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An Interesting Case of Cystinuria complicated by End Stage Renal Disease: A Case Report

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Abstract

Cystinuria is a genetic disorder that causes recurrent nephrolithiasis. Cystinuria accounts for about 1-2 % of adult kidney stones and carries significant morbidity beginning at a young age. All patient with Cystinuria requires frequent clinical follow-up and medical therapy to prevent cystine stone formation, chronic kidney disease, and eventually end-stage kidney disease progression.

We report a case of a 28year older woman with a history of Cystinuria who presented to the emergency department after a syncopal episode with complaints of generalized weakness, decreased urine output, reduced appetite, metallic taste, and hand tremors. Her laboratory studies at presentation were significant for anemia, hypocalcemia, hyperphosphatemia, metabolic acidosis, and elevated creatinine. The Patient's symptoms and laboratory findings were suggestive of uremia. The Patient eventually required hemodialysis to resolve symptoms and improve laboratory findings. Cystinuria progressing to End stage renal disease is preventable.

Keywords: Cystinuria, Nephrolithiasis, Chronic Kidney disease, End stage renal disease

Introduction

Cystinuria is a rare autosomal recessive disorder caused by impaired absorption of dibasic amino acids, which include cystine, ornithine, lysine, and Arginine from proximal renal tubules and gastrointestinal tract **[1-4]**. Cystine has poor solubility at normal urine pH, and this property causes stone formation in the urinary tract. It accounts for 1 % of renal calculi **[5]**. Cystinuria has been estimated to be 1:15000 in the United States (US). Cystinuria is a remarkable genetic disorder causing recurrent nephrolithiasis requiring patients to undergo several surgical interventions impacting their quality of life **[6-8]**. The high recurrence rate of cystine stones is associated with a high prevalence of chronic kidney disease compared to other renal stones **[9]**. Cystinuria is seldom implicated as the cause of End stage renal disease (ESRD). A retrospective study done among 120 patients with Cystinuria in the United Kingdom (UK) showed that 57.6 % of the Patients had stage 2 chronic kidney disease (CKD),17.8 % had stage 3 CKD, no case of CKD stage 4 or 5 and ESRD was reported **[10]**. Early and life-long medical treatment to reduce stone formation is critical in preventing CKD and ESRD in Cystinuria **[11,12]**. We present an interesting case of a Patient with Cystinuria who progressed to end-stage renal disease.

Case Summary

A 28-year-old woman with a history of recurrent nephrolithiasis (cystine stones) complicated by bilateral hydronephrosis requiring multiple extracorporeal shockwave lithotripsy and bilateral ureteral stent, recurrent urinary tract infections, hypertension, and Stage 3a chronic kidney disease. She had previously followed up with a geneticist for an organic urine test demonstrating a marked elevation of cysteine and moderate elevation of ornithine, lysine, and Arginine. She presented to the emergency department after an episode of syncope with complaints of generalized weakness, decreased urine output, appetite, metallic taste, and hand tremors.

At presentation, vital signs were significant for hypothermia with a temperature of 32 degrees Celsius, with otherwise stable vitals. Physical examination findings were notable for pallor, asterixis, mild facial puffiness, and mild pitting pedal edema.

Laboratory results revealed anemia with hemoglobin of 5.5mg/dL (reference range 11-14.5mg/dL), hypocalcemia with calcium of 5.6mg/dL (reference range 8.7-10.4), hyperphosphatemia with the phosphorus of (12.4mg/dL; reference range 2.4-5.1mg/dl), metabolic acidosis with bicarbonate at 13mmol/L (reference range (20-31mmol/L), elevated blood urea nitrogen of 119 mg/dL (reference range of 9-23mg/dl), elevated creatinine at 20.59 mg/dL (reference range 0.5 to 0.80mg/dl), low GFR at 2ml/min/1.73m2 (reference range 90-120mL/min/1.73m2), hyperparathyroidism with the parathyroid hormone of 906.7 pg./ml (reference range 18.5-88 pg/ml), low vitamin D 25 hydroxy level at 18ng/ml (reference range 30-100 pg/ml), prothrombin time of 25 secs (reference range of 11.8 to 14.6 secs), the international normalized ratio of 2.0 (reference range 0.8-1.2). Additional workup, which included HIV, hepatitis panel, complement levels, serum protein electrophoresis with

immunofixation, and ANA, were all normal. Abdominal ultrasound revealed generalized increased echogenicity indicative of sequelae of chronic kidney disease.

Echocardiography showed normal systolic function with an Ejection fraction of 60-65 %.

She was transfused with 2 units of blood, phosphate binders for hyperphosphatemia, and calcitriol for vitamin D deficiency. She resumed her antihypertensive medication. Due to her worsening renal function, volume overload, metabolic acidosis, and concern for uremia, hemodialysis was initiated with a resolution of metabolic acidosis, volume overload, and signs of uremia. She was discharged to continue outpatient with hemodialysis and nephrology follow-up. However, the Patient passed away after missing multiple hemodialysis sessions outpatient.

Discussion

Cystinuria is a rare genetic disorder that causes recurrent cystine stones. It is often diagnosed in childhood. Clinical features of Cystinuria are attributed to the formation of rocks, including hematuria, flank pain, nausea, vomiting, and dysuria. Patients with Cystinuria often develop recurrent urinary tract infections and chronic kidney disease (CKD) but rarely end-stage renal disease (ESRD). Few cases of Cystinuria with end-stage renal disease have been reported. In a retrospective study conducted in France with a population of 442 cystinuria patients, it was observed that 5 patients had ESRD, and hypertension was prevalent among this population **[9]**.

Patients with Cystinuria often form large staghorn calculi needing frequent urology intervention. On imaging, cysteine stones are radiopaque but less dense than calcium-based stones.

The genetic cause of Cystinuria has been linked to a mutation in the SLC3A1 gene on chromosome 2 and the SLC7A9 gene on chromosome 19. Based on this congenital disability, Dello Strologo et al. classify Cystinuria into types A, B, and AB **[2,3,13]**.

Cystinuria is commonly confirmed with a quantitative 24hr urine test and stone chemical analysis. Routine urinalysis may show characteristic hexagonal urine crystals, the initial test of choice. The sodium-Cyanide nitroprusside test is often used as a screening test for Cystinuria. **[3,5,7, 11,14]** Renal biopsy in Cystinuria reveals bellini ducts plugged with cystine crystals deposit but is not frequently performed for diagnosis. **[2,15]**

Treatment of Cystinuria is majorly targeted at preventing the recurrence of stone formation and its complications and improving patient quality of life. **[3]** Conservative measures attain this through dietary modification by reducing protein intake, alkalinization of urine to aid cystine stone solubility with potassium citrate, and hyper-diuresis with hydration. **[3,11,14]** If conservative management is insufficient, pharmacology therapy could be sought with chelating agents such as Penicillamine and Tiopronin. **[2,14]** Urology intervention is often required in patients with recurrent symptoms, with no adequate response to conservative measures, and these include extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy **[5,7]**. Adherence to dietary modification and medical therapy plays a significant role in averting stone recurrence; however, this could be demanding for most patients. **[8]**

In the index case, the Patient was diagnosed with Cystinuria with recurrent cystine stone formation requiring multiple urology interventions. She had poor clinical follow-up and was not adherent to her diet or medications. She had a progressive renal decline, ultimately leading to ESRD **(Figure 1).**

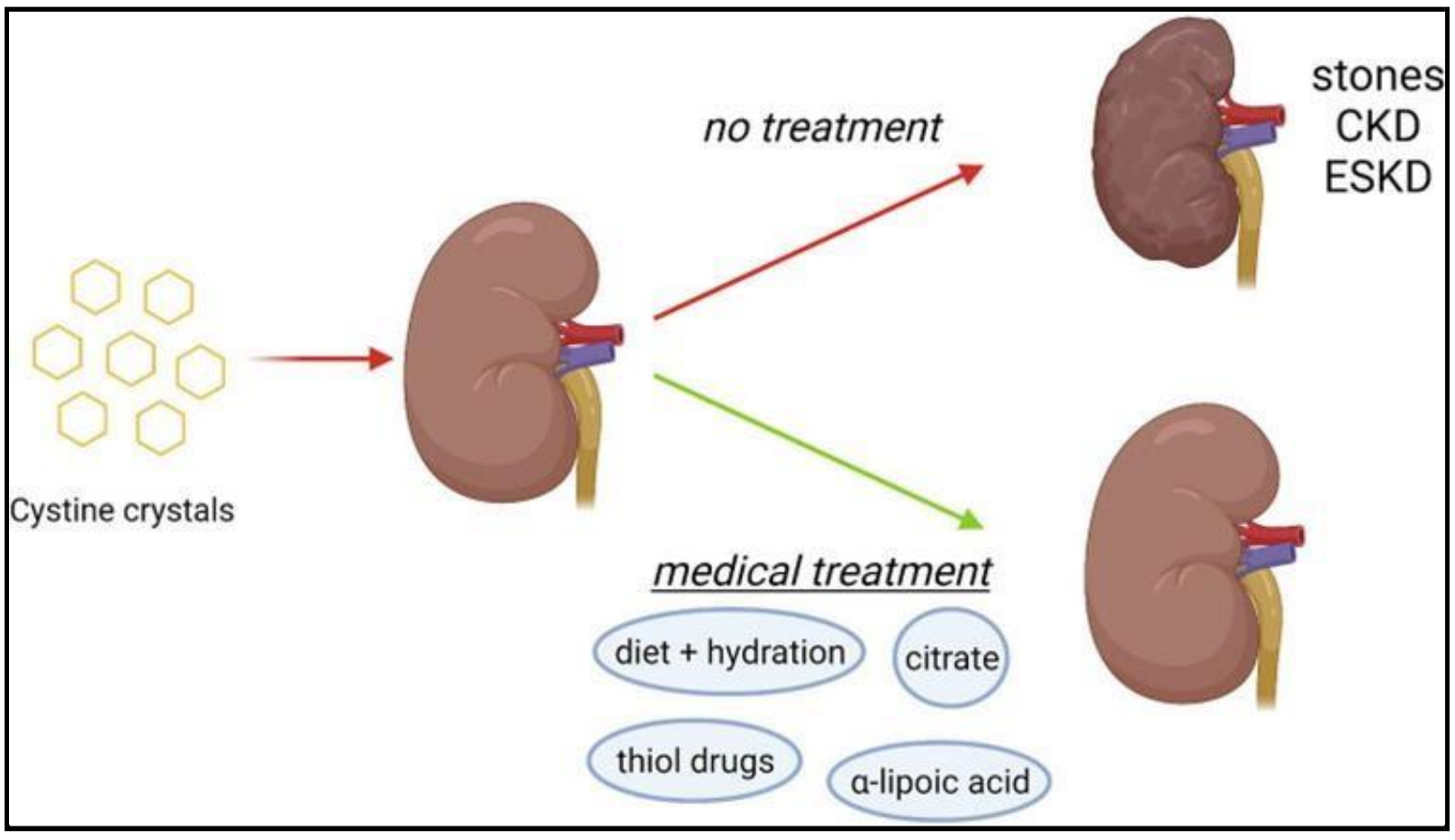

Figure 1: Complications of cystinuria and effects of preventive medical treatment **[11]**

Conclusion

Cystinuria is a lifelong disease. Preventing stone formation is crucial to avoid complications like an end-stage renal disease. A patient who are compliant with their treatment have a lower rate of cystine stone formation, thereby reducing the risk of chronic kidney disease and end-stage renal disease.

Conflict of interest: No conflicts of interest regarding the publication of this paper.

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