

Posterior segment optical coherence tomography findings in a case of nephropathic cystinosis

Omar Al Abdulsalam

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Abstract:

Cystinosis is a rare autosomal recessive lysosomal storage disorder characterized by abnormal accumulation of intracellular cystine in various tissues including the brain, kidneys, bones, and eyes. Infantile nephropathic cystinosis is the most severe phenotype of cystinosis that has been associated with a wide spectrum of ocular features. In this report, the author describes a posterior segment spectral-domain optical coherence tomography (SD-OCT) finding that has not been previously reported in a case of nephropathic cystinosis.

Keywords:

Cystinosis, nephropathic cystinosis, optical coherence tomography

INTRODUCTION

Cystinosis is a rare autosomal recessive lysosomal storage disorder characterized by abnormal accumulation of intracellular cystine in various tissues including the brain, kidneys, bones, and eyes. Genetically, cystinosis is due to the mutation of the cystinosin (CTNS) gene that codes for cystinosin, the lysosomal cystine transporter. There are three main phenotypes of cystinosis: Infantile nephropathic cystinosis, the classic form; juvenile cystinosis, the less severe late-onset variant; and adult cystinosis, the benign non-nephropathic form.^[1]

The most frequently described ocular manifestation, associated with all types of cystinosis, is crystal deposition in the cornea. This crystal accumulation begins in infancy, increases with age, and gradually leads to significant photophobia.^[2] In addition to corneal involvement, crystal accumulation within the conjunctiva, iris, ciliary body, choroid, fundus, and optic nerve have been reported.^[3] This report describes a posterior segment spectral-domain optical coherence tomography (SD-OCT) finding that has not been previously reported in a case of nephropathic cystinosis.

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CASE REPORT

A 19-year-old woman presented to our ophthalmology department with severe photophobia and decreased visual acuity in her both eyes since childhood. She was diagnosed initially with nephropathic cystinosis at the age of 3 years for which oral cysteamine therapy was given. The patient had also chronic kidney disease secondary to Fanconi syndrome and had been undergoing hemodialysis for treatment.

On initial ophthalmic examination, the patient's best-corrected visual acuity (BCVA) was 20/50 in the right eye and 20/200 in the left eye. The intraocular pressure readings were 12 and 14 mmHg in the right and left eye, respectively. Slit-lamp examination of both eyes showed moderate corneal haze and multiple refractile polychromatic crystal deposits in the cornea. [Figure 1a and b]. The view of the retina in both eyes was obscured by the corneal crystals during fundus examination, color fundus photography, and fluorescein angiography. Imaging with SD-OCT (Heidelberg Engineering, Inc., Heidelberg, Germany) scans through the macula could be performed. The right eye SD-OCT scans showed a focal dome-shaped subfoveal hyperreflective material, while the left eye showed hyperreflective foci throughout the retinal layers, cystoid spaces, and hyperreflective

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Ophthalmology Division,
King Abdulaziz Hospital,
Ministry of National Guard
Health Affairs, Al Ahsa,
King Abdullah International
Medical Research Center
(KAIMRC), Saudi Arabia

Address for correspondence:

Omar Al Abdulsalam,
Ophthalmology Division, King
Abdulaziz Hospital, Ministry of
National Guard Health Affairs,
P.O. Box 233, Al Ahsa 31982,
Saudi Arabia.
E-mail: dr.omar300@hotmail.
com

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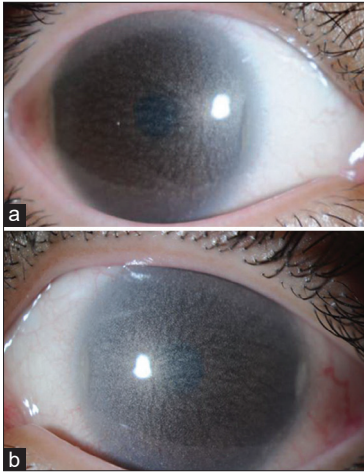


Figure 1: Slit-lamp photographs at initial presentation showing cystine crystal deposition in the cornea of (a) the right eye, and (b) the left eye

band anterior to the retina suggestive of epiretinal membrane [Figure 2a and b]. Topical cysteamine treatment was instituted, in addition to the previously administered oral cysteamine therapy, but there was no improvement in the patient's BCVA or symptoms.

Nine-months later, the patient underwent renal transplantation and showed for ophthalmic evaluation six-months posttransplantation. She reported improvement in the photophobia. However, there was no change in her BCVA or SD-OCT findings during a three-year follow-up.

DISCUSSION

Ocular complications are among the most common causes of discomfort and disability in patients with cystinosis, affecting almost all patients with nephropathic cystinosis if left untreated.^[1] In 1941, Burki was the first to describe the presence of cystine crystals within the cornea and conjunctiva.^[4,5] These needle-shaped, highly reflective cystine crystals are pathognomonic for cystinosis and have been observed in all subsequently reported cases.^[5] Furthermore, other ocular structures also suffer from cystine accumulation.^[6]

The most commonly described posterior segment abnormality in nephropathic cystinosis patients consists of patches of depigmentation with pigmentary mottling.^[7] This finding usually precedes the appearance of corneal crystals and has been seen as early as 5 weeks of age. As the patient grows older, changes progress posteriorly; macular abnormalities have been described as early as 6 years of age.^[8] Other reported retinal abnormalities in older patients include bone spicules and pigment clumps resembling retinitis pigmentosa, constricted visual fields, and decreased cone and rod function on electroretinogram.^[7]

In our patient, the densely packed corneal cystine crystals prevented detailed retinal examination. Moreover, the view was poor during conventional photography and fluorescein

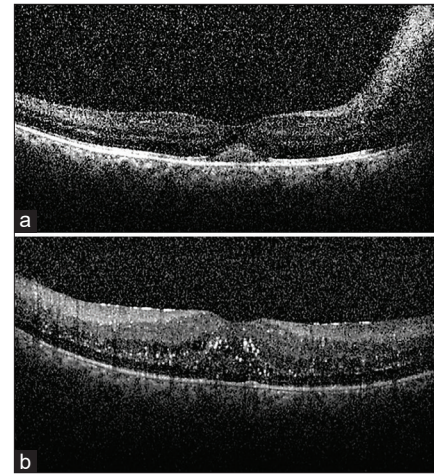


Figure 2: Spectral-domain optical coherence tomography of the macula at initial presentation showing (a) a focal dome-shaped subfoveal hyperreflective material in the right eye, and (b) hyperreflective foci throughout the retinal layers, cystoid spaces, and hyperreflective band anterior to the retina in the left eye

angiography, but imaging with SD-OCT provided a clear view to delineate macular changes.

Flockerzi *et al.* reported the SD-OCT findings in a case of nephropathic cystinosis after penetrating keratoplasty.^[9] Their examination revealed intraretinal cystine crystals and a cystoid macular edema which was treated with a bevacizumab injection. In our patient, the SD-OCT scans of the left eye revealed intraretinal cystine crystals as well as cystoid spaces, which corresponds to Flockerzi *et al.* description. However, the right eye SD-OCT scans showed a focal dome-shaped subfoveal hyperreflective material, which has not been previously described. This SD-OCT finding in the right eye could be attributed to the degenerative changes in the outer retinal layers with focal destruction of the photoreceptor outer segments, which had been observed in some older cystinosis patients.^[7,10]

Oral cysteamine is the mainstay of cystinosis therapy.^[5] Tsilou *et al.* investigated the effect of chronic oral cysteamine therapy on the frequency of cystinosis retinopathy. They found positive correlation between the frequency of cystinosis retinopathy with time off of cysteamine therapy, and negative correlation with time on cysteamine therapy.^[7] Our patient presented with retinal abnormalities despite the early initiation and the long-term use of oral cysteamine. She continued to use oral cysteamine after the diagnosis of cystinosis retinopathy and showed no progression in the retinal changes during a three-year follow-up.

Although oral cysteamine alleviates most of the symptoms associated with cystinosis, it is not effective on the corneal crystal accumulation, because of the corneal avascular nature. Topical cysteamine treatment has long been shown to be effective in reducing corneal crystal density and alleviating symptoms.^[3] In our patient, topical cysteamine treatment led to symptomatic improvement but failed to show decrease in corneal cystine crystals.

In conclusion, we report this case to describe a new SD-OCT finding in nephropathic cystinosis. Further studies are needed to confirm our findings and to investigate other possible SD-OCT features in nephropathic cystinosis patients.

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Conflicts of interest

There are no conflicts of interest.

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