Photo Essay

Ocular cystinosis: Rarity redefined

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Key words: CTNS gene, cysteamine hydrochloride, cystine, ocular cystinosis

Cystinosis is an extremely rare autosomal recessive lysosomal storage disorder, characterized by accumulation of cystine in the lysosomes of the affected cells.[1] Of the three forms of the disease, the infantile severe form is associated with severe or truncating mutations on both the alleles, whereas the juvenile and the adult form are associated with at least one mutation.

A 15-year-old female presented with insidious onset, gradually progressive, and painless diminution of vision. Relevant ophthalmic, systemic, and family history was negative. Best Corrected Visual Accuity (BCVA) on Snellens chart was 6/12. Slitlamp examination showed fine birefringent deposits in the corneal stroma. Ref. Figs. 1-3. Rest ocular examination was unremarkable. There was no evidence of pedal edema or pericoular edema or oliguria ruling out renal dysfunction. Urine examination did not reveal any crystals. Renal function tests were well within normal limits. Leucocyte assay revealed elevated levels of Cysteine. A diagnosis of Ocular Cystinosis was made and the patient is now on follow-up.

Genetic mapping revealed the CTNS variant c. 1042_1044del p.(Val348del), which is an in-frame deletion of 3 bps in exon 12, which causes the loss of residue Val at position 348. It is classified as variant of uncertain significance (Class 3) according to the recommendations of ACMG.

Discussion

The presence of cystine crystals with in the cornea and conjunctiva was first described by Burki in 1941. He described them as a myriad of shinning, small, white sequin like crystals, deposited in the superficial layers of parenchyma, respecting the limits of epithelium, and endothelium.[2]

The gold standard for diagnosis is detection of increased cystine levels in WBSs. The WBC cystine levels are in the range of 3–20 nmol half cystine/mg protein in the newly diagnosed cystinosis patients, whereas the heterozygous carriers and the controls have levels <1.0 and <0.2 nmol half cystine/mg protein, respectively.[3]

Molecular testing of the CTNS gene (which has 12 exons but only 10 are coding) can reveal 95% of the disease carrying mutation, but is time consuming.

The cystine depleting properties of cysteamine were first described in 1976 by Thoene and colleagues.[4] Upon treatment with cysteamine, a cysteamine-cysteine mixed disulfide compound is formed which can exit the lysosome through the PQLC2 (PQ-loop repeat-containing protein 2) transporter.

Topical cysteamine hydrochloride eye drops (0.1%) have been shown to be effective in reducing the symptoms and the corneal crystal density, but there are several problems associated with it like the frequency of administration, bioavailability, and stability.

A more viscous formulation of cysteamine hydrochloride (0.55%), CYSTADROPS® is the first orphan drug approved in the European Union for the treatment of corneal crystal deposits in adults and children aged >2 years with cystinosis. (Cystadrops, manufactured by Orphan Europe S.A.R.L., France).[5] Recently CYSTARAN 0.44% is the first and only FDA approved drug for ocular cystinosis. It contains a sterile ophthalmic solution containing 6.5 mg/mL of cysteamine hydrochloride equivalent to 4.4 mg/mL of cysteamine (0.44%) and requires hourly administration.[6]

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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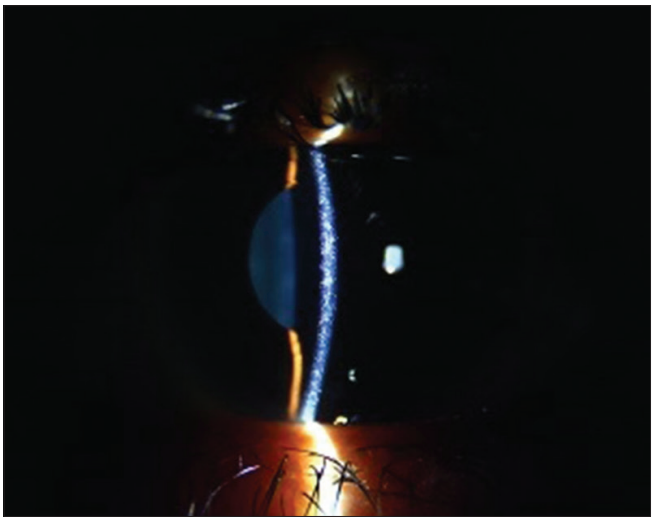

Figure 1: Slit Lamp section showing deposition of cysteine crytals in the corneal stroma

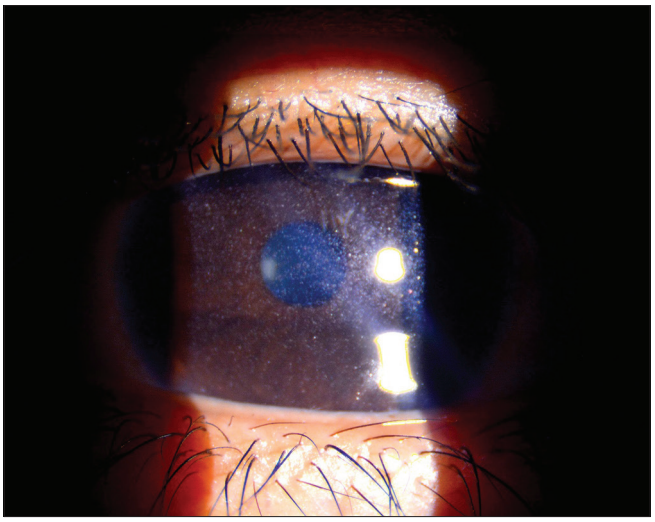

Figure 2: Diffuse slit lamp photograph of the cornea depicting the crystals

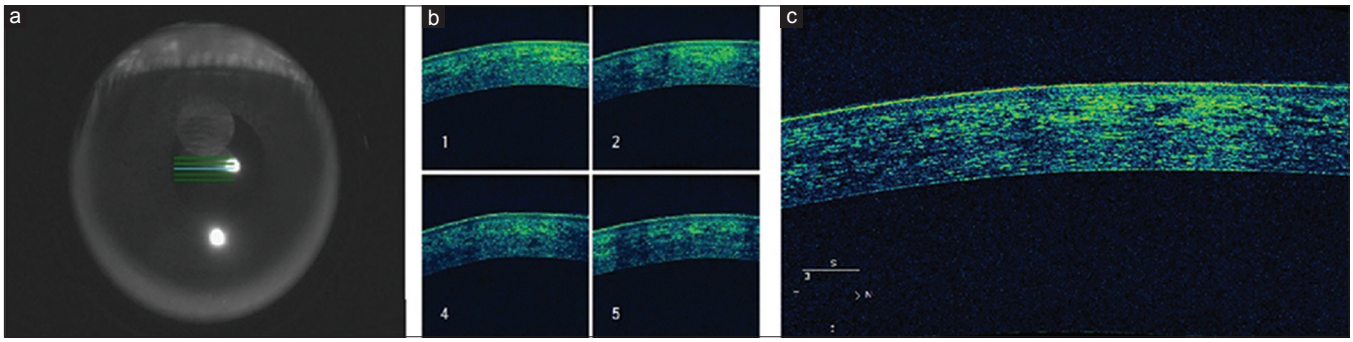

Figure 3: Anterior segment OCT showing absence of any other pathology. (a) ASOCT sections through the central cornea. (b) OCT depiction through sections 1-2-4-5. (c) Enlarged OCT image through central section 3

Conflicts of interest

There are no conflicts of interest.

References

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