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Case Report

Eyes are a gateway to the kidney – A rare case of cystinosis

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ABSTRACT

A 6-year-old girl born through third-order consanguinity (the other two siblings girls and parents have no kidney disease). She presented with failure to thrive, polyuria, polydipsia, photophobia, poor social interaction, poor eating, and a craving for salt. On examination, growth retardation and severe malnutrition were discovered. Height for age below the third percentile, weight for age below the third percentile, severe pallor, and rickets features were also present. Anaemia, non-oliguric renal dysfunction, normal anion gap metabolic acidosis, urine anion gap positive, rickets on wrist X-ray, hypophosphatemia, hypocalcaemia, hyponatraemia, and hypokalaemia were reported. On ophthalmology examination, cystine crystals deposits in the stroma of the cornea were noted. Fundus examination showed crystalline retinal deposits. On Genetic workup, homozygous 4 base pair deletion in exon 3 of the CTNS gene (chr17: g.3640224_3640227del; Depth: 78×) that results in a frameshift and premature truncation of the protein 7 amino acids downstream to codon 7 (p.Thr7phefster7; ENST00000381870.8) was detected. Cystinosis can be diagnosed using specific symptoms, a complete clinical evaluation, a full patient history, and a range of specialist tests. To get the most out of the preventive and therapeutic effects of cystine depleting drugs, cystinosis must be diagnosed as early as possible.

Keywords: Cystinosis, Genetic, Rickets

INTRODUCTION

Cystinosis is a rare autosomal recessive lysosomal condition characterised by cystine buildup in lysosomes. The prevalence of cystinosis is substantially lower in Asian than in Caucasian populations. According to its obvious and severe clinical signs, which include symptoms of the kidneys and eyes, the majority of cystinosis is the infantile nephropathic variety. Patients with proximal tubulopathy of unknown aetiology should undergo molecular testing and a cysteine-binding protein assay.

CASE REPORT

A 6-year-old girl born in a third-order consanguineous union (the other two sibling girls and parents have no kidney disease). She presented with failure to thrive, polyuria, polydipsia, photophobia, poor social interaction, poor eating, and salt craving was present. She has a history of several admissions for dehydration. On examination, growth retardation and severe malnutrition were present. Height

Figure 1: A picture demonstrating the clinical features in our child – Frontal bossing, Harrison sulcus, Metaphyseal widening, Visceroptosis, Genu Valgum, proportionate short stature and Blepharospasm.

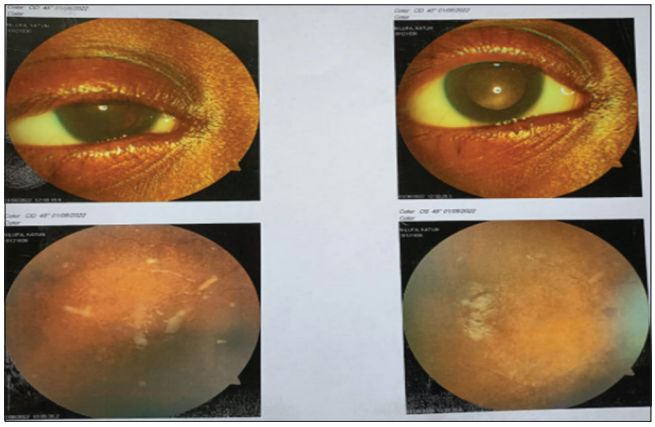

Figure 2: Ophthalmological evaluation of child showing retinal deposits.

Figure 3: Slit lamp showing corneal deposits of cystine.

for age below the third percentile, weight for age below the third percentile, severe pallor, and rickets that did not improve with Vitamin D supplementation was noted [Figure 1]. Investigations revealed hypophosphatemia (2.1 mg/dL), hypocalcaemia (7.6 mg/dL), hyponatremia and hypokalaemia as well as anaemia (9.6 g/dL), non-oliguric renal failure, severe normal anion gap metabolic acidosis, urine anion gap positivity and rickets on wrist X-ray. An ophthalmological examination revealed deposits of crystalline retinal deposits and cystine crystals in the stroma of the cornea [Figures 2 and 3]. Genetic workup showed homozygous 4 base pair deletion in exon 3 of the CTNS gene (chr17: g.3640224_3640227del; Depth: 78×) that results in a frameshift and premature truncation of the protein 7 amino acids downstream to codon 7 (p.Thr7phefsTer7; ENST00000381870.8).

DISCUSSION

A rare autosomal recessive condition called cystinosis is brought on by an aberrant build-up of cystine in the lysosome.[1] In most tissues, cystine crystals form as cellular cystine levels rise 10–1000 times. Cystinosis is categorised clinically as either nephropathic (MIM 219800) or non-nephropathic (MIM 219900). Renal failure is very common in nephropathic cystinosis (NC) and is linked with multi organ damage. Cystinosis patients get Fanconi's syndrome symptoms between 6 and 12 months of age if they do not receive cystine-depleting medication and they progress to end-stage renal failure around the age of 10.[2] Cystinosin, a malfunctioning lysosomal cystine transporter, provides the molecular basis for cystinosis. (CTNS gene)

With seven transmembrane domains, CTNS is predicted to be an essential lysosomal membrane protein. The CTNS gene, which has 12 exons and occupies a region of genomic DNA measuring 23 kb, is found on chromosome 17p13.3. The symptoms of CTNS mutations include everything from the complete absence of the gene product to the wrong intracellular location of CTNS to CTNS mutant proteins with residual or abnormal function.[3] Age at disease onset and disease severity is connected to genotypic variation.[4] According to Meikle *et al.*, the birth prevalence of cystinosis is 1 in 100,000–200,000 in European and American populations.[5] The majority of patients are fair-skinned people of European heritage. The incidence of cystinosis has also been reported in African American, Mexican, and Indian ancestry, Iranian children, Taiwanese sisters, and Japanese infants.[5]

Vitamin D or calcium insufficiency are two common dietary factors linked to rickets. Although malnutrition is the primary cause of the majority of instances in developing nations, it is still important to rule out endogenous reasons

such as renal fanconi syndrome (RFS). Even with proper mineral supplementation, persistent renal phosphate or calcium wasting will not improve a patient's condition. Chronic deficits can cause rickets-related physical symptoms, linguistic regress, and failure to thrive.[6] RFS may result from a multiorgan illness or underlying genetic problem.[6]

The most typical cause of RFS in children is NC, commonly known as infantile cystinosis. It is the first genetic disease that is taken into account when determining the etiology of RFS due to its frequency. Around 6–9 months of age is when failure to thrive first appears and by the age of 18 months, polyuria, polydipsia and rickets symptoms are present.[7]

The presence of corneal cystine crystals on slit lamp examination by 12 months of age, an elevated cystine concentration in polymorphonuclear leukocytes, biallelic pathogenic mutations in the CTNS gene, and an elevated cystine level in cultured fibroblasts or the placenta at birth are all necessary for a conclusive diagnosis of NC.[8] The mainstay of treatment is replacing nutrients that have been lost and cysteamine, which prevents cystine from accumulating inside cells. NC's prognosis is based on early diagnosis and treatment beginning. Due to broad cystine deposition in tissue, many patients continue to experience difficulties even after receiving cysteamine treatment. Renal failure, hypothyroidism, myopathy, retinopathy, pulmonary insufficiency, and hypergonadotropic hypogonadism are examples of long-term consequences.[9] The overall morbidity and mortality of patients who received treatment continuously for at least 8 years, however, significantly decreased.[9]

The patient's protracted clinical course in the case we have provided demonstrated the negative consequences of a delayed diagnosis. It is possible that RFS and NC would have been identified earlier if rickets had been diagnosed earlier.

Treatment includes supportive therapy to prevent acidosis and hypophosphatemic rickets by preserving a healthy fluid and electrolyte balance. After 6–9 months of age, indomethacin can be used to treat polydipsia and polyuria linked to RFS.[10] Cystine depletion utilising cysteamine bitartrate in either an immediate-release or slow-release form is a specific treatment for cystinosis. Early detection, adequate cystine-depleting therapy and prevention or postponement of extra-renal involvement can all greatly slow the progression to chronic kidney disease 5. In the context of treatment, barriers to accessing treatment in poorer countries as well as poor treatment compliance may be to blame for the discrepancy brought on by the absence of effective cysteamine treatment.[9,11]

In our scenario, the patient received supportive care before beginning cystine depleting medication for cystinosis (Sapiens Health Foundation).

CONCLUSION

Cystinosis can be diagnosed using specific symptoms, a complete clinical evaluation, a full patient history and a range of specialist tests. A complicated disease with the ability to affect several organ systems, NC can cause severe morbidity and mortality. Further testing for total renal wasting and cystinosis can help with quick therapy and nutrient replenishment in rickets instances where malnutrition as aetiology is not clearly diagnosed. To get the most out of the preventive and therapeutic effects of cystine depleting drugs, cystinosis must be diagnosed as promptly as possible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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