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# Sarcoidosis revealed by simultaneous optic nerve and eyelid involvement: A case report

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ABSTRACT

*Purpose:* Ocular disease can be the initial manifestation in patients with sarcoidosis. It is most often associated with uveitis, but eyelid or optic nerve disease can also be presenting features. Although uncommon and easy to overlook in a patient presenting with visual loss, paying attention to the presence of eyelid granulomas in our patient proved to be very helpful in our diagnostic work up for optic neuropathy.

*Observations:* A young otherwise healthy patient was addressed with a 3 month history of bilateral painless visual loss. At presentation, best-corrected visual acuity was counting fingers in both eyes. Anterior segment slit-lamp examination was completely normal in both eyes. Eye fundus examination revealed subtle optic disc swelling in the left eye. Interestingly, flesh-colored nodular eyelid lesions were found bilaterally. Basic work-up for optic neuropathy showed elevated levels of serum lysozyme and serum angiotensin converting enzyme. More importantly, a biopsy specimen of an eyelid nodule demonstrated multiple non-necrotizing granulomas, a hallmark sign of sarcoidosis. Despite a delay in treatment of several months after onset of symptoms, response to systemic corticosteroids was prompt and important with visual acuity improving to 20/20 in both eyes as well as complete resorption of all eyelid lesions.

*Conclusion and importance:* In the diagnostic work-up for optic neuropathy, the answer can sometimes be hiding where it's least expected: the possible presence of eyelid lesions should not be overlooked as they may orient us towards sarcoidosis as an underlying etiology.

## 1. Introduction

Sarcoidosis is a systemic multi organ involving inflammatory disease of unknown cause that is characterized by granuloma formation in affected organs, most often in the lungs.[1] Clinically, sarcoidosis can be classified in many different ways, such as by type of onset, by natural history or by organ involvement.[1]

Ocular disease may be the initial manifestation in about 20% of cases (ranging from 5 to 40%). Uveitis is the most common ocular manifestation, followed by conjunctival and lacrimal gland involvement.[2] Involvement of the skin of the eyelids in patients with cutaneous sarcoidosis may also be seen. However, sarcoidosis granulomas within the eyelid appear to be an uncommon finding.[3] Neurological involvement can be recognized in 5–10% of patients with sarcoidosis, with the facial nerve being the most commonly affected cranial nerve (ranging from 15 to 39%) closely followed by the optic nerve (ranging from 4 to 35%).[4]

We hereby present a rare case of a young otherwise healthy patient with simultaneous bilateral optic nerve and eyelid involvement, leading to disease diagnosis.

## 2. Case report

A 26-year- old patient of African descent was addressed to our hospital with a 3 month history of bilateral acute painless visual loss. Initially the patient was still able to continue his daily activities, but unfortunately, visual impairment progressed 6 weeks after onset, resulting in a best-corrected visual acuity of "counting fingers" in both eyes at the time of presentation in our hospital. The patient had also noted bilateral appearance of eyelid lesions that emerged simultaneously with the first symptoms of vision loss. Medical history was unremarkable and not indicative for possible toxic substance ingestion or malnutrition.

Goldmann visual field testing showed limited concentric loss for the V4e isopter in the left eye, whereas an altitudinal inferior loss was found in the right eye. The patient failed to respond to smaller or less bright

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testing lights. Intraocular pressure was 19 mmHg in both eyes. There was no relative afferent pupillary defect, but both pupils showed relative mydriasis with sluggish response to light, especially in the right eye. Eye movements were full and painless. Slit-lamp examination of the anterior segment revealed no signs of intraocular inflammation in both eyes. Near the medial canthi of both eyes small, flesh-colored nodular lesions were found on the upper and lower eyelid of the right eye and on the lower eyelid of the left eye [Fig. 1a]. Funduscopic examination revealed asymmetry of optic disc cupping with a Friesen grade 1 optic disc swelling of the left optic nerve [Fig. 2], but was otherwise normal. Macular OCT showed normal morphology of retinal layers with a slightly thinned ganglion cell layer thickness in both eyes [Fig. 3a and b], whereas peripapillary retinal nerve fiber layer (RNFL) measurements were slightly thickened in the left eye [Fig. 4a and b]. Fluorescein angiography and indocyanine green angiography were completely normal.

Initial work-up for bilateral optic neuropathy showed normal levels of vitamins A, B6, B9, B12 and homocysteine and a subtle zinc deficiency (64μg/dL with normal values range 80–120μg/dL). Serum angiotensin converting enzyme (ACE) level was elevated at 128U/L (normal values 8–55 U/L) as well as serum lysozyme level (34 μg/mL – normal values 9.56–17.14 μg/mL). Calcium level was normal. Tuberculin skin test and QuantiFERON assay for tuberculosis were negative. Cerebral magnetic resonance imaging (MRI) of the optic nerves and optic chiasm showed no hyperintense lesions on fluid-attenuated inversion recovery (FLAIR) or fat suppressed T2 sequences. Coronal T2 sequences showed important bilateral perioptic nerve sheath distension secondary to optic atrophy. Interestingly, nodular lesions at the parotid glands were also found.

Based on initial work-up, a diagnosis of sarcoidosis was highly suspected. Thoracic computerized tomography scan imaging (CT scan) revealed bilateral non-necrotizing hilar and mediastinal lymphadenopathy as well as parenchymatous lesions typical for sarcoidosis. Diagnosis was then confirmed by microscopic examination of a biopsy specimen of an eyelid nodule, showing multiple non-necrotizing granulomas containing epithelioid macrophages, as well as some multinucleated giant cells and some lymphocytes.

It was decided to start systemic methylprednisolone (1 g/day intravenous pulses for 3 consecutive days, followed by oral administration of initially 32 mg/day). A dramatic improvement of visual function was observed: after only 1 pulse of intravenous treatment, visual acuity improved from seeing “hand movements” to 20/100 in the right eye and from 20/40 to 20/20 in the left eye. Visual acuity was 20/20 in both eyes after two weeks of treatment, with resolution of the subtle optic disc swelling in the left eye and evolution towards bilateral optic nerve atrophy on OCT scan [Fig. 3c and d & 4c-d]. Eyelid lesions resolved completely [Fig. 1b].

## 3. Discussion

The clinical picture of a patient with bilateral painless visual acuity loss with funduscopic and OCT evidence of subtle optic disc swelling and/or relative loss of macular ganglion cell layer thickness preceding RNFL loss mimics the characteristic description of so-called “mitochondrial optic neuropathies” typically seen with toxic, nutritional or genetic disorders. The same clinical presentation has also been documented in compressive disease[5,6,7,8].

However, the simultaneous appearance of eyelid lesions in this patient should attract our attention as this type of nodular lesions has previously been documented in association with sarcoidosis.[3,9] Eyelid involvement may be the first feature of sarcoidosis. Its incidence in adnexal sarcoidosis ranges from 11.5 to 17% and it may be seen in the form of “millet seed “nodules, ulcerated nodules, plaques, diffuse eyelid swelling, papules and destructive skin lesions.[3,10]

The non-necrotizing granulomas found on microscopic examination of an eyelid biopsy specimen in our patient are a hallmark sign of sarcoidosis.[11] The histological confirmation of non-necrotizing granulomatous inflammation, together with the thoracic CT –scan findings compatible with stage II disease, and the elevated serum level of ACE, meet multiple major and minor diagnostic criteria suggested for the diagnosis of sarcoidosis.[11] According to recently proposed diagnostic guidelines, the presence of optic nerve disease in our patient would also allow us to establish the diagnosis of “definite” neuro-ophthalmic sarcoidosis.[12]

Involvement of the optic nerve in sarcoidosis may be due to inflammation of the nerve itself or to meningeal inflammation within the optic nerve sheath (causing optic perineuritis). Alternatively, there might be compression or infiltration by sarcoid granulomas within the disc itself, by an inflammatory mass adjacent to the anterior visual pathway or as a consequence of intracranial hypertension. Secondary involvement through ischemic complications of retinal and choroidal inflammation and/or glaucoma is also possible.[2,13] A recently published prospective series including 52 patients with optic neuropathy related to sarcoidosis identified two main clinical subtypes.[13] Subacute optic neuropathy that evolved over days resembling optic neuritis was the more common presentation and was found in 43 cases, of which 12 were bilateral (8 sequential bilateral and 4 synchronous). A more slowly progressive optic neuropathy in which the symptoms evolved over weeks was found in 6 cases, all of which were unilateral and all were shown to have a more widespread neurologic involvement (all showing evidence for adjacent meningeal inflammation). Pain was a feature in


**Fig. 1.** (a) Photograph showing numerous flesh-colored nodules medially on both eyelids of the right eye and on the lower eyelid of the left eye. (b) Photograph taken after two weeks of systemic corticosteroids showing complete resolution of eyelid lesions.

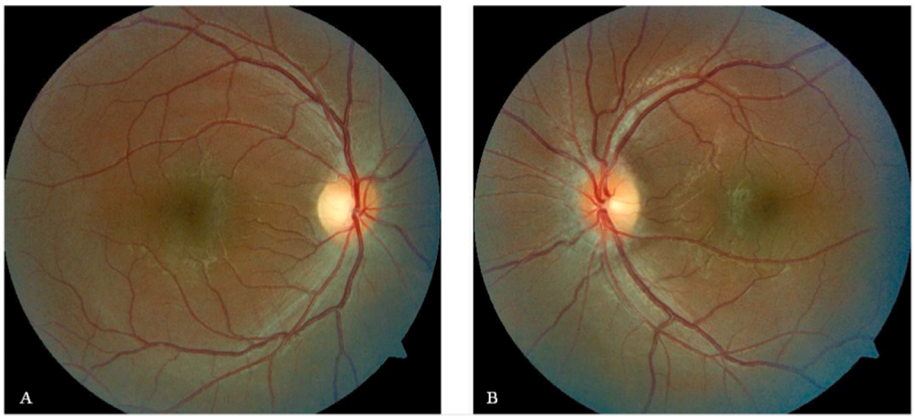


**Fig. 2.** Eye fundus at presentation showing clear vitreous and asymmetry of optic disc cupping with optic disc margins showing sharp edges in the right eye (a) and a Friesen grade 1 optic disc swelling in the left eye (b).

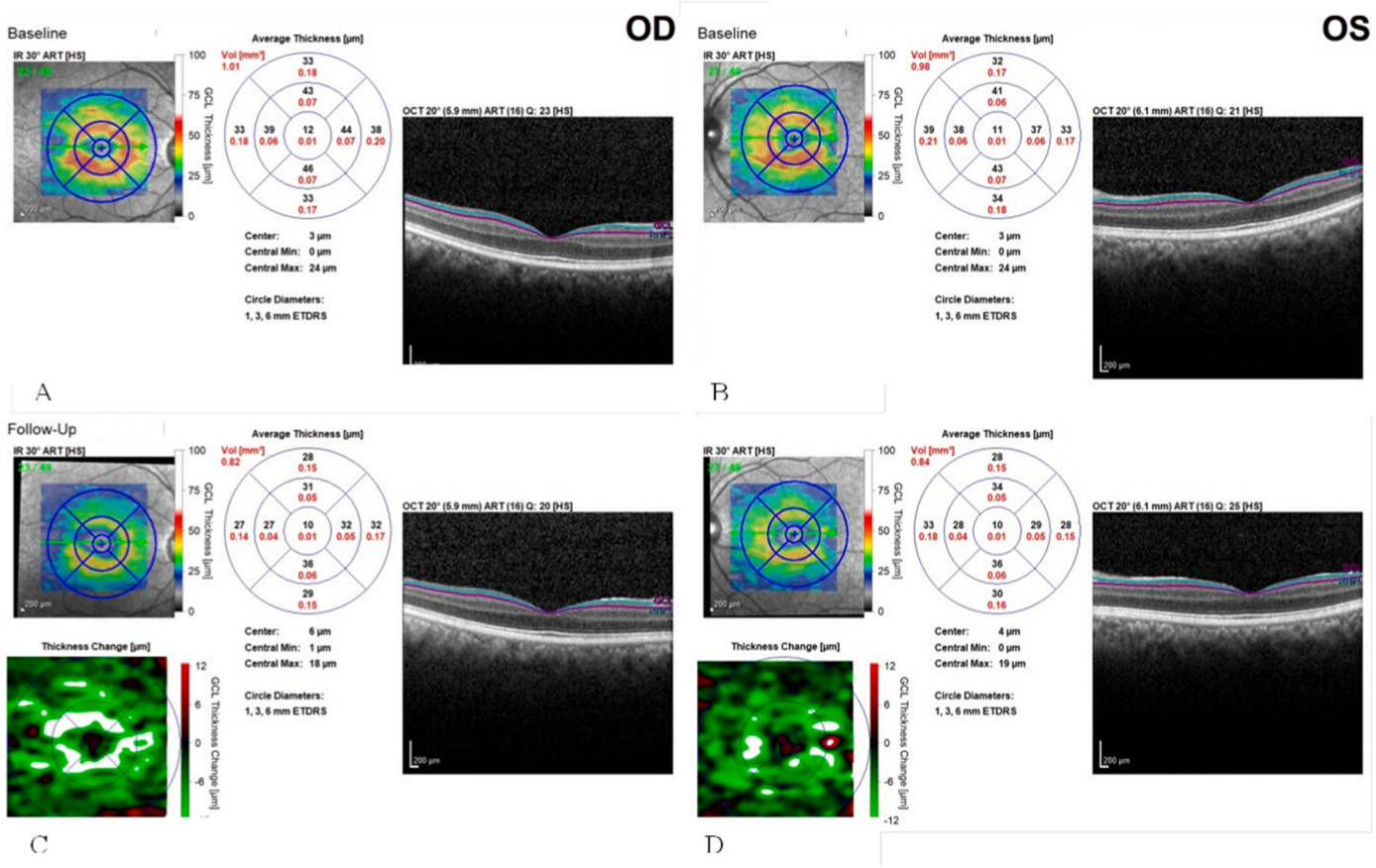


**Fig. 3.** Optical coherence tomography showing macular ganglion cell layer thickness at presentation (a,b) and 6 weeks later (c,d).

27% of cases overall, and (predominantly mild) intraocular inflammation was seen at the same time as the optic neuropathy in 36% of cases. Substantial improvement in vision, even after several weeks without treatment, was seen in the patients with the subacute syndrome, whereas those in the progressive subgroup showed no improvement in visual acuity with treatment (even though the disease process required, in general, a higher and more prolonged dose of steroids and/or concurrent immunosuppression).[13] Despite only administered several months after onset of visual loss, our patient also showed prompt and dramatic improvement of vision with systemic corticosteroids. This evolution is most compatible with the above described subgroup presenting with subacute optic neuropathy.

Cerebral MRI in our patient failed to show hyperintens lesions on T2 weighted images at the level of the optic nerves. Due to availability issues, contrast weighted T1 sequences were not obtained, therefore we could not adequately evaluate any meningeal (though not identified on other sequences) nor optic nerve sheath enhancement (in search of the so called 'tram-track' and doughnut' signs on axial and coronal images respectively),[14] the latter to exclude possible (concomitant) optic perineuritis. Cases of optic perineuritis due to sarcoidosis presenting with painless and/or progressive visual loss have been reported, thereby often masquerading both the radiological and clinical appearance of optic nerve sheath meningiomas[15,16,17,18] Visual loss experienced by patients with optic perineuritis usually takes place over several weeks,

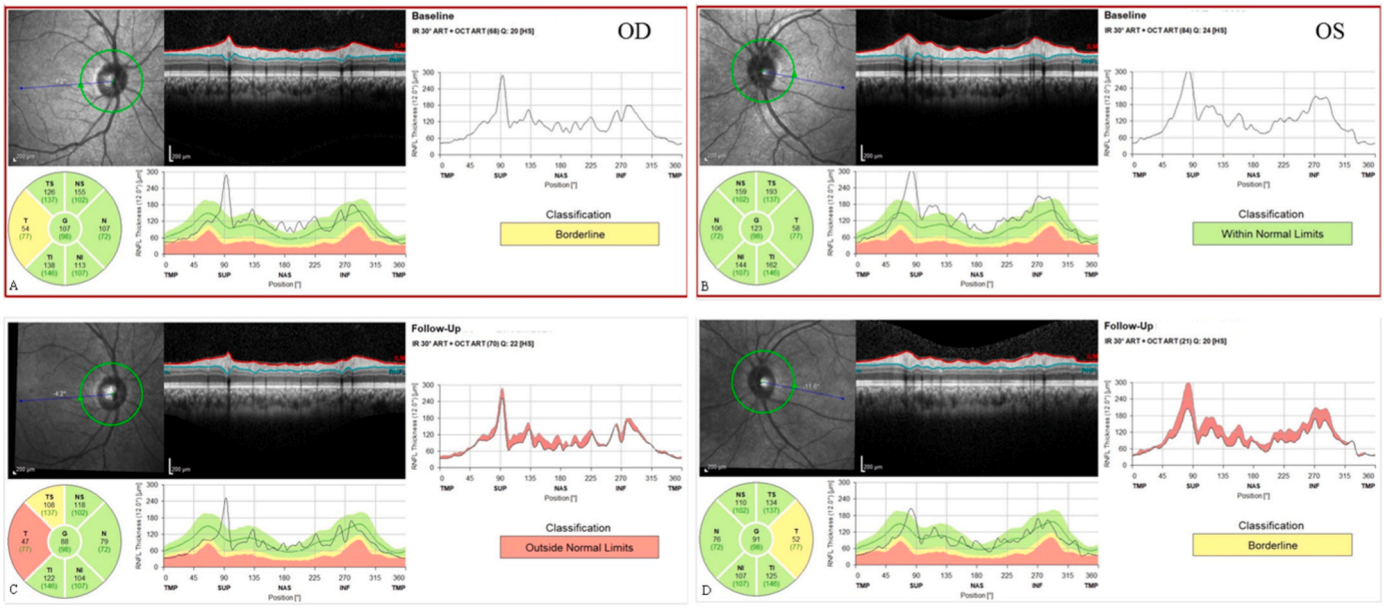


**Fig. 4.** Optical coherence tomography showing peripapillary retinal nerve fiber layer thickness at presentation (a,b) and 6 weeks later (c,d).

often with sparing of central vision. Response to corticosteroids is usually very good, with often prompt (within hours) relief of pain, and rapid improvement in visual symptoms[17,18,19,20]. Important to our case however, is the notion that the outcome in optic perineuritis seems to be dependent on time between onset of symptoms and initiation of corticosteroid treatment, with poor prognosis associated with delays to the initiation of treatment, making it less likely to be relevant in our patient.[19,20]

Both eyelid and optic nerve disease separately can be the isolated and/or presenting feature in (ocular) sarcoidosis.[3,13] We presented a rare case of a young patient with simultaneous involvement of both structures without additional signs of intra-ocular inflammation on clinical examination, fluorescein angiography or indocyanine green angiography. Despite a delay in treatment of several months after onset of symptoms, response to systemic corticosteroids was prompt and dramatic for both components.

## 4. Conclusion

In the diagnostic work-up for optic neuropathy, the answer can sometimes be hiding where it's least expected. The possible presence of nodular eyelid lesions should not be overlooked as they oriented us towards sarcoidosis as the underlying etiology in our patient.

## Patient consent & ethics approval

Informed consent was obtained from the patient for the purpose of publication.

Approval by the Ethics Committee of the CHU Saint-Pierre hospital in Brussels was acquired.

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## Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

## Declaration of competing interest

The authors report no conflicts of interest.

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