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Case Report
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Successful Renal Transplantation in a 15-Year-Old Girl with Nephropathic Cystinosis: A Case Report

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ABSTRACT

Cystinosis is an autosomal recessive lysosomal storage disorder(bi-allelic mutations in the CTNS gene) characterized by the defective transport of the amino acid cystine out of the lysosome due to a deficiency of cystinosin, the lysosomal cystine transporter. Patients have lysosomal cystine ac- cumulation in various tissues, leading to cellular stress and damage, particularly in the kidney, cornea, and other extrarenal tissues. Cysteamine, a cystine-depleting agent, improves survival and delays the progression of disease, but it does not prevent the development of either renal failure or extrarenal complications. Furthermore, the drug has severe adverse effects that significantly reduce patient compliance. Allogeneic hematopoietic stem cell transplantation (HSCT) is currently established as a therapeutic option for many inborn errors of metabolism, where the main pathologic driving factor is an enzyme deficiency. Nephropathic cystinosis is a rare autosomal recessive lysosomal storage disorder that leads to progressive renal failure, often necessitating renal transplantation. We present the case of a 15-year-old girl with end-stage renal disease (ESRD) secondary to nephropathic cystinosis, successfully managed with a live donor renal transplantation.

KEYWORDS: *Transplantation, Cystinosis, Renal*

INTRODUCTION

Cystinosis is characterized by lysosomal cystine accumulation and crystallization, and manifests clinically with severe polyuria and loss of a diverse range of substances normally reabsorbed in the kidney proximal tubules (renal Fanconi syndrome), leading to end-stage renal disease (ESRD) during childhood or early adolescence. Extrarenal manifestations include photophobia, retinopathy, endocrine dysfunction (hypothyroidism, endocrine pancreatic insufficiency, hypogonadism), peripheral myopathy, and central nervous system complications, which mostly develop during the second and third decades of life. In cystinosis patients, phagocytic cells, such as blood granulocytes and bone marrow and tis- sue macrophages, accumulate large amounts of cystine due to their phagocytic nature and their inability to process the phagocytized crystals. The only available treatment for cystinosis is the cystine-

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depleting amino thiol cysteamine. However, this drug does not prevent progressive disease, but merely postpones the development of ESRD and extrarenal complications. Moreover, cysteamine has numerous side effects that severely limit patient compliance. Renal transplantation is the treatment of choice for ESRD in these patients. However, post-transplant management must address systemic manifestations of cystinosis, including growth retardation, skeletal deformities, and ocular complications.

There are 3 major phenotypes for cystinosis. Infantile nephropathic cystinosis is the most severe type, and constitutes >95% of cases. This disease presents with renal impairment during the first year of life, and development of renal failure by the end of the first decade, along with multiorgan damage. Few cystinosis patients present with juvenile nephropathic cystinosis, which is a milder form of the dis- ease that induces renal injury at a later age. Thirdly is the ocular type, which manifests only with photophobia due to corneal cystine crystal deposition, and spares other organs.

Case Presentation

A 15-year-old girl presented with complaints of renal failure and had been on maintenance hemodialysis for two years through a left radiocephalic arteriovenous fistula (AVF). She exhibited growth retardation with bowed legs and impaired visual acuity, necessitating cysteamine eye drops. Her blood group was A positive, and due to the absence of a compatible related donor, she was placed on a paired donor list. She subsequently underwent renal transplantation on April 30, 2024.

Pre-Transplant Management

Six weeks prior to transplantation, she was initiated on oral cysteamine (mercaptamine bitartrate), starting at 50 mg four times daily (QID) and titrated up to 100 mg QID, along with ophthalmic cysteamine. Pre-transplantation assessment revealed normal thyroid function, neurological status confirmed on MRI brain, and cardiac status which were within normal limits. However, she had secondary hyperparathyroidism with normal calcium, elevated phosphorus, and an intact parathyroid hormone level of 230 pg/ml, managed with alfacalcidol.

Transplant Details

She received a blood group-compatible, A-positive, live-nonrelated kidney transplant from a 35-year-old female donor through a paired donor exchange program. HLA matching revealed a 6/8 mismatch, with negative flow cross-match and Luminex results, allowing the transplant to proceed per hospital protocol.

Induction Therapy

- rATG: 6 mg/kg cumulative divided over three days
- IV Methylprednisolone: 250 mg once daily for three days
- Tacrolimus: 2 mg twice daily (initiated 24 hours before transplantation), maintained tacrolimus trough levels between 8-10 ng/ml in the first 3 months.
- Mycophenolic acid: 500 mg twice daily (initiated 24 hours before transplantation)

Post-Transplant Course

The transplant surgery was uneventful. The patient achieved a nadir serum creatinine of 0.8 mg/dL and was discharged on the fourth post-operative day.

One-Year Post-Transplant Follow-Up

- Maintained baseline creatinine around 0.9 mg/dL
- IMMUNOSUPPRESSION REGIMEN:
- Tacrolimus levels stabilized around 7 ng/mL
- Mycophenolic acid 500 mg TWICE daily, Prednisolone 5 mg daily

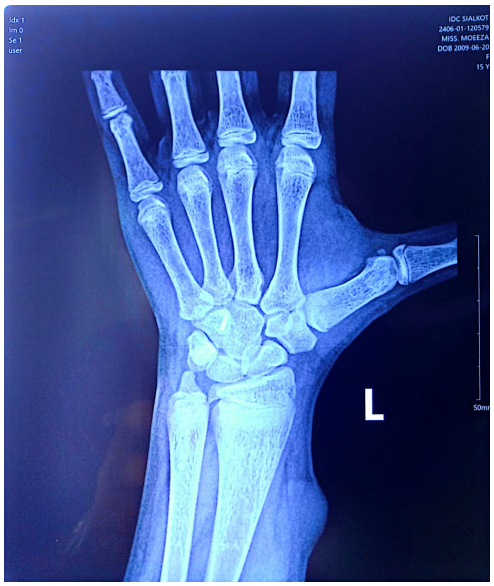
- Persistent hypertension managed with Carvedilol
- Increased linear growth by approximately 5 cm; however, growth hormone therapy was not pursued due to concerns over immunological rejection and unsatisfactory bone age findings.

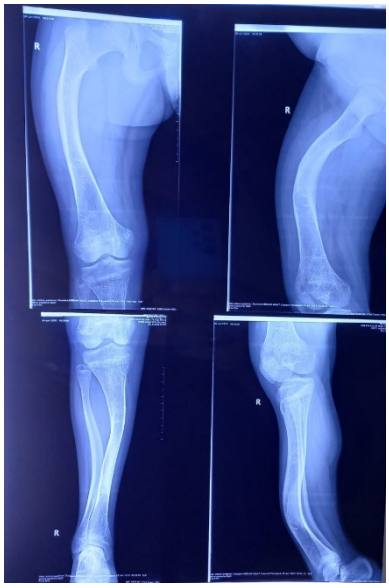
Challenges and Future Considerations

Despite successful renal transplantation, the patient continues to experience growth retardation and bowed legs. A multidisciplinary approach involving endocrinology and orthopedic specialists is essential for long-term management. The role of cysteamine therapy in mitigating extra-renal manifestations remains a key focus in her ongoing care.

CONCLUSION

This case highlights the feasibility and success of renal transplantation in patients with nephropathic cystinosis. While renal function post-transplant has been excellent, extra-renal complications such as skeletal abnormalities and growth delay require continued attention. Early diagnosis and comprehensive multidisciplinary care remain crucial in optimizing long-term outcomes for these patients.





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