Med. 2020;41:673-88. doi: 10.1055/s-0040-1710536.
14. Karagiannidis A, Karavalaki M, Koulaouzidis A. Hepatic sarcoidosis. Ann Hepatol. 2006;5:251-6.

Corresponding Author/
Autor Correspondente:

João Romana
Rua da Junqueira 126,
1349-019, Lisboa, Portugal
E-mail: joaoromana37@gmail.com

ORCID: 0009-0000-4991-0767