CASE REPORT

CYSTINURIA: Crystals that Make a Baby Cry

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Abstract Cystinuria is a common aminoaciduria due to a COAL transporter defect in renal tubular epithelium. Increased level of cystine in urine with occasional cystine crystal can be diagnostic. With reference to clinical examinations, symptoms and laboratory reports we present a case of primary cystinuria. Prevention of complication in cystinuric relies on detection at early stage and targeting treatment towards maintaining low level of urinary cystine level.

Keywords Cystinuria · Aminoaciduria · Crystal · Ammoniacal silver nitroprusside test · IEM

Introduction

Cystinuria is a common aminoaciduria which affects both genders equally. It is an autosomal recessive disorder, also known as dibasic aminoaciduria. Though basic defect is unknown, Cystine shares COAL membrane bound protein transporter present in renal tubular epithelium with dibasic amino acid viz, Ornithine, Arginine, lysine for its reabsorption. Due to a defective transport of the renal tubular epithelial cell, cystine cannot be reabsorbed and excreted in

urine [1, 2]. At physiological pH of urine, among four amino acids only cystine has relatively low solubility due to which it forms characteristic hexagonal crystals and if levels are higher it may get clumped as calculi [3].

We would like to present a case of Cystinuria detected at our Department because, recognizing symptoms of Cystinuria at the earliest is important to protect the patient from complications arising at a later age.

Case Report

A 7 month male child was brought by parents to the out-patient pediatric clinic of a private nursing home at Bijapur with chief complaint of fever from the last 2 days, four episodes of loose stool in the last 24 h and the baby cries before urination.

History of Present Illness

Patent had Fever for the last 2 days and passed loose stool four times in the last 24 h. The mother informed that, baby has some trouble while urination for a week or so as he cries before urination other times active and playful. The mother denied any eye or nose irritation, no sign of cough or difficulty in breathing, no report of fever in family member nor any medication given to baby in the past 1 month. Immunization was up to date.

Past Medical History

Baby born FTMVD. No birth complication. The couple has Non consanguineous marriage. The family belongs to a middle socioeconomic group. There is no history of allergic occupation of father.

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Physical Examination

All Vitals checked were normal, baby show normal activity, muscle tone was ok, no periorbital swelling or vision impairment was detected. Skin was warm and dry, No skin rashes were observed.

Clinical Examination

Baby showed mildly delayed milestone with signs of rickets. Baby was pale, anemic having mild breathing difficulty.

After taking patients' history and clinical examination, a suspicion was raised about underlying metabolic abnormality. To rule out any possibility of inborn error of metabolism, the fresh morning urine sample was sent for screening to Department of Biochemistry of our hospital.

Biochemical tests performed at the Department of Biochemistry for screening of inborn error of amino acid and carbohydrate metabolism revealed following results (Table 1).

From Table 1, Sodium Nitroprusside test for cystine turned out positive (Fig. 1) which was correlated well with urinary cystine spot detected on TLC. Test of thin layer chromatography of the patient's urine was repeated with individual separate standard solutions of Glycine,

Fig. 1 Nitroprusside test for Cystinuria

Histidine, Arginine, Lysine and Glutamine as these amino acids show close zone of separation on TLC, also to rule out Fanconi syndrome. After development of chromatogram with Ninhydrin spray, spots of cystine, lysine and Arginine were confirmed in a patient's urine suggesting primary cystinuria (Fig. 2).

Plasma sample of the patient's blood was first deproteinized with alcohol and 5 ml of protein free filtrate was loaded on TLC to detect the possibility of type-II/III cystinuria. It has shown negative results.

Small part of urine was concentrated by evaporation on boiling water bath and a drop of it was subjected to microscopic examination. A typical highly reflectile hexagonal crystal of cystine was observed under microscope validating our chemical findings (Fig. 3; 40× and 100×).

After assessing the complete clinical history and laboratory reports, patient was diagnosed as a case of primary cystinuria. Screening for Family members were advised, but due to distance and inconvenience of time; parents' refused for analysis.

The patient's mother was instructed about the condition and asked to maintain a high fluid intake along with K-Citrate (5 ml/day-BD) and Acetazolamide (5 mg/kg/day-BD). Regular follow up after every 15 days was advised. At first follow up after 15 days, patient was relieved of most symptoms.

Discussion

Cystinuria is a common aminoaciduria. Reported prevalence for Cystinuria is 1 among 7000–10,000 lives worldwide but, it is less common in Asian population [6]. Among these 6–8 % pediatric cases having Cystinuria have been reported. A mutation in SLC3A1, which is responsible for the defect in dibasic amino acid transport causes type I—primary cystinuria [7, 8]. Increased urinary cystine may either be detected in primary cystinuria or Fanconi

Table 1 Result of biochemical test for screening of IEM on Fresh morning Urine sample [4, 5]

Biochemical test	Result
pH of urine	5.4 (Acidic)
Benedict's test for reducing sugars	Negative
Rothera's test for Ketone bodies	Mildly positive
Sulphosalicylic acid test for protein	Negative
Ninhydrin test for free amino acids	Positive with good intense colour
Tests for aminoaciduria	
DNPH test for keto acids	Negative
Ferric chloride test for PKU	Negative
Methyl malonic acid test	Negative
Nitrosanaphthol test for tyrosine	Negative
Ammoniacal silver nitroprusside test for cystine	Positive
Test for MPS	
Spot test for MPS	Negative
CPC citrate turbidity test	Trace Positive
Thin layer chromatography	
Urine-	Presence of cystine, arginine, lysine
Plasma-	No amino acid spot developed
Urine microscopic examination	Hexagonal crystal of cystine

Fig. 2 Urine Cystine crystals under microscope (40× & 100×)

Fig. 3 Thin Layer Chromatography Plate (Patient's Urine & Standard Amino acid spots)

syndrome. In Fanconi syndrome increased excretion of Histidine, Glycine, Serine, Alanine and Glutamine is reported along with cystine. Whereas Hexagonal polarizable crystals of cystine as noted in the present case along with increased excretion of dibasic amino acids viz, Ornithine, Arginine and Lysine substantiate primary cystinuria. Though, formation of cystine crystal in urine depends on various factors like the degree of saturation, presence of crystal inhibitors or pH of urine. It is important here to state that only a fraction of patients with Cystinuria present crystal in urine. Oxidized dimer, cystine precipitate leads to crystal formation [9].

As cysteine is non essential amino acid and can be synthesized from Methionine, excretion does not have much clinical significance. Clinical concern of Cystinuria is to prevent stone recurrence [10] and minimize morbidity.

Conclusion

With reference to clinical examinations, symptoms and laboratory reports we conclude that the patient is a case of primary cystinuria. Prevention of complication in

cystinuric relies on detection at early stage and targeting treatment towards maintaining low level of urinary cystine level.

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Compliance with Ethical Standards

Ethical Approval This study is purely a self funded study, and approved by the institutional ethical committee.

Conflict of interest The authors of this case report have declared that they have no conflict of interest.

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