Introduction

Metachromatic leukodystrophy (MLD) is an autosomal recessive lysosomal storage disorder characterized by the deficiency of the enzyme arylsulfatase A \(^1\). It is characterized by demyelination and deposition of metachromatic material in the central and peripheral nervous system and visceral organs \(^2\). Ultrastructural analysis of the metachromatic granules shows that they are composed of different types of inclusions \(^3\).

A literature review did not reveal previous reports of viscera from MLD being used for organ donation.

Case Presentation

The donor presented at two years of age with psychomotor retardation and cognitive decline and was diagnosed with MLD. He suffered an unexplained cardiac arrest at age ten and his parents requested that the organs be transplanted.

One of the kidneys was transplanted to a 61 year old female with diabetic nephropathy. The graft started functioning effectively immediately. There was one episode of acute cellular rejection which was treated with steroids. Currently, the patient is well with a creatinine of 1.1 mg/dl.

The renal surveillance biopsies were performed at time zero, 3, 12, 24, and 36 months and examined by light and electron microscopy.

<table>
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<tr>
<th>Light microscopy</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
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<tr>
<td>Acute cellular rejection</td>
<td>No evidence of rejection with subcapsular scar</td>
<td>No evidence of rejection</td>
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| Thick sections | Pale targetoid vacuolated structures in less than 5% of the distal tubules | Dark brown intracytoplasmic metachromatic inclusions in 20% of the distal tubules | Previously described inclusions are absent |

| EM | Membrane bound concentric whorled inclusions with alternating light and dark circular bands in the proximal and distal tubules | Prominent inclusions of varying sizes | The inclusions are fragmented and dispersed. There is focal disruption of the proximal tubular brush border with extrusion of the inclusions |

Figure 1: A. H&E: Intact proximal and distal tubules. B. PAS stain: normal glomerulus C. Toluidine blue stain: intracytoplasmic metachromatic granules D. Toluidine blue stain: dark brown intracytoplasmic targetoid inclusions in the distal tubules

Figure 2: A. Electron microscopy reveals distal tubules with intracytoplasmic inclusions (x 4000). B. Higher power showing the membrane bound whorled concentric inclusions with alternating dark and light bands (x 30000) C. Proximal tubule with dispersed fragmented inclusions (x 4000). D. Focal disruption of the proximal tubular luminal brush border with extrusion of the inclusions into the lumen

Conclusion

1. In MLD patients metachromatic inclusions were observed in the distal convoluted tubules, thin limb of the loop of Henle, collecting tubules, tubular lumen and urine \(^4\), \(^5\). In our case, the inclusions were present in the cytoplasm of the distal and proximal tubules and tubular lumen.

2. The morphology of the inclusions in MLD may be quite variable. Large lamellae, herring bone, tublstone and zebroid inclusions have been observed \(^4\), \(^5\). The inclusions in our case resemble the zebroid type and type III inclusions described by Joosten et al \(^5\).

3. The inclusions are present in few tubular epithelial cells. Toluidine blue stain highlights the targetoid vacuolated structures within the epithelial cells. Extensive ultrastructural examination is often needed to identify and characterize the inclusions \(^4\).

4. During early post-transplant period, the inclusions are large and membrane bound within the cytoplasm. 5. Three years after transplantation, fragmentation of the inclusions and extrusion into the tubular lumen is observed.

6. Simultaneous expulsion probably indicates that the lysosomal pathology is being remedied, most likely due to uptake of host arylsulfatase A enzyme by the allograft \(^7\).

7. There are no reports of impaired renal function in patients with MLD, except for one case of proximal renal tubular acidosis \(^8\). The kidney function in the recipient has markedly improved due to transplantation.

8. The three year follow-up study, suggests the possibility that MLD patients can be potential renal donors, although further long term studies are required.

References


