Choroidal neovascularization complicating sclerochoroidal calcifications

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ABSTRACT
Purpose: Sclerochoroidal calcifications (SCC) are rare conditions characterized by unifocal or multifocal well-defined scleral deposits of calcium. The present study describes two cases of SCC complicated by the onset of choroidal neovascularization (CNV).
Method: Five patients affected by SCC were enrolled in the study and two cases were complicated by CNV. Both patients underwent complete ophthalmic examination with multimodal imaging including optical coherence tomography angiography (OCTA).
Results: In the two patients with CNV (1 male), BCVA was 20/40 and 20/50 in the affected eyes. Fundus examination revealed an irregular yellow-white lesion close to the superotemporal arcade in both patients, with exudation. The diagnosis of CNV was performed by means of fluorescein angiography in one patient and OCTA in the other patient. The patients received a total of 3 and 9 ranibizumab injections respectively over a six-year follow-up, reaching a final BCVA of 20/25 in both patients with stabilization of the CNV.
Conclusions: SCC may be complicated by CNV, with good management obtained by intravitreal anti-VEGF injections.

1. Introduction
Sclerochoroidal calcifications (SCC) are unifocal or multifocal well-defined scleral deposits of calcium of variable size and form, with predilection to the vicinity of the retinal vascular arcades. 1–4 Choroidal neovascularization (CNV) is rarely reported in SCC. We describe the management of two patients with SCC-related CNV responding to intravitreal ranibizumab treatment.

2. Methods
The study was designed as a prospective case series with a planned follow-up of at least two years. Consecutive patients referred for SCC to the Ophthalmology Department of San Raffaele Hospital between 2010 and 2018 were examined. The study was approved by the Ethical Committee of IRCCS San Raffaele Hospital (Milan, Italy) (protocol MIRD), in accordance with Helsinki declaration. All the patients, once informed about the study, signed an informed consent. Inclusion criteria were the identification of both SCC and CNV. Any other conditions potentially correlated to the development of CNV were considered as exclusion criteria. All the patients underwent a best corrected visual acuity BCVA using EDTRS chart, biomicroscopic evaluation of the anterior and the posterior segments, color fundus photography, blue-light fundus autofluorescence (FAF), and spectral domain optical coherence tomography (OCT) (Spectralis, Heidelberg, Germany). CNV management was planned as pro-re-nata regimen after a single ranibizumab injection at baseline. The detection of any fluid on structural OCT was considered as indication to further ranibizumab re-injection. Primary outcome of the study was the functional and anatomical outcomes after the treatment.

3. Results
Five patients had the diagnosis of SCC, and two patients were found to have associated CNV in the right eye. These two patients were 67-year-old diabetic hypertensive man without diabetic retinopathy and 77-year-old hypertensive woman, both complaining of progressive visual deterioration in the right eye. Screening for SCC was negative in both family members, considering the parents of both patients, one son of the male patient and both one son and one daughter of the female**
Fig. 1. First case of sclerochoroidal calcification complicated by choroidal neovascularization. Baseline fundus appearance shows an irregular yellowish lesion close to the superotemporal vascular arcade (A). Fluorescein angiography detects a mainly hyperfluorescent lesion with increased leakage in late phases (B). The fundus image acquired at the last follow-up visit shows fibrotic changes (C) and fluorescein angiography detects only staining of the lesion without leakage (D).

Fig. 2. Second case of sclerochoroidal calcification complicated by choroidal neovascularization. Baseline fundus examination shows a yellowish lesion developed in the superior vascular arcade (A). This lesion turned out to be almost fibrotic at the last follow-up examination (B). Structural OCT shows totally disrupted retinal structures in the context of the growing lesion (C). The patient is characterized by macular edema at baseline (D), regressing due to anti-VEGF treatments (E).
patient. No relevant information available for the other generations of relatives.

BCVA was 20/40 and 20/50 in the right eye, respectively. The unaffected left eye had a BCVA of 20/20 in the first patient and counting fingers in the second patient from amblyopia. Anterior segment and intraocular pressure were normal.

Biomicroscopic fundus examination revealed an irregular yellow-white lesion close to the superotemporal arcade in both patients, showing fluid exudation extending to the fovea (Fig. 1 and Fig. 2). One eye also showed a pucker with pseudomacular hole. Fundus autofluorescence at the level of the SCC revealed an irregular hypofluorescent signal, whereas structural OCT of the lesions showed thinning and disruption of the outer retinal bands, along with choroidal thinning. There was evidence of intraretinal cysts in both patients. Fluorescein angiography was performed in the first patient, disclosing irregular staining of the SCC, and slight, late leakage from the CNV. OCTA was carried out in the second patient, revealing the neovascular network at the inner border of the SCC (Fig. 3).

The patients underwent intravitreal ranibizumab injections following a pro-re-nata regimen on the basis of the identification of fluid on structural OCT. Overall the patients received a total of 3 and 9 injections respectively over a six-year follow-up. At the last examination BCVA improved to 20/25 in both patients with stabilization of the CNV and resolution of the intraretinal cysts (Fig. 4).

4. Discussion

Sclerochoroidal calcifications are usually asymptomatic discrete yellowish lesions.1–6 SCC can be either idiopathic or secondary to systemic disorders, including parathyroid tumors, hyperparathyroidism, chronic renal disease, Bartter syndrome, and Gitelman syndrome.1–6 CNV may complicate the course of SCC, showing variable clinical outcomes.5,7–11 When the CNV is asymptomatic and distant from the fovea, no treatment may be required, a frequent monitoring being sufficient to ascertain the stabilization of the CNV.5,7 On the other hand, several treatment modalities are available when CNV showed exudative manifestations, including laser photocoagulation, photodynamic therapy and anti-VEGF injections.7–12 Intravitreal anti-VEGF treatment was used to stabilize the SCC-related CNV activity in a few cases, with variable results.10–12 In particular, in a single case, a series of bevacizumab injections failed to control the CNV-related retinal exudation,11 whereas in another case the macular edema and subretinal fluid was reduced after an unspecified number of intravitreal anti-VEGF injections in combination with a single posterior subtenon injection of triamcinolone.
Our experience in two consecutive patients affected by CNV secondary to SCC suggests that intravitreal ranibizumab can achieve positive functional and anatomical outcomes over a six-year follow-up. Interestingly, a single injection was not enough to promote the CNV stabilization, being necessary to administer 3 and 9 injections respectively, over a six-year follow-up. The advanced age of the patients may have had a role in the required number of injections, as, supposedly, younger patients may require less treatment with a prompter response. Nevertheless, CNV seems to complicate the course of SCC in advanced age, since all the described cases are above 70. OCT angiography in one case demonstrated choroidal ischemia in the area of SCC and it is possible that the choroidal hypoperfusion or RPE compression by SCC can lead to CNV formation. Of interest is the close similarity between CNV in choroidal osteoma and CNV in SCC, knowing that up to half of eyes with choroidal osteoma can develop CNV and are best treated with anti-VEGF injections. We acknowledge that indocyanine green angiography examination, not performed for these patients, would have improved the multimodal imaging assessment of the disease. Further studies are warranted to analyze the effects of anti-VEGF approach, along with the specific indications for the most appropriate management of exudative CNV secondary to SCC.

Patient consent

Consent to publish this case report has been obtained from the patient in writing.

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Authorship

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

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Declaration of competing interest

All the authors have no conflict of interest.
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