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End-Stage Renal Disease in Childhood – A rare biopsy-proven diagnosis

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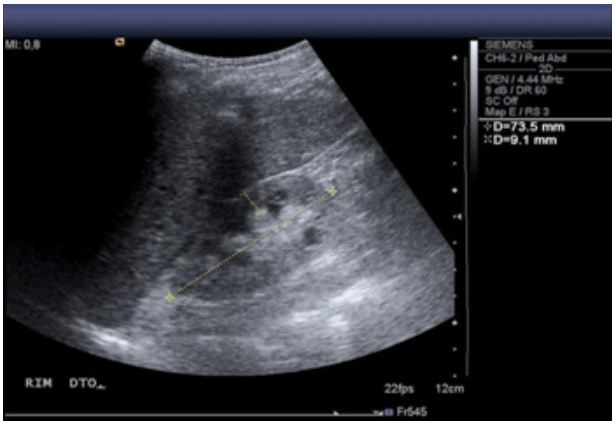
CLINICAL PRESENTATION

A 16-year-old male was referred to our paediatrics nephrology department for severe renal dysfunction. He complained of polydipsia and polyuria for several years and had recently developed symptoms of asthenia and anorexia. On admission he was normotensive and euvolaemic. Skin and mucous membranes were pale and there was a notorious growth retardation and delayed puberty. The remaining physical examination was unremarkable. Laboratory tests were as follows: serum creatinine 14mg/dL, urea 361 mg/dL, haemoglobin 6.3 g/dL, pH 7.28, serum bicarbonate 14.4 mEq/L, ionized calcium 0.6m Eq/L and phosphate 9.1 mg/dL. Urinalysis showed a low density of 1.005, innocent sediment and a protein/creatinine ratio 2180 mg/g. Serologic, autoimmunity and immunologic study was negative. On renal ultrasound screening, kidney dimensions were within the inferior normal range and cortical thickness was reduced, and there were multiple small corticomedullary cysts (Figure 1).

Figure 1
Kidney ultrasound.



He had a previous medical history of enuresis until he was six years old. No familiar history of renal disease was known.

A kidney biopsy was performed.

HISTOLOGICAL FINDINGS

The paraffin-embedded fragment showed kidney cortical and medulla with a total of sixteen glomeruli and several small and medium-sized arteries.

All glomeruli presented global sclerosis and there was an extensive interstitial fibrosis (Figure 2 – Masson's trichrome).

Figure 3 and 4 represents the routine staining with Periodic acid-Schiff (PAS) and shows tubular atrophy and basement membrane disruption with duplication and thickening, as well as dilatation of distal tubules.

Figure 5 represents a PAS positive material deposition in the interstitium of cortico-medullar region. Figure 6 shows that the material deposited correspond to uromodulin (Tamm-Horsfall protein) that was extruded from the tubules.

Figure 2

Masson´s Trichrome 40.

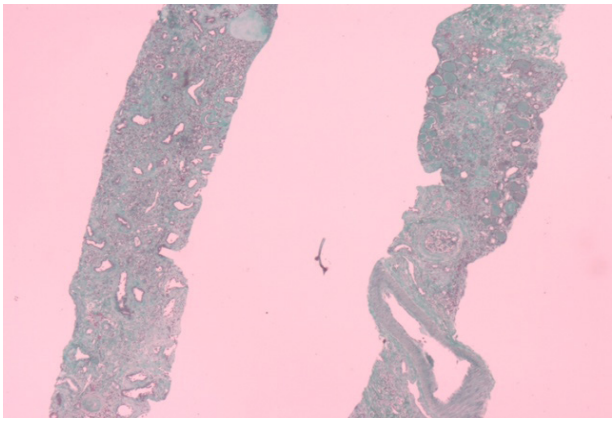


Figure 3

Periodic acid-Schiff 200X.

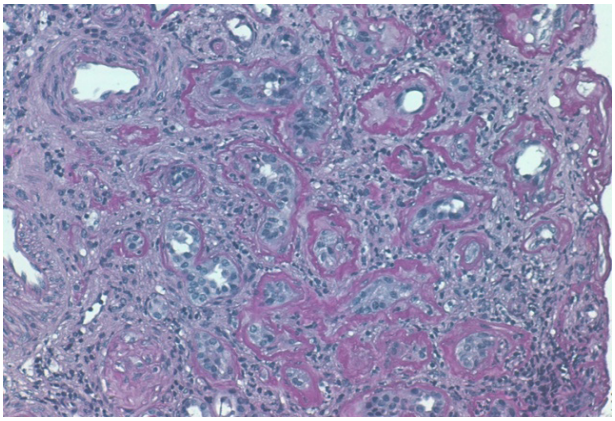


Figure 4

Masson's Trichrome 400X.

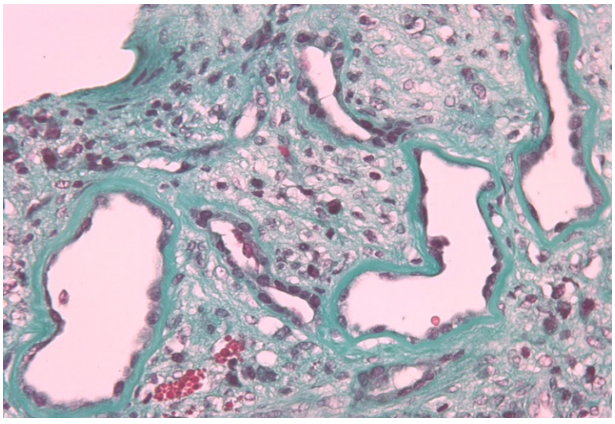


Figure 5

Periodic acid-Schiff 200X.

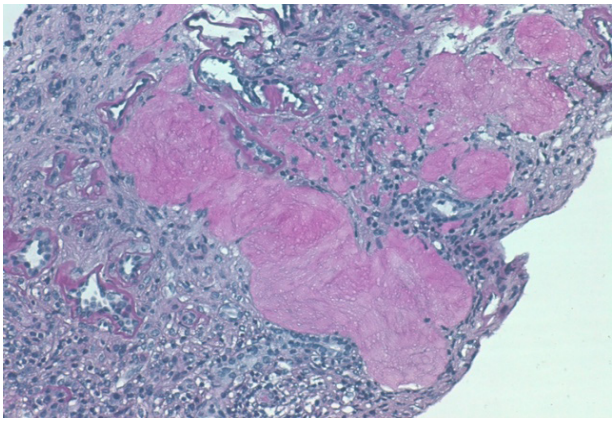
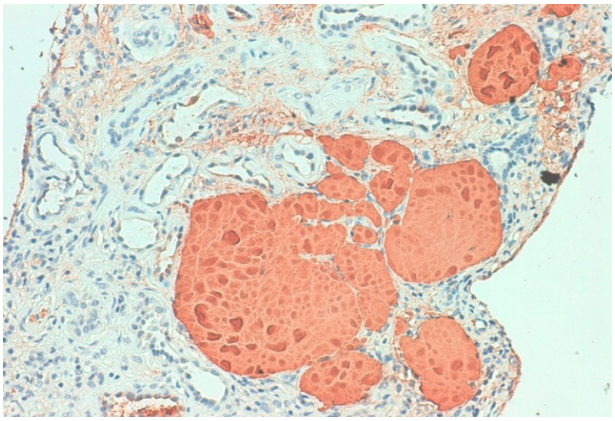


Figure 6

Uromodulin imunochemistry 200X.



Anatomical diagnosis

Nephronopthisis.

EVOLUTION AND TREATMENT

A Tenckhoff catheter was placed and the patient was started on peritoneal dialysis.

DISCUSSION

Nephronophthisis (NPHP) is an autosomal recessive cystic kidney disease and one of the most common

genetic disorders causing end-stage renal disease (ESRD) in children and adolescents[1].

Correlating with the age of onset of ESRD, three clinical subtypes of NPHP have been distinguished: infantile, juvenile, and adolescent, which manifest with ESRD at the median ages of 1, 13, and 19 years, respectively[2].

There are several genes underlying NPHP, most of which express nephrocystins, a protein present in primary cilial and basal body structures. Some other nephrocystins are believed to be part of adherens junction and focal adhesion kinase protein complexes[3].

Common symptoms of NPHP are usually mild and consist of polyuria, polydipsia and secondary enuresis, due to an urinary concentration defect[4]. Advanced renal disease is accompanied by anaemia and growth retardation[5].

Extrarenal symptoms are present in up to 20% of cases, in particular, retinitis pigmentosa (Senior-Løken syndrome), cerebellar ataxia (Joubert syndrome), oculomotor apraxia Cogan type, mental retardation, bone anomalies and hepatic fibrosis[6].

Typical ultrasound features include normal or reduced renal size, loss of corticomedullary differentiation and corticomedullary cysts[3].

On histological examination, a characteristic triad of corticomedullary cysts, tubular basement membrane thickening or disruption and tubulointerstitial nephropathy is usually found, although there are no pathognomonic characteristics[1,4]. Interstitial extrusion of uromodulin is a typical finding in NPHP[7].

The clinical features of patients with NPHP are not specific, so a genetic diagnosis is required for a definitive diagnosis of NPHP[5]. Mutations in eight different genes (NPHP1, 3, 4, 5, 6, 7, 8, and 9) have been associated to juvenile NPHP, whereas in the infantile form, mutations have been found in the NPHP2 gene[6].

Since there is no specific treatment for NPHP, conservative management of CKD is necessary[5]. Disease recurrence has never been reported in kidney graft after transplantation[2].

The clinical course of our patient, the renal ultrasound and histological findings confirm the diagnosis of NPHP, and he is still waiting for the results of genetic study for a better characterization of NPHP.

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