

**CYSTINOSIS: A RARE CASE PRESENTATION**

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**ABSTRACT** - Cystinosis is a systemic disease caused by defect in metabolism of Cystine. It typically presents as Fanconi syndrome with metabolic acidosis, polyuria, failure to thrive, glucosuria, phosphaturia and aminoaciduria. Our patient did not display metabolic acidosis at presentation and had features suggesting Bartter's syndrome.

**KEYWORDS** - Cystinosis, Metabolic Acidosis, Bartter's Syndrome

**INTRODUCTION**

Cystinosis is a systemic disease caused by defect in metabolism of Cystine. It typically presents as Fanconi syndrome with metabolic acidosis, polyuria, failure to thrive, glucosuria, phosphaturia and aminoaciduria. Our patient did not display metabolic acidosis at presentation and had features suggesting Bartter's syndrome.

**CASE PRESENTATION**

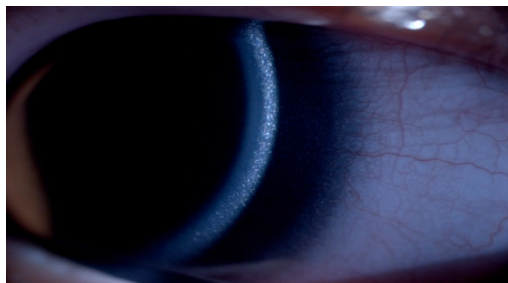
A 2 year girl presented with history of failure to thrive and polyuria since 9 month of age. She had grown well prior to that. She was born at term, normal vaginal delivery, birth weight 2.7kg, length 47cm and head circumference 34cm. Her initial physical milestones were normal but she never walked and language was appropriate for age. Presenting at 2 years of age her weight was 5.9kg, height 68cm and head circumference 44 cm. Blood pressures was normal. She had severe polyuria (urine output more than 6 ml/kg/hr). Venous blood gas showed a pH of 7.48 with the HCO<sub>3</sub> value of 20. She had hyponatremia (serum sodium 126 mEq/L), severe hypokalemia (serum potassium 1.0 mEq/L) and hypochloremia (serum chloride 84

mEq/L). Hypercalciuria (urine calcium: creatinine 0.6) was also noted. Serum creatinine was normal (0.4 mg/dL).

She also had a low serum phosphorus (2.9mg/dl) and calcium (7.4mg/dl) with mild elevation of alkaline phosphatase (307IU/lit). The 25 OH Vit D levels were high. The urine electrolytes showed a high urine chloride (39mmol/lit). The combination of hypokalemia, hypochloremia, no metabolic acidosis and a high urinary chloride was suggestive of Bartter's syndrome. However the hypophosphatemia was not in concurrence. Hence other possibilities were kept in mind and investigations including an ophthalmic examination recommended though therapy was commenced for Bartter's syndrome.

There was irregular follow-up and the ophthalmic examination was not done early. 6 months later she presented with severe metabolic acidosis along with severe hyponatremia (107meq/lit), hypokalemia (2.1meq/lit) and hypochloremia (72meq/lit). The hypophosphatemia (2.6mg/dl) persisted and investigations also revealed aminoaciduria. Ophthalmic evaluation was done

which revealed Cystine deposits in cornea on slit lamp examination. This confirmed a diagnosis of cystinosis.



**Figure 1(a) – Cystine Crystals in Cornea on Slit lamp examination**

### **DISCUSSION**

Cystinosis is an autosomal recessive lysosomal storage disorder caused by defective transport of amino acid cystine out of lysosome (1). This stored cystine is poorly soluble and crystallizes within lysosome of many cell types leading to widespread tissue and organ damage. It has 3 variants (Infantile onset, late onset and ophthalmic). Children with Infantile cystinosis present early, usually in the first year of life with failure to thrive and polyuria, metabolic acidosis, hypokalemia and features of Fanconi syndrome (2). Severe hypophosphatemia is the hallmark due to tubular loss of phosphorus (3).

This child presented with polyuria, polydipsia, and failure to thrive but had hypokalemia, hypochloremia with a raised urinary chloride and no evidence of metabolic acidosis. These are classical features of Bartter's syndrome (4, 5). However, Bartter's syndrome usually does not show a low phosphorus level and if they do develop nutritional rickets, they will show low levels of Vitamin D. This girl had low phosphorus with normal/high levels of Vitamin D. hence there was a suspicion that this was not so straightforward. The confirmatory test for cystinosis is ophthalmic evaluation which classically demonstrates the

cysteine crystals in the cornea. The girl had evidence of this and she eventually did present with severe metabolic acidosis and all features of Fanconi syndrome. This is an extremely rare presentation of Cystinosis but has been described earlier (6-8). As to the reason why this type of presentation occurs is not completely understood but there are theories. One of the theories is that before cysteine accumulates in sufficient quantities in the lysosomes to cause the typical Fanconi syndrome, the accumulation probably damages the sodium-potassium ATPase in the tubular cell lining thereby causing a leak of all these electrolytes simulating Bartter's syndrome (9). Eventually as the cysteine accumulation progresses, the typical clinical picture emerges (10- 13).

Treatment consists of Soda mint to correct acidosis, potassium supplements, phosphate supplements like Joulie's solution and good nutrition. Specific therapy is with cysteamine that helps cysteine to egress the cell (14). However it is a dreadful illness with a poor prognosis. Untreated, children will go into end stage renal disease by adolescence. Even with cysteamine treatment which is very intensive, they will eventually reach ESRD by 25 to 30 years of age (15). It also affects other organs like the pancreas, thyroid etc causing hypothyroidism, diabetes mellitus etc. Hence even after a renal transplant, cysteamine treatment is usually required lifelong. Cysteamine drops for the eyes are also used to reduce deposits in the cornea.

### **CONCLUSION**

Cystinosis is a dreadful illness with a uniformly poor prognosis in terms of renal function. On the other hand, Bartter's syndrome has many electrolyte abnormalities but most children will do well in the long term. Hence it is extremely important to be aware of this masquerading nature

of Cystinosis with regards to Bartters syndrome so that the diagnosis is not missed.

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