



## Retinal and pre-retinal nodules: A rare manifestation of probable ocular sarcoidosis

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### ABSTRACT

**Purpose:** To report a case of multiple pre-retinal and intra-retinal lesions in the context of probable sarcoidosis. **Observations:** A 31-year-old black woman presented with a bilateral panuveitis and multiple pre-retinal and retinal nodules. The workup showed enlarged mediastinal lymph nodes as well as meningitis with an increased cerebrospinal fluid angiotensin-converting enzyme (ACE) [0.36 UI/L (1.44 × normal)] leading to the diagnosis of probable sarcoidosis. The nodules were hyper-reflective, with posterior shadowing on OCT imaging, and appeared as multiple hypoautofluorescent spots: their characteristics were suggestive of intra and preretinal granulomas. The intraretinal nodules were located in the ganglion cell layer. The posterior segment manifestations were limited to the retina while the choroid appeared uninvolved including on indocyanine green angiograms. The lesions disappeared after corticosteroid treatment. **Conclusions and importance:** Retinal and pre-retinal nodules have rarely been reported as the sole posterior manifestations of ocular sarcoidosis without choroidal involvement.

### 1. Introduction

Sarcoidosis is a multisystemic autoimmune granulomatous disease of unknown cause. Ocular involvement is the presenting symptom in approximately 20–30% cases.<sup>1</sup> The choroid is the usual site of the posterior manifestations of ocular sarcoidosis and the most characteristic lesions are multifocal choroiditis.<sup>2</sup> Vitritis, retinal vasculitis, macular edema and papillitis are also common. However, the intraretinal localization of sarcoidosis-related granulomas is rare.<sup>3</sup> We report a case with pre-retinal and retinal sarcoid lesions analyzed by multimodal imaging and we review the literature regarding these manifestations.

### 2. Report of a case

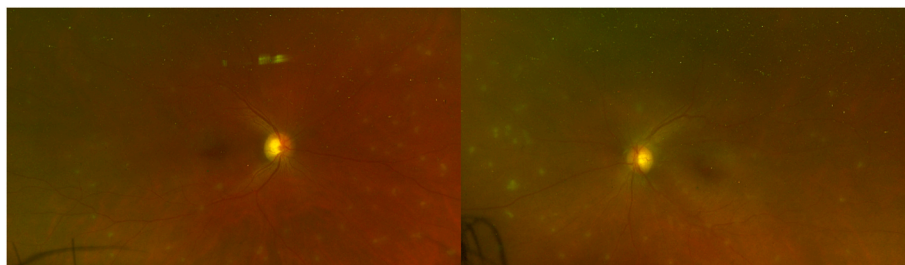
A 31-year-old black female patient with no past medical history complained of bilateral painless visual loss and fatigue, with headaches, speech disorder and fever (39 °C). The decimal Best Corrected Visual Acuity (BCVA) was 0.8 in the right eye and 0.4 in the left eye. The slit-lamp examination showed 1+ cells in both anterior chambers, numerous non-granulomatous keratic precipitates and iris nodules. A 1+ vitritis was seen and multiple bilateral yellowish retro-hyaloid lesions and some

intraretinal lesions were observed on the fundus examination (Fig. 1). Superficial hemorrhages and periphlebitis were detected in both eyes.

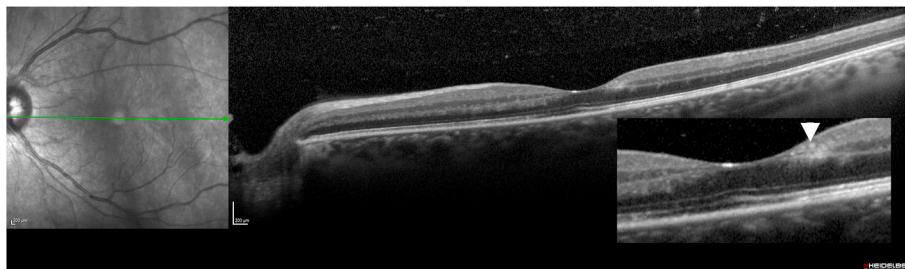
Spectral-domain optical coherence tomography (SD-OCT) showed a normal macular profile, with a hyperreflective band at the level of the inner nuclear layer, sparing the outer retina (Fig. 2). On SD-OCT the retro-hyaloid lesions appeared as pre-retinal nodules which were hyper-reflective with posterior shadowing; moreover, an intra-retinal lesion was seen (Fig. 3). The pre-retinal nodules also appeared as multiple hypoautofluorescent spots on infrared autofluorescence (IRAF) (Fig. 4). The parafoveal area was hyporeflective on the infra-red imaging. The ultra-widefield fluorescein angiograms showed bilateral leakage of the dye from the retinal venules and the optic nerve head, due to retinal vasculitis and papillitis, while the indocyanine green angiograms were normal (Fig. 5).

A systematic work-up was performed. The combination of headaches and fever led to a lumbar puncture and the analysis of the CSF showed a lymphocytic meningitis (170 elements, 80% lymphocytes) with an increased angiotensin-converting enzyme (ACE) [0.36 UI/L (1.44 × normal)]. The brain magnetic resonance imaging (MRI) was normal. The serum ACE and the electrophoresis of blood proteins were both normal, and the following serologies for infectious diseases were negative:

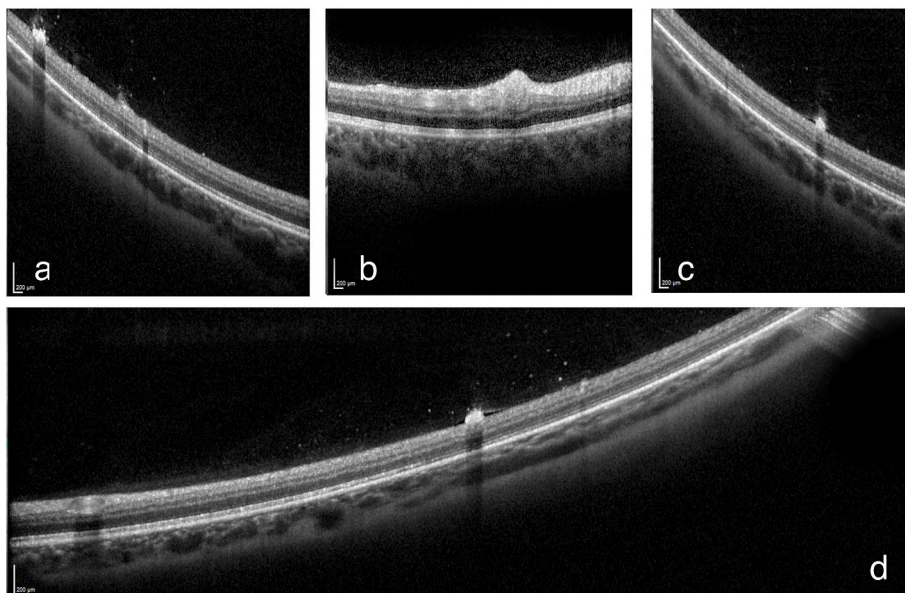
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**Fig. 1.** Ultra-wide-field color funduscopy at presentation showing numerous bilateral yellowish pre-retinal lesions. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2.** Optical coherence tomography (OCT) and near-infrared reflectance (NIR) imaging of the left eye showing an hyperreflective band at the level of the inner nuclear layer (white arrowhead).



**Fig. 3.** OCT imaging showing multiple pre-retinal lesions with posterior shadowing located between the posterior hyaloid and the retina (3a, 3c, 3d) as well as one intraretinal lesion (3b).

rickettsiosis, coxsackie, toxoplasmosis, syphilis and bartonella. The interferon-gamma release assay and the tuberculosis skin-test were also negative. An accessory salivary gland biopsy was normal. The chest CT-scan was performed only after the onset of corticosteroid treatment and showed enlarged mediastinal lymph nodes. Although a definitive diagnosis of sarcoidosis with the identification of non-caseating granulomas composed of islands of epithelioid cells and a few Langhans giant cells was not made, the combination of the findings was sufficient to make a diagnosis of probable sarcoidosis with ocular manifestations, including pre-retinal and retinal granulomas.

The patient was treated by intravenous methylprednisolone pulses (10 mg/kg per day) for three days. At day three, decimal BCVA

improved to 1.0 in the right eye and 0.8 in the left eye. The inflammation of the anterior chamber and the vitreous cleared, as well as most of the pre-retinal granulomas. All systemic symptoms subsided a few days later. The quick and effective response to corticosteroids was an added criterion for the diagnosis of sarcoidosis. The treatment was pursued with oral prednisone 1mg/kg/day followed by a progressive tapering over 12 months. The following parameters were monitored and showed that the treatment was well tolerated: intra-ocular pressure, blood pressure, weight, fasting blood glucose and serum potassium. At the 12-month-follow-up visit, decimal BCVA was 1.0 on both eyes with a normal ocular examination.

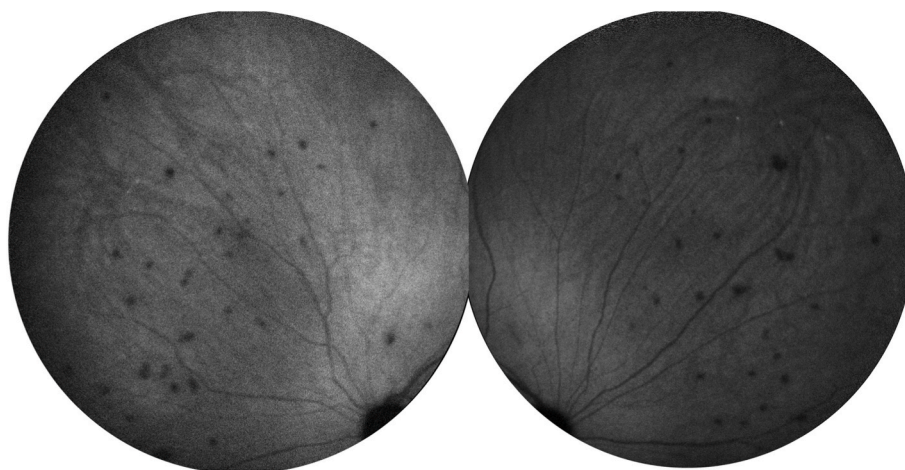


Fig. 4. Infrared autofluorescence (IRAF) imaging showing hypoautofluorescent spots at the site of the pre-retinal nodules.

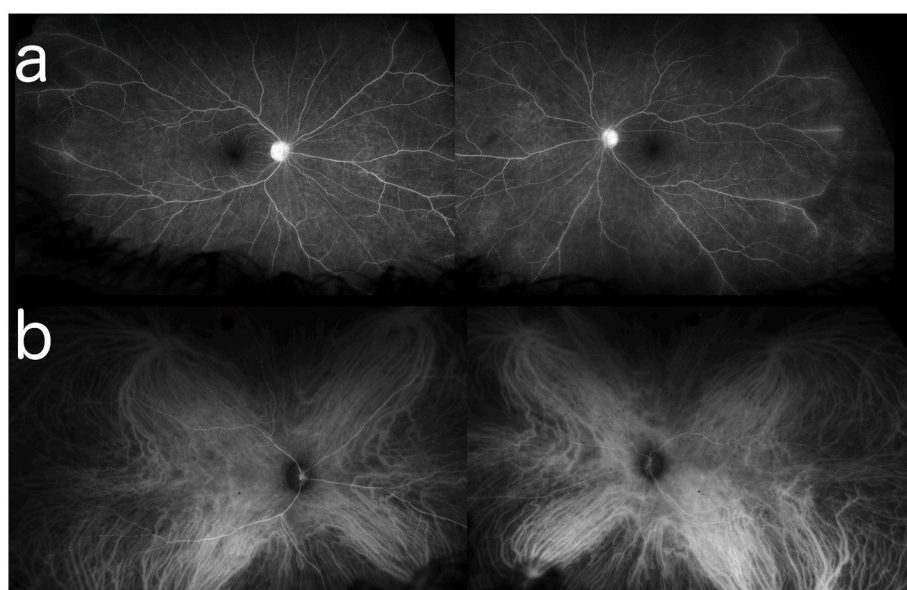


Fig. 5. Ultra-widefield fluorescein angiograms showing peripheral venous vasculitis and bilateral papillitis (5a) and normal ultra-widefield indocyanine angiograms (5b).

### 3. Discussion and conclusion

When sarcoidosis cannot be biopsy-confirmed, the diagnosis relies on a combination of findings and ocular manifestations are often helpful. In our case the association of the neurological and ophthalmic manifestations was key to the diagnosis. According to the International Workshop on Ocular Sarcoidosis (IWOS), the diagnosis of sarcoidosis in our case was considered probable as there was a combination of three intraocular signs (iris nodules, segmental peri-phlebitis and bilateral involvement) and two biological criteria (negative interferon-gamma release assay and increased ACE - although in the CSF but not in the peripheral blood).<sup>4</sup> Although rare cases of retinal nodules have been reported in other conditions such as syphilis or as a satellite manifestations of toxoplasmic retinochoroiditis, these diagnoses were ruled out in our patient.

Retinal or pre-retinal granulomas have rarely been reported as manifestations of ocular sarcoidosis and our case was particularly unusual because these multiple lesions were not associated with choroidal or optic nerve granulomas. Our survey of the literature identified only two similar reports: (1) a patient with skin-biopsy-proven sarcoidosis for

whom pre-retinal nodules appeared on OCT anchored in the retina and bulging in the vitreous; (2) a patient with proven sarcoidosis who died in a car accident and for whom the pathology showed pre-retinal granulomas without caseous necrosis.<sup>3,5</sup>

Why granulomas are more frequently localized in the choroid rather than in the retina remains unexplained. One hypothesis is that the choroidal vasculature may be more susceptible to lead to the development of granulomas because the choroidal vascular flow is greater than that of the retina. Moreover, areas of fenestration are present in the wall of the choroidal vessels only. Another factor may be that the choroidal environment allows more interactions between lymphocytes and macrophages leading to granuloma formation than the retina. Additionally, the blood-retinal external barrier might shield the retina from most of these manifestations, despite the macrophage-like potential of Müller cells. This may parallel the role of the blood-brain barrier which shields some sarcoidosis-associated manifestations resulting in a low incidence of neuro-sarcoidosis. In our case, it might not have been coincidental that a presentation with neurological manifestations was associated with retinal ones.

### Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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### Declaration of competing interest

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