Rare disease

An ocular presentation of familial tumoral calcinosis

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Summary

This case report presents the ophthalmic features and complications of a 56-year-old Caucasian woman with familial tumoral calcinosis. She presented to our ophthalmology clinic with a 3-month history of blurring of her vision. She had been diagnosed 14 years earlier with familial tumoral calcinosis. Ophthalmological examination revealed calcific depositions on the eyelid margins, perilimbal calcific deposits and angioid streaks. An optical coherence tomography scan of the left eye revealed a choroidal neovascular membrane. Deterioration in vision occurred secondary to subretinal haemorrhage, resulting from the angioid streak. The patient was treated with a series of three intravitreal ranibizumab injections to her left eye, which led to an improvement in her visual acuity (VA). The patient is being closely followed up with monthly appointments, and to date, after 6 months of follow-up, there has been no further deterioration in her VA or reactivation of the choroidal neovascular membrane.

BACKGROUND

Tumoral calcinosis is a rare disorder of phosphate metabolism. The term was first coined in the literature in 1943.¹ It is characterised biochemically by elevated serum phosphate levels, increased renal tubular phosphate reabsorption and normal or elevated serum 1,25-dihydroxyvitamin D levels. Calcium and parathyroid hormone levels are generally within the normal range.² Ectopic deposition of calcium in soft-tissue para-articular regions, dental pulp, skin and the vasculature are other characteristic features.^{1 3–5} A recessive homozygous mutation in the fibroblast growth factor-23 gene, leading to the substitution of glycine for serine at residue 71, is known to be a cause of familial tumoral calcinosis and was the mutation identified in this case.⁶ Ocular involvement in tumoral calcinosis has been reported to include calcific-lid lesions of the eyelids, conjunctival calcific deposits, band keratopathy and angioid streaks.^{1 5 7–12} Ocular features of tumoral calcinosis have rarely been described in the literature. To the authors' knowledge, there has been no previous report in the literature of such a presentation of ophthalmic tumoral calcinosis.

CASE PRESENTATION

A 56-year-old woman presented to our ophthalmology clinic in September 2009, with sudden onset of blurred vision occurring 3 months earlier. She also reported metamorphopsia and micropsia. She had no past ophthalmic history. She was referred by an optometrist to our clinic after a routine visual check.

She had been diagnosed at the age of 42 with tumoral calcinosis after presenting with a painful right foot.¹³ She was of a consanguineous union.⁶ Her sister was also affected with the condition and her two brothers, while asymptomatic, were both carriers. Her parents had never been tested for this condition.

Her previous history was significant for large joint arthralgia, renal stones and calcification of the placenta

noted after her two pregnancies.¹³ At diagnosis she was noted to have osteoarthritis of both hands, calcification of the soft tissue of the left thigh, diminished pedal pulses in the right lower limb and widespread calcification of the upper- and lower-limb vasculature. A biochemical profile at this time revealed elevated serum phosphate, normal serum calcium, normal 1,25-dihydroxyvitamin D, normal alkaline phosphatase and normal parathyroid hormone levels.¹³

General examination at the ophthalmology clinic in 2009 revealed irregular dentition and swelling of the proximal interphalangeal joints of both hands related to calcium deposition. No evidence of soft-tissue calcification was observed. Blood pressure was noted at 128/74. Otherwise the systemic examination was normal.

On ophthalmological examination, the patient's corrected visual acuity (VA) was 6/6 in the right eye and 6/36 in the left eye. Examination of the eyelids revealed approximately 8–10 yellow/white calcific nodules on the lower-eyelid margins bilaterally (figure 1). These were located near the grey line, just posterior to the meibomian openings, and were more prominent towards the lateral canthi. Anterior segment examination revealed shiny, white, perilimbal calcific deposits in the left-nasal conjunctiva (figure 1). These were not present in the right eye. No other abnormal calcific deposition was noted. The corneae were clear in both eyes. Both lenses were normal. Gonioscopy and tonometry were normal. Retinal examination of the right eye revealed two small, flame-shaped, haemorrhages adjacent to the optic disc (figure 2). Retinal examination of the left eye revealed an elevated fibrotic macular mass with overlying fluid (figure 3). Along the superior border of this mass, an area of haemorrhage was noted. Angioid streaks were observed in both eyes.

INVESTIGATIONS

An optical coherence tomography (OCT) scan of the left eye showed macular intraretinal and subretinal fluid typical

Figure 1 External photograph of the patient's left eye, illustrating perilimbal calcific deposits in nasal conjunctiva and calcific deposits on the lower-lid margin.

Figure 2 Fundus photograph of the patient's right eye, illustrating two small, flame-shaped, haemorrhages adjacent to the optic disc.

Figure 3 Fundus photograph of the patient's left eye, illustrating an elevated fibrotic mass with underlying fluid, on the macula. A single angioid streak is also observed.

Figure 4 OCT of the patient's left-eye – pre-treatment – illustrating intraretinal and subretinal fluid due to choroidal neovascularisation.

of a choroidal neovascular membrane (figure 4). Fundus fluorescein angiography (FFA) of the left eye revealed a sub-foveal choroidal neovascular membrane at the base of an angioid streak.

TREATMENT

This patient was treated with a series of three intravitreal ranibizumab injections (anti-vascular endothelial growth factor) to her left eye, after which her VA improved from

Figure 5 RFA of the patient's left eye after treatment, illustrating staining but no active leakage.

6/36 to 6/18 in the left eye. The patient also reported a subjective improvement in both vision and metamorphopsia.

An OCT scan post-treatment showed no intraretinal or subretinal fluid. Staining but no active leakage was seen on repeat FFA (figure 5).

OUTCOME AND FOLLOW-UP

This patient is being followed up monthly with clinic appointments that include OCT and where appropriate, FFA. To date, after 6 months of follow-up, there has been no deterioration in VA or reactivation of the choroidal neovascular membrane.

DISCUSSION

To our knowledge this is the first report in the literature of a patient with a background of tumoral calcinosis presenting with a sudden deterioration in vision due to choroidal neovascularisation (CNV), secondary to an angioid streak. It is interesting that the ocular features only became evident 14 years after diagnosis, though soft-tissue and vascular

calcifications were observed at a much earlier stage. Similarly, a previous case in the literature reported that the ocular involvement only became apparent in a patient 29 years after diagnosis.¹⁴ Perhaps the ocular features manifesting at a later stage during the course of the disease are a feature of this syndrome.

Angioid streaks are small breaks in Bruch's membrane, an elastic membrane of the retina. They can lead to CNV with subsequent deterioration in VA. Previous treatments such as photodynamic therapy have yielded poor results, with most eyes showing poor visual outcomes in the long term.¹⁵ More recently, the anti-VEGF therapies using ranibizumab and bevacizumab have been used to treat CNV. Case reports in the literature have reported favourable results with these treatments, with most eyes showing a maintenance or improvement in VA with treatment, as in this case.^{16 17}

A recent case report in the literature looking at the use of intravitreal ranibizumab for CNV secondary to angioid streaks found an improvement in VA after four injections, with VA remaining stable for 1 year after treatment.¹⁸

Ranibizumab appears to be an effective and promising treatment for CNV secondary to angioid streaks.

The fact that patients with tumoral calcinosis can develop angioid streaks and CNV indicates that they should be strongly advised to present urgently to an eye department, should any deterioration in vision occur. In our case, the presence of flame-shaped haemorrhages in the fellow eye indicates a need for close, long-term monitoring to determine whether similar complications develop in this eye.

Further study is required to determine the full spectrum of ocular involvement in this condition. Further investigation is also necessary to more accurately determine the immediate and long-term benefits of anti-VEGF therapies in the management of CNV secondary to angioid streaks, using larger numbers of patients.

Finally, though tumoral calcinosis is a rare condition, it is important for ophthalmologists to be aware of it as part of a differential diagnosis and to be aware of the potential complications that can arise from ocular involvement.

Learning points

- ▶ Tumoral calcinosis is a rare disorder of phosphate metabolism, typically presenting with ectopic deposition of calcium in soft-tissue para-articular regions, dental pulp, skin and the vasculature. Ocular involvement includes calcific-lid lesions of the eyelids, conjunctival calcific deposits, band keratopathy and angioid streaks.
- ▶ The anti-VEGF therapies ranibizumab and bevacizumab appear to be an effective and promising treatment for CNV secondary to angioid streaks, including for patients with tumoral calcinosis.
- ▶ Patients with tumoral calcinosis should be routinely followed up by an ophthalmologist to help prevent visual deterioration and ocular complications from this condition.

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Competing interests None.

Patient consent Obtained.

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