CASE REPORT

AN INTERESTING CASE OF NEPHROPATHIC CYSTINOSIS – LIGNAC FANONIS SYNDROME

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ABSTRACT: Cystinosis is a rare autosomal recessive lysosomal storage disorder characterized by the intracellular accumulation of cystine crystal in various organs. Three forms have been described infantile, adolescent and adult. Cystinosis is diagnosed by the presence of typical cystine crystals in the cornea on slit-lamp examination or the 50 to 100 fold elevated levels of free, non-protein cystine within polymorphonuclear leucocytes or cultured fibroblasts. We report a 10 yr old female who presented with infantile form of cystinosis.

KEYWORDS: Cystinosis, Fanconi syndrome, Corneal deposit.

CASE REPORT: A 10 yrs old female was brought to hospital by her mother to our hospital with complaints of haziness in both corneas since 5 months of age which was progressively increasing and that baby avoided looking at bright light since one year of age more so since past two years.

On ocular examination both eyes were orthophoric, anterior segment examination of both eyes showed hazy cornea (Fig. 1) with deposition of multiple crystals in entire thickness of corneal stroma more in periphery than at the centre (Fig. 2) Iris details were hazy with normal AC depth, pupillary reaction and clear lens in both eyes. Fundus examination of both eyes showed a mildly hazy media due to overlying corneal changes. Mild disc pallor was noted with normal retinal vasculature. Macular examination showed chorioretinal degeneration with absent foveal reflex (Fig 3, 4). Best corrected visual acuity in both eyes was 6/60.

General examination showed mental retardation with short stature (Fig 5), stunted growth, sparse hair and defective dentition (Fig 6). CVS and RS were normal and abdominal examination showed hepatomegaly.

Fig. 1

Fig. 2

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Fig. 3 **Fig. 4** **Fig. 5** **Fig. 6**

BIRTH HISTORY: Third degree consanguineous marriage. Antenatal period of mother was uneventful. Fourth born female child, full term normal delivery. First male sibling died of hydrocephalus at age of four months. Second male sibling died of cardiac anomalies at age of eighteen months. Third male sibling died of gastrointestinal tract anomalies of seven months.

DEVELOPMENTAL HISTORY: Delayed motor and social milestones. Not able to stand or walk, even with support. Able to comprehend commands but unable to express herself.

SYSTEMIC HISTORY: Can take only semisolid food, vomits frequently. Passes copious volume of urine, no specific odour. Patient has had repeated attacks of UTI from age of 2yrs. Patient had pathological fracture of Supracondylar fracture of left femur at age of 4 yrs.

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TREATMENT HISTORY: At age of 6months patient was diagnosed as nephropathic cystinosis with generalized aminoaciduria and at age of 4yrs with associated Renal Rickets. On Urine Chromatography all amino acids were detected.

Patient is on treatment with oral cysteamine 50 mg/kg QID, Pottasium citrate, Calcitriol, Ferrous sulphate and multivitamins. Patient has been instructed to take plenty of oral fluids. Periodic assessment of renal parameters is being carried out by the nephrologist. Topical cysteamine 0.5% QID has been started and is being followed up with regular ocular examinations.

DISCUSSION: First described by Abderhalden¹ in 1903 cystinosis is a rare autosomal recessive lysosomal storage disorder resulting from mutations in the gene CTNS mapped to chromosome no 17p. Mutation causes the defective transport of the amino acid cystine out of the lysosome² leading to its intracellular accumulation in various organs. The incidence of nephropathic cystinosis is approximately 1 in 100,000-200,000 live births³ with highest prevalence in patients with French – Canadian ancestry.

In 1941, Burki first reported the corneal crystal as an ocular manifestation associated with nephropathic cystinosis⁴. The histological findings of cystine crystals in the choroid was first published by Bickel et al in 1952.⁵ Francois described the clinical appearance of presumed tapetoretinal degeneration in 1964.⁶

Three types of cystinosis have been described, including infantile (nephropathic), adolescent, and adult (non-nephropathic) type. Most common form is the infantile or nephropathic type form and is characterized by Fanconi syndrome with growth retardation, renal rickets, hypokalemia, polyuria, hypothyroidism and progressive renal failure.⁷ Generally renal fanconis syndrome becomes apparent 3-6 months after birth in nephropathic calcinosis and leads to end stage renal disease at age of 10 – 20 years.⁸

Adolescent cystinosis was first described by goldmen et al characterized by the onset in the first or second decade of life with a mild nephropathy and the typical corneal and conjunctival cystine deposits but with the absence of retinopathy.⁹ Adult or benign type is characterized by characteristic corneal crystals and absent or minimal photophobia and absence of renal involvement.¹⁰

Ocular manifestations is characterized by deposition of crystals in cornea, iris, anterior lens surface and retina.¹¹ Corneal crystals may be absent or minimal in first year of life¹² with progressive crystal deposition leading to gradual loss of visual acuity.¹³ Photophobia and visual impairment increase with age and deposition of crystals.

Retinal involvement includes patchy depigmentation of the retinal pigment epithelium, mottled depigmentation of the macula that is more prominent and irregular toward the periphery.¹⁴

Other complications include corneal infiltration, filamentous and band keratopathy, impaired tritan colour vision.

Early diagnosis and treatment with renal transplantation and oral cysteamine can change the course of this disease.¹⁵ Renal transplantation has improved the prognosis for nephropathic cystinosis. After renal transplantation, fanconi syndrome does not develop in the recipients and cystinosis does not recur in the graft however, cystine deposition continues to accumulate in non-renal tissue leading to multi-system dysfunction.¹³

Cysteamine (β -mercaptoethyamine) specific agent that has a biochemical structure similar to cysteine and can deplete cystine from the patients' cells. Oral cysteamine, especially given before 2

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years of age, has been demonstrated to lower the intracellular cystine content by 95% and has proven efficacy in delaying renal glomerular deterioration, enhancing growth, preventing hypothyroidism and lowering muscle cystine content.¹⁶ The dosage for cysteamine treatment is 50-90 mg of free base/kg every 6 hours to maintain leukocyte cystine levels to less than 1nmol of half cystine per mg of protein when measured five hours after a dose.

The treatment for ocular complication include supportive treatments, topical cysteamine and corneal transplantation. Systemic cysteamine has demonstrated no effect on corneal accumulation and does not improve ocular symptoms.¹⁷

Topical cysteamine 0.5% given every 1 hour or at least 6 times a day has been shown to reduce corneal crystal deposition. After penetrating keratoplasty, grafts usually maintain clear with minimal crystals deposition.¹⁸

CONCLUSION: Cystinosis is a rare autosomal recessive disorder. The characteristic deposition of corneal crystals is one of the diagnostic criteria, which is very useful and could be discovered with general slit lamp examination. Early diagnosis and treatment with renal transplantation and oral cysteamine can lead to improvement in overall life expectancy. Topical cysteamine and corneal transplantation in advanced cases for ocular complications have shown promising results.

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