Optical coherence tomography: Angiography visualization of retinal oxalosis in primary hyperoxaluria, a case report

A Barigali, Aswin PR, SM Abdul Khadar

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Oxalate is a byproduct of normal metabolism and is excreted from the body by the kidneys through urine. Systemic oxalosis can result from endogenous sources due to break down of ascorbic acid and amino acids. Exogenously, crystalline deposits may be precipitated due to excessive dietary intake of oxalate rich foods, usually leafy vegetables or high dose vitamin C in patients with renal compromise. Primary hyperoxaluarias are rare autosomal recessive inborn errors of glyoxylate metabolism that can lead to oxalate accumulation, recurrent nephrocalcinosis and retinal oxalosis.[1] We present a case of primary hyperoxaluria with an identified alanine–glyoxylate aminotransferase (AGXT) gene mutation which resulted in nephrocalcinosis and retinal oxalosis.

A 56-year-old lady presented with sudden diminution of vision for about two weeks. She had a history of recurrent renal calculi requiring lithotripsy, hypertension, ureteric stenting and chronic renal failure necessitating thrice weekly hemodialysis. Further evaluation had revealed primary oxaluria with AGXT gene mutation. She was referred by the nephrologist for evaluation of her ocular symptoms.

The systemic evaluation revealed a blood pressure (BP) of 208/112 mmHg. Nail beds and tarsal conjunctiva showed gross pallor. There was a bruit in the left forearm with an arterio-venous (AV) fistula for hemodialysis.

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On ocular examination, her best corrected visual acuity (BCVA) was 5/60 in both eyes. Anterior segment findings were within normal limits. On fundus examination, both eyes showed clear media with pale disc with multiple cotton wool spots with superficial and deep retinal hemorrhages and whitish crystalline deposits and inferior exudative retinal detachment. Considering differential diagnoses of hypertensive retinopathy, OIS, combined retinal vascular occlusion or non-arteritic anterior ischemic optic neuropathy, the patient was referred back to the nephrologist for urgent control of hypertension and elevated serum oxalate levels.

Fundus photography confirmed ophthalmoscopic findings with whitish crystalline deposits diffusely deposited in the retinal layers bilaterally [Fig. 1a and b]. There was a striking granular appearance delineating the arterial tree. The veins appeared normal without any crystalline deposits. The crystals appeared more numerous and clearly delineated in the red-free photo compared to autofluorescence image [Fig. 2]. The veins appeared strikingly spared. As fundus fluorescein angiography (FFA) was contraindicated by the nephrologist, we proceeded with optical coherence tomography (OCT) [Fig. 3a] and OCT-Angiography (OCTA) [Fig. 4], which showed outer retinal and sub-retinal crystalline deposits in the macula with arteriolar wall studded with crystalline deposits which render the vessel wall hyperreflective and well delineated against a homogenous retinal reflectivity. Foveal section showed deposits at the level of the inner plexiform layer corresponding to the inner retinal arteriolar plexus.

Follow-up OCT images after two weeks also showed the retinal precipitates that appear to have migrated into more subretinal or pre-retinal pigment epithelium (RPE) locations [Fig. 3b].

With a final diagnosis of retinal oxalosis with secondary OIS, the patient underwent sequential anti-VEGF injections in the left eye and then the right eye. At three months follow-up, fundus examination showed deep retinal and subretinal migration of the crystalline deposits with persistence of intra-arterial granularity suggestive of improving clinical picture. The BCVA improved in right eye to 6/36 and left eye remained 5/60 [Fig. 1c and d]. She has been asked to review monthly to look for development of retinal neovascularization.

Discussion

Our patient had autosomal recessively inherited mutation in the AGXT gene. This resulted in high levels of oxalate in the serum with subsequent nephrocalcinosis and recurrent nephrolithiasis, which are hallmarks of primary hyperoxaluria. Recurrent renal damage led to end-stage renal failure, causing hypertension and further accumulation of calcium oxalate. Retinal oxalosis and the subsequent hypertensive vaso-occlusive ischemic retinopathy was resultant of this pathogenetic mechanism. Garner described retinal oxalosis in 1974 in an enucleated eye of a 13-year-old male with chronic retinal detachment following trauma. Histochemical and X-ray diffraction pattern of crystals on the deep surface of the detached retina proved oxalosis, leading him to believe that retinal oxalosis is of necessity a pathological diagnosis. Meredith et al., in 1984, and Wells et al., in 1989, through histopathological examination, showed ocular calcium oxalate deposition in the walls of the retinal blood vessels in a patient with chronic renal failure on dialysis. Munir et al. reported a case of retinal oxalosis in primary hyperoxaluria type 1, confirmed with renal and liver biopsy, after noting crystals in the retina and RPE and delayed arteriolar filling with severe capillary non-perfusion of macula on FFA. With the advent of OCT imaging, it is no longer needed to confirm location of the crystals through histopathology, as shown by Querques et al. in 2009 and Scruggs in 2018. While Querques et al. showed oxalate deposits within areas of dome-shaped RPE, Scruggs showed in OCTA reflective deposits and capillary nonperfusion in all retinal layers with sparing of the choriocapillaris and choroid.

The salient features of previously reported cases have been summarized in Table 1. As FFA was contraindicated by the nephrologist in our patient, we proceeded with OCTA.

![Figure 1: Fundus color photographs showing distribution of cottonwool spots and retinal crystals at presentation (a and b) and at follow-up (c and d)](image)

![Figure 2: Red-free (a) and fundus autofluorescence (b) images showing diffusely distributed retinal and intra-arteriolar deposits better appreciated in red-free image)](image)
| Author (year of publication) | Age | Gender | Duration of ocular symptoms | Visual acuity | Etiology | Pathology | Fundus photography | Fundus fluorescein angiography | OCT |
|-----------------------------|-----|--------|-----------------------------|---------------|----------|-----------|-------------------|-------------------------------|-----|
| Garner et al. (3) 1974      | 21  | Male   | 8 years since trauma        |               | Traumatic with secondary retinal detachment | Oxalate crystals in chronically detached retina with degenerative changes |                  |                               |     |
| Meredith et al. (4) 1984    | 14  | Female | 6/18                         |               | Primary oxalosis | Oxalate deposits disrupting to RPE | Blockage of background fluorescence by pigmented areas |                  |     |
| Meredith et al. (4) 1984    | 4 months | Male   |                              |               |          |           |                   |                               |     |
| Wells et al. (5) 1989       | 55  | Female |                              | Primary oxaluria type 1 | Secondary oxaluria - Chronic renal failure with excessive vitamin C intake | Birefringent crystals apparent in the inner retina and retinal arterial wall | Peri-arterial crystalline deposits and extensive crystal deposition in the macula |                  |     |
| Munir et al. (6) 2004       | 59  | Female | 3 months                     |               |          |           | Scattered peripapillary and intra-arteriolar crystalline deposits asymmetrically deposited in the posterior pole | Delayed arteriolar filling with severe capillary non-perfusion of the macula | Oxalate deposits as tiny hyper-reflective lesions localized within areas of dome-shaped elevated RPE |     |
| Querques et al. (7) 2009    | 19  | Male   |                              | Primary oxaluria type 1 | Retinal crystalline deposits, widely distributed in the fundus, interposed between the RPE and neurosensory retina | Hyper-fluorescent dots and ring-shaped areas of hyper-fluorescence with central hypo-fluorescence | Reflective deposits and capillary non-perfusion in all retinal layers with sparing of the choriocapillaris and choroid |                               |     |
| Scruggs et al. (8) 2018     | 70  | Female | 2 weeks                      | Secondary to chronic renal failure and vitamin C intake | Retinal and arteriolar crystals, disc pallor, nerve fiber layer infarcts, and dot, blot, and flame-shaped hemorrhages | Mid-phase blockage from hemorrhages, poor perfusion in some venules and substantial capillary non-perfusion | Deposits at the level of the inner plexiform layer corresponding to the inner retinal arteriolar plexus |                  |     |
| Barigali et al., 2021       | Female | 2 weeks |                              | Primary oxaluria with alanine-glyoxylate aminotransferase (AGXT) gene mutation | Retinal and arteriolar crystals, disc pallor, nerve fiber layer infarcts, and dot, blot, and flame-shaped hemorrhages | Reflective deposits and capillary non-perfusion in all retinal layers with sparing of the choriocapillaris and choroid | Deposits at the level of the inner plexiform layer corresponding to the inner retinal arteriolar plexus |                  |     |
imaging, which revealed intra-arteriolar crystal deposition with sparing of the venules. The follow-up images show subretinal or pre-RPE locations of the crystals. This could be a true movement of the crystalline deposits due to absorption at the RPE, or it could be an imaging artefact due to the resolution of subretinal fluid approximating the retinal layer to the RPE. This case highlights the importance of OCT and OCTA as a safe, non-invasive tool in retinal oxalosis.

Retinal oxalosis is a retinal crystallosis with oxalate crystals in the retinal arterial tree and interstitium. In lieu of FFA, OCT and OCTA helped us to confirm our diagnosis and also showed the intra-arteriolar and sub-retinal location of the crystals. This sign usually occurs late in the disease and prompt multidisciplinary treatment is needed to improve the quality of life and safeguard vision while preventing vaso-occlusive events in the ocular and systemic vascular tree.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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