

FOCAL SCLERAL NODULE AND SCLERODERMA: REPORT OF ONE CASE AND AN OBSERVATIONAL SERIES

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ABSTRACT – Objective: a) To report an original case of focal scleral nodule (FSN) in a patient affected by collagen's systemic disease; b) to investigate the possible correlation between the two clinical entities by means of an observational case series.

Case Presentation: A 74-year-old Caucasian woman was referred on the suspicion of choroidal tumor. She was affected by Systemic Sclerosis (SSc), with a history of an ancient ovarian tumor and a recent severe bacterial pneumonia. Ocular investigations, associated with total body oncological follow up and blood investigations for granulomatous diseases, supported the diagnosis of FSN. Mydriatic funduscopy was then performed in cohort of 62 eyes of patients affected by confirmed SSc excluding other similar conditions.

Conclusions: The simultaneous presence of FSN and SSc has never been reported. The present series has excluded these concomitant findings in a cohort of confirmed SSc subjects. It is probable that SSc alone is not a sufficient condition to promote FSN formation. Further events (e.g., bacterial infections) may play a role in triggering a type 1 collagen over-deposition.

KEYWORDS: Focal scleral nodule, Systemic scleroderma, Pathogenesis.

INTRODUCTION

The ophthalmological alteration dealt in the present study was firstly described in 1997 under the earlier name of unifocal helioid choroiditis because of its “sun-like” appearance ¹. In 2002 Shields et al² described 60 similar lesions renamed solitary idiopathic choroiditis (SIC). The large availability of the optical coherence tomography (OCT), particularly implemented with the enhanced depth imaging technique (EDI-OCT), enabled to observe that the characterizing lesions were actually located into the sclera/outer choroid complex ³. These and further imaging and clinical insights have led to the present definition of focal scleral nodule (FSN) ⁴. The FSN is an extremely rare finding consisting of scleral lesions of approximately 1 disc diameter which typically appear stable, solitary, yellow-white, and located in the peripapillary region. So far, no patient has shown association with an extraocular inflammatory process, or with any active systemic inflammatory and/or immune disorder.



In the herein study we first described a case of FSN in a patient with Systemic Sclerosis (SSc). This peculiar finding drove us to perform mydriatic funduscopy in a series of patients with confirmed SSc with the aim of investigating the possible correlation between the two clinical entities.

Case Report and observational series

A 74-year-old Caucasian woman was referred to the Eye Clinic of the Local University Hospital (Parma, Italy) for suspicion of ocular amelanotic malignancy in her right eye (RE). The patient denied any ongoing ocular or systemic symptom and the lesion, originally remarked during a routine fundus examination, was as in Figure 1A. The medical history of the patient included the following items:

- Ongoing treatment for: hypothyroidism (levothyroxine); arterial hypertension (beta-blocker); supra-ventricular tachycardia (antiplatelet agent).
- Ovarian epithelial tumor surgically removed 22 years earlier, without any subsequent relapse and/or dissemination.
- “Limited” SSc diagnosed 7 years earlier based on the presence of Raynaud’s phenomenon, anti-centromere antibodies (ACA 1:320), sclerodactylia and positive capillaroscopy⁵. When the ocular lesion was discovered, SSc was being controlled with nifedipine (10 mg/day) and behavioral regimen.
- Bacterial pneumonia treated by a three-week course of double antibiotic therapy occurred about 5 months earlier.

To investigate the etiology of the ocular nodule, a broad-spectrum systemic work-up was performed. It included: 1. oncological evaluation with high-resolution chest CT scan repeated after 6 months, cranial magnetic resonance, total body positron emission tomography/CT, blood tumor-related markers. 2. Blood withdrawal for autoimmunity (including the angiotensin-converting enzyme), which tested regular except for the confirmation of the ACA titer at 1:320. 3. Blood investigations for infectious diseases (including QuantiFERON, toxoplasma, syphilis, SARS-CoV-2 immunoglobulins), all negative too. Other less common compatible pathologies such as *Toxocara canis* infestation, Lyme disease, Wegener’s granulomatosis, were excluded according to the medical history. Rheumatological evaluation assessed the status of clinical quiescence of the SSc.

Ophthalmological evaluation provided the following evidences: best-corrected visual acuity of 20/20 in both eyes; intraocular pressure of 18 mmHg in the affected eye (15 mmHg in the LE). Initial lens cataract, no sign of inflammation in the anterior and posterior segment in OO. B-scan ultrasound showed in the RE a dome-shaped formation protruding 1.2 mm from the choroidal plane and having the largest basis of 3.5 mm. Internal echogenicity was minimally hyperreflective with no signs of calcification or extraocular extension. Fundus autofluorescence, showed stippled hyperautofluorescence of the lesion area. Fluorescein angiography was as shown in Figure 1(B,C).

Indocyanine green angiography demonstrated constant hypocyanescence. In OCT angiography (OCTA) the lesion appeared avascular and choroidal flow void was demonstrated in the choriocapillaris region overlying the lesion (Figure 2A); EDI-OCT showed a dome-shaped lesion confined to the sclera. The choroidal layer above the scleral nodule was devoid of vascular lacunae, without evidence of subretinal fluid and drusen (Figure 2B). According to fundus imaging and the systemic investigations described above, we diagnosed FSN.

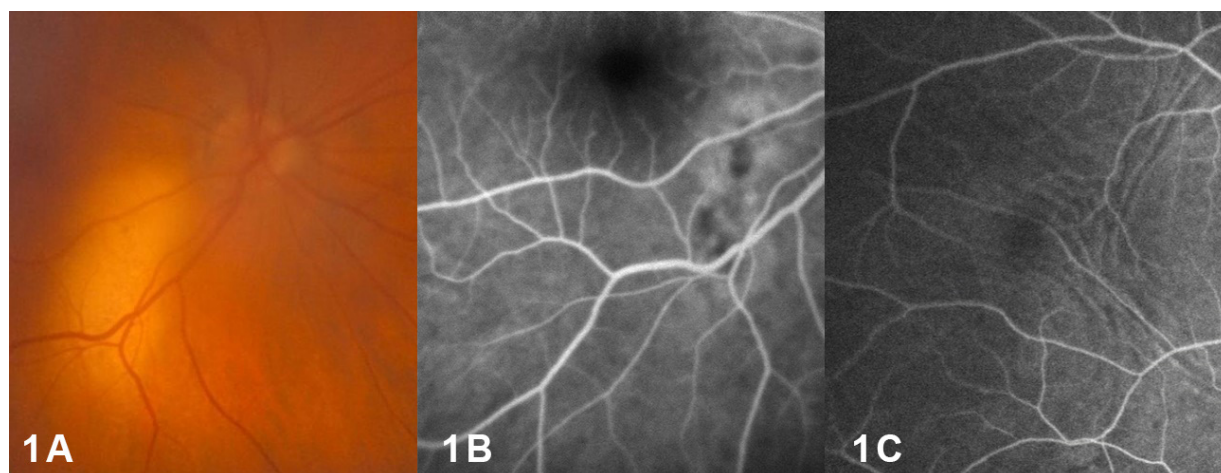


Figure 1. A, Fundus color photograph showing the yellow/white amelanotic lesion; B, fluorescein angiography with early hyperfluorescence around the margins of the lesion; C, choroidal folds irradiated up to the macular region.

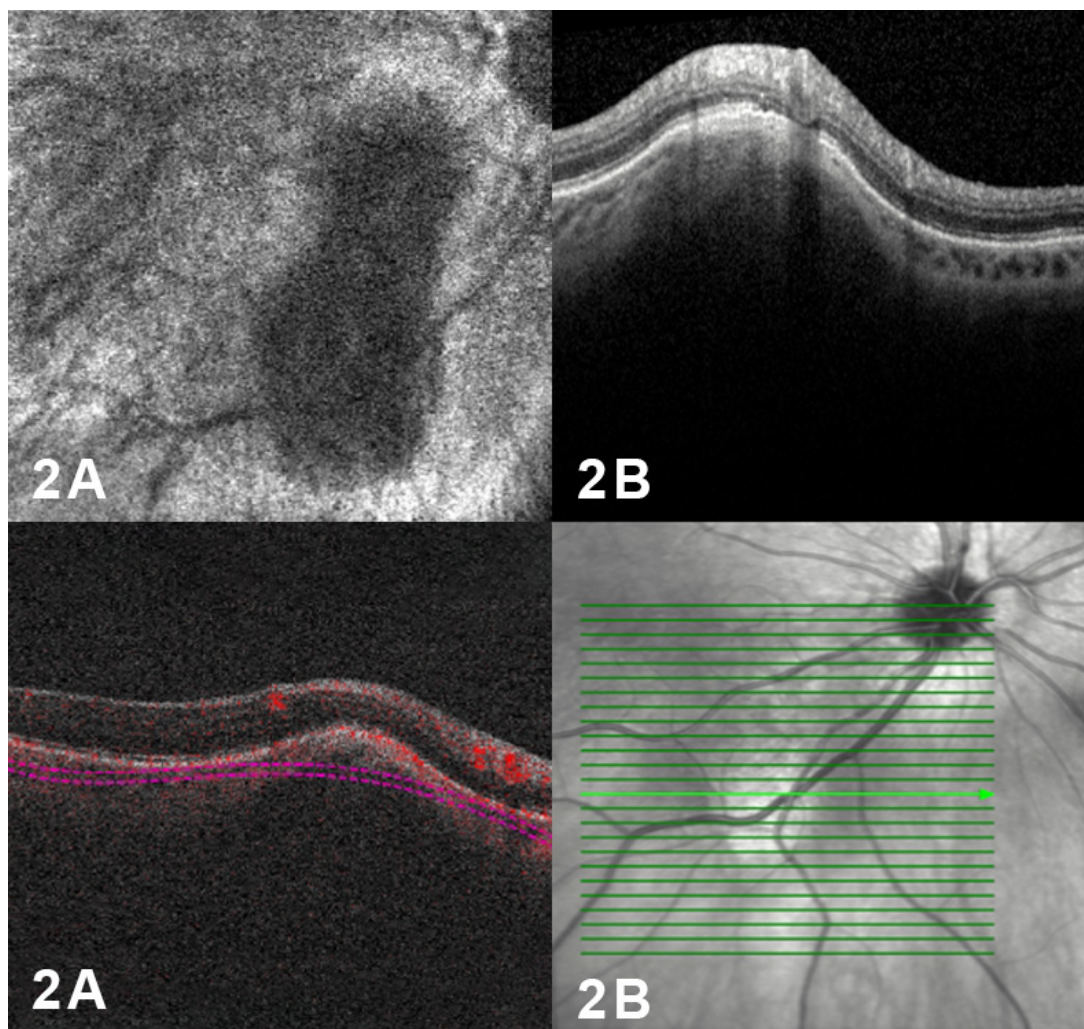


Figure 2. *A*, In OCT angiography the lesion appeared avascular and choroidal flow void was observed in the overlying choriocapillaris region. *B*, The OCT showed a dome-shaped lesion confined to the sclera. The corresponding choroidal layer was devoid of vascular lacunae, without evidence of subretinal fluid and drusen.

The finding of a FSN in a patient with SSc led us to plan mydriatic funduscopy in all the available patients with SSc on their presence at the Internal Medicine and Rheumatology Unit of the hospital to undergo the Iloprost weekly regimen (performed for five consecutive days every 8 weeks during the coldest period of the year). Since the FSN is almost invariably asymptomatic, a screening evaluation in selected subjects could disclose a possible correlation between these two independent diseases, both characterized by altered collagen metabolism and deposition. The evaluation respected the tenets of the declaration of Helsinki and was authorized by the local Ethics Committee (protocol number 34379). Indirect funduscopy under mydriasis with tropicamide 1% was performed on 62 eyes of thirty-one subjects with confirmed SSc (27 women and 4 men; mean age 60 years, range: 38 - 83 years). In 55 eyes the examination tested completely silent; in the remaining eyes the following unrelated anomalies were recorded: advanced nuclear cataract in 2 eyes; raised optic nerve cup excavation in 2 eyes; background diabetic retinopathy in 1 eye; atrophic age-related maculopathy in 1 eye; choroidal nevus in 1 eye. No case deserved further investigations for nodular formations in the posterior segment of the eye.

DISCUSSION

At present the characteristics of about seventy FSN cases, mostly from North America and Australia, have been described in the literature^{3,4}. These series agreed that FSN is not associated with extraocular disorders; it chiefly affects adult white women presenting as a solitary, yellowish lesion, often located in the peripapillary region and without predilection for laterality. The lesion tends to remain stable, and

the diagnosis always requires the exclusion of malignancies and infectious granulomas. A recent report describes 2 cases of FSN in whom the localized reduction in blood flow was documented by laser speckle flowgraph⁶. Based on the seminal article by Shields et al² and the following literature, FSN was never found associated with chronic systemic disease, especially autoimmune disorders^{1,3,4,7-11}.

We described a case of FSN appeared in a patient with prior diagnosis of limited SSc. The type 1 collagen, specifically involved in the pathogenesis of SSc, is the same substance that sclera is composed of. Briefly, SSc is a chronic autoimmune disease resulting from an overproduction and accumulation of collagen in body tissues, predominantly skin, connective, and parenchyma⁵. There are two SSc patterns: diffuse or limited. About 50% of patients shows the limited pattern, which is more benign and characterized by a slower progression typically confined to the fingers, hands, and face. In diffuse SSc, instead, the skin thickening occurs more rapidly and extends more widely than in the limited pattern. Patients with diffuse SSc have higher risk of developing fibrous hardening of the internal organs.

CONCLUSIONS

We report the characteristics of a patient presenting with an original association between FSN and limited SSc. Patient's medical history also included severe pneumonia (SARS COV-2 infection excluded) occurred few months before the first observation of the scleral nodule. The presence of FSNs was then excluded in a cross-sectional series of other thirty-one patients presenting with SSc. Based on the present results, it is inferable that SSc alone is not a sufficient condition to support direct correlation with FSN. Further events (e.g., bacterial infections) may play a role in triggering an overproduction/deposition of collagen matrix involving the sclera, namely a different place than those typical for SSc. The lack of histopathological data from the scleral nodules still limits a deeper characterization of the pathogenesis of the ocular disease.

CONFLICT OF INTEREST:

None of the authors has conflicting relationship.

FINANCIAL SUPPORT:

None.

INFORMED CONSENT:

The involved patients gave written consent for the processing of personal data and images.

ETHICS COMMITTEE APPROVAL:

The evaluation respected the tenets of the declaration of Helsinki and was authorized by the local Ethics Committee (protocol number 34379).

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