Retinal Oxalosis: Case Report and Review of Histopathology

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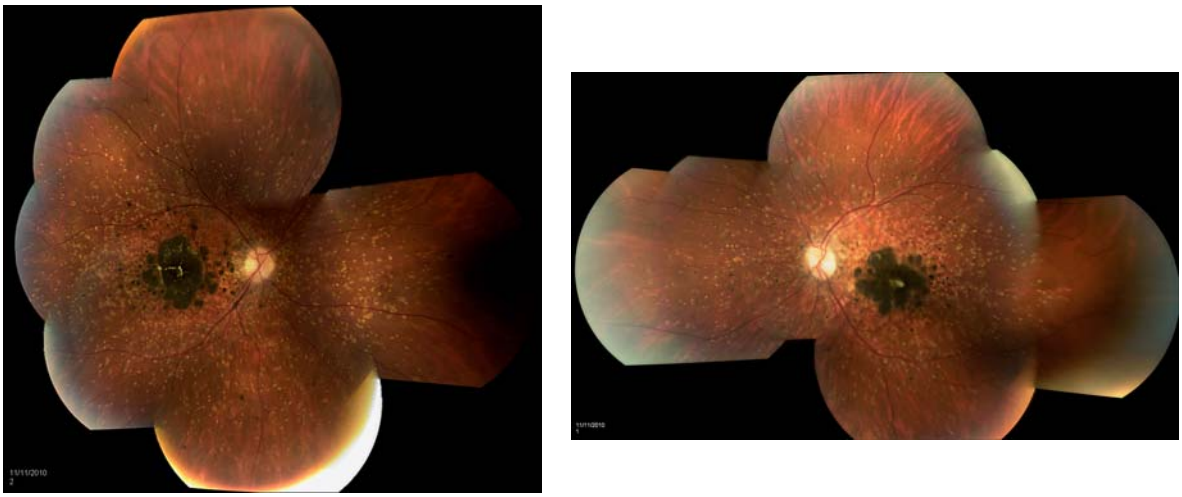
Abstract: Oxalosis involves the deposition of calcium oxalate crystals throughout the body, including the eye and specifically the retina. Primary oxalosis involves an inborn metabolic defect in glyoxalate metabolism while secondary oxalosis occurs with excess oxalate ingestion, absorption, or acquired defects in its metabolism or excretion. Characteristic deposits are noted funduscopically, and crystal deposition primarily within retinal pigment epithelial cells ultimately leads to macular scarring and atrophy. Profound visual loss typically occurs as a result of advanced disease. Such findings are illustrated in the present case of a 27 year old woman with primary oxalosis.

Keywords: Oxalosis, retina, crystalline retinopathy.

INTRODUCTION

Oxalic acid is a common organic acid formed as a metabolic product that can combine with ionized calcium to yield the insoluble salt calcium oxalate [1-4]. Oxalosis is a condition characterized by hyperoxaluria with the deposition of calcium oxalate crystals throughout the body. Primary oxalosis involves an inborn defect in glyoxalate metabolism due to a hepatic enzyme deficiency. Increased plasma oxalate levels ensue with resultant generalized calcium oxalate crystal deposition in various organs, including ocular tissues [5]. Because oxalate must be excreted through the kidneys, marked renal tract crystal deposition, nephrolithiasis, and renal failure typically occur early in life [5]. Secondary oxalosis may occur due to excessive ingestion of oxalic acid or its precursor ethylene glycol, hyper-absorption of oxalate post ileal resection, or secondary defects in oxalate metabolism in cirrhosis, or its excretion in renal failure [5]. Also, prolonged exposure to the anesthetic agent methoxyflurane, a metabolic precursor of oxalic acid, may cause secondary oxalosis. This was the underlying etiology in Bullock *et al.*'s pioneer report of systemic oxalosis with histopathologically-proven retinal involvement [1]. In either primary or secondary forms of the disease, characteristic oxalate crystal deposition may be observed funduscopically. The following case report illustrates the clinical and diagnostic features of retinal oxalosis.



a **b**

Figure 1: Color montages of right (**a**) and left (**b**) eye showing diffuse oxalate crystalline deposits, left optic disc pallor, and black geographic maculopathy.

CASE REPORT

A 27 year old woman with primary oxalosis presented with progressive visual loss. She had undergone bilateral renal transplants approximately 15 years prior

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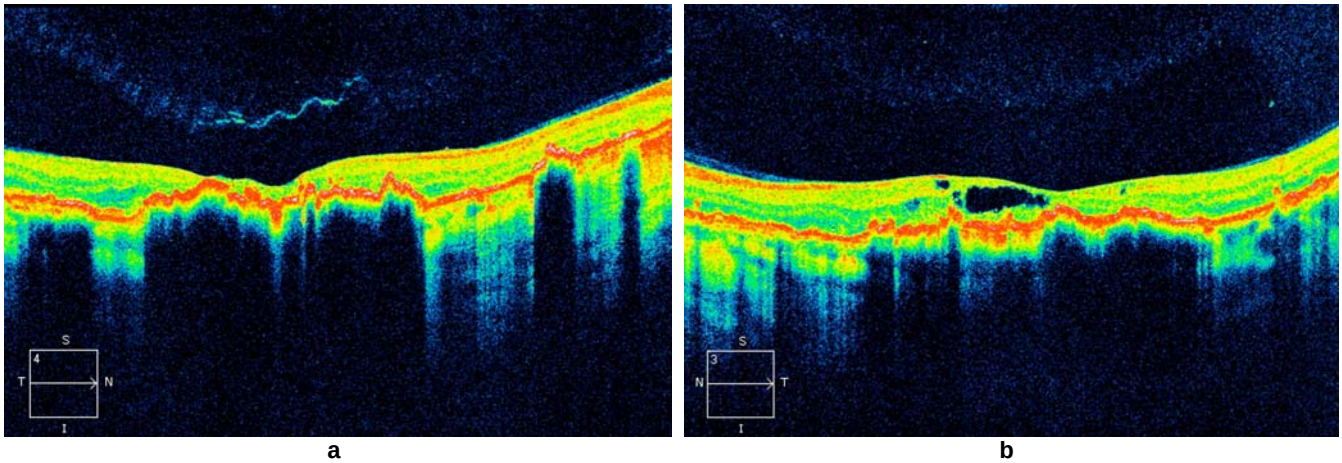
to presentation. The presenting distance visual acuity was 20/100 OU. Funduscopic examination revealed diffuse bilateral black crystalline deposits at the posterior pole and associated geographic maculopathy and left optic disc pallor (Figure **1**). Optical coherence tomography showed a thin atrophic retina with hyper-reflectivity in the region of the retinal pigment epithelium corresponding to deposition of material. Details of the choriocapillaries were obscured due to overlying retinal pigment epithelium hyperpigmentation (Figure **2**). On fluorescein angiography, the crystals appeared as hyperfluorescent spots and there were areas of blockage of fluorescence corresponding to areas of retinal pigment epithelial hyperpigmentation (Figure **3**).

DISCUSSION

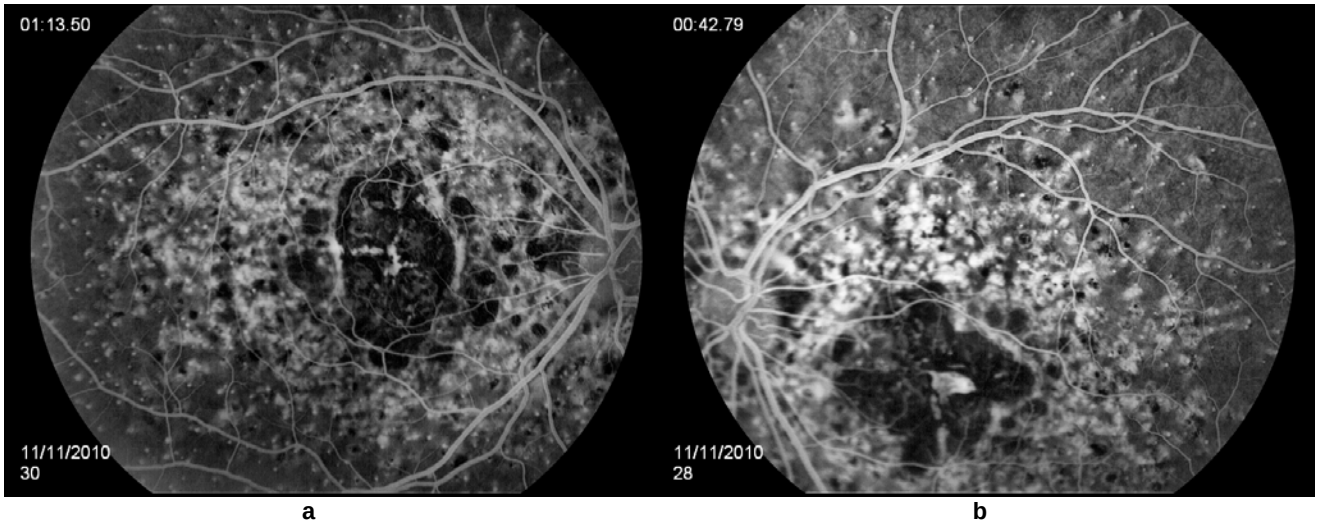
Bullock *et al.* [1] performed extensive postmortem histopathological studies of a patient with systemic and retinal oxalosis secondary to methoxyflurane anesthesia. Birefringent crystalline deposits were found in the retinal pigment epithelium, seemingly intracellularly, and close to Bruch's membrane within the cells. Fewer crystals were found in the inner retina, ciliary body epithelium, and lens. They postulated that enlargement of intracellular crystals likely disrupts the cells and accounts for their scattered extracellular appearance. A propensity for crystalline deposition in the macular area and ciliary body has been thought to be secondary to the high vascularity of these regions [5].

Funduscopically, oxalate crystals are noted predominately in the posterior pole, and rarely, anterior to the equator. Optic atrophy, retinal pigment epithelial hyperpigmentation, subretinal fibrosis, and black geographic maculopathy (as seen in the present case) are typically seen late in the course of the disease [6-8]. Punjabi *et al.* [7] reported a case of a one year old male with primary hyperoxalosis. Electroretinography



a **b**

Figure 2: Optical coherence tomography showing broad thickening and elevation of the retinal pigment epithelium with obscuration of the underlying choriocapillaries, (**a**) right and (**b**) left eye.



a **b**

Figure 3: Late phase fluorescein angiography showing hyperfluorescent spots corresponding to the oxalate crystals and areas of blockage corresponding to the areas of retinal pigment epithelial hyperpigmentation, (**a**) right and (**b**) left eye.

showed extinguished electrical activity to both photopic and scotopic stimuli, presumably due to basic retinal dysfunction secondary to crystalline deposition. The only waveform that was present was the high-intensity, white scotopic waveform [7]. Crystal deposition may occur intravascularly as well, which can contribute to retinal ischemia, edema, hemorrhages, and even neovascularization [9,10]. Yuan and Ehlers reported a case of a 55 year old female with primary oxalosis and renal failure with retinal crystalline deposition, neovascularization, ischemia, and macular edema requiring treatment with panretinal photocoagulation and intravitreal bevacizumab [10]. Querques *et al.* reported a case of a 19 year old male with primary hyperoxaluria in which both fundus autoflourescence and fluorescein angiography showed hyperflourescent dots and ring-shaped areas of hyperflourescence with central hypoflourescence associated with crystal deposition, and on spectral-domain optical coherence tomography, oxalate crystals appeared as hyper-reflective lesions within areas of dome-shaped elevated retinal pigment epithelium [11]. Enhanced depth imaging optical coherence tomography has shown hyper-reflective deposits at the level of the retinal pigment epithelium as well as the inner and outer retina and the choroid [12]. Our patient demonstrated the diffuse thickening of the retinal pigment epithelium seen in patients with black geographic maculopathy, likely related to oxalate deposition and subsequent retinal pigment epithelium hyperplasia as described by Bullock *et al.* [1]. Clinical course of the ocular component of oxalosis is dependent upon the underlying cause and severity of the systemic disease, and improvement may occur with dialysis in some cases [9,10]. This case report demonstrates the pertinent clinical and diagnostic findings important in the evaluation and diagnosis of a patient with suspected retinal oxalosis.

CONFLICT OF INTEREST

The authors have no financial interests, disclosures, or conflicts of interest pertaining to this manuscript.

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