A cutaneous disease with multisystem involvement: hypomelanosis of Ito may be associated with proteinuria, focal segmental glomerulosclerosis and end-stage renal disease

Sir,

We report the case of a young girl with Hypomelanosis of Ito who developed focal segmental glomerulosclerosis (FSGS) and end-stage renal disease.

In this child from Pakistan, hypomelanosis and multiple dysmorphic signs were noted during the neonatal period: patches and streaks of hypo- and hyperpigmented areas involving the whole integument (Figure 1), muscular weakness, syndactyly and clinodactyly, hypertelorism, flat bridge of the nose, converging eyebrows, prominent upper lip (Figure 2). Chromosomal abnormalities were not found.

During the course of several years the patient developed contractures of the limbs, progressive scoliosis of the lower spine, and short stature. She also suffered from severe deafness and could not speak; intelligence seemed normal. Voiding cystourethrography and urodynamic investigations were normal. At the age of 7.5 years, proteinuria (1.4 g/day) with a normal GFR (Ccr 125.5 ml/min x 1.73 m²) were documented.

Conflict of interest statement. None declared.
On admission at the age of 11 years, proteinuria was 43 mg/kg/day and the Ccr 56 ml/min × 1.73 m². There was no oedema or hypertension. The complement factors C3 and C4 were normal, and ANA, ds-DNA and anticardiolipine antibodies (ACLA) were negative. Abdominal ultrasound showed hyperechogenic kidneys. Renal biopsy (20 glomeruli) showed global sclerosis in 12 and segmental sclerosis in two glomeruli associated with widespread interstitial fibrosis, tubular atrophy and mild arteriosclerosis (Figure 3). The findings by electron microscopy were unspecific. Immunohistology showed segmental deposits of IgM, C1q, C3c and C3d. Treatment with captopril reduced proteinuria; however, renal function decreased rapidly. At the age of 13, the Ccr was 20.1 ml/min × 1.73 m². Haemodialysis was initiated at age 15 and the patient received a kidney transplant after 27 months. Unfortunately, she died shortly after transplantation due to treatment-resistant pneumonia and cardiac arrest.

Hypomelanosis of Ito is a neuroectodermal disease frequently involving different organ systems [1,2]. Involvement of the kidneys has been reported very rarely [3]. A unique form of glomerulopathy was described by Chevalier [4] in a four-year-old boy with proteinuria and normal renal function. Eussen [5] described a boy with tuberous sclerosis, polycystic kidney disease and alpha-thalassaemia. Coward [3] described a 17-year-old girl who had multiple cysts in both kidneys which diminished renal function.

The genetic background of Hypomelanosis of Ito (OMIM 300337) is not known. An autosomal dominant, x-linked or recessive inheritance, chromosomal aberrations, mosaicism and other abnormalities have been described [6]. In patients with balanced X-autosomal translocations, paternal imprinting was recognized [6]. It is known that disruption of imprinted genes is associated with characteristic patterns of inheritance and a multisystem phenotype, which may include cutaneous features; clinical examples include the Beckwith–Wiedmann, Silver–Russell, Prader–Willi, McCune–Albright syndromes and others [7].

This seems the first case of Hypomelanosis of Ito with end-stage renal disease due to FSGS.

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Rapamycin-induced hypokalaemic nephropathy in a middle-aged hypertensive male

Sir,

Rapamycin-induced hypokalaemic nephropathy is rarely reported in renal transplant patients. Rapamycin, an mammalian target of rapamycin (M'TOR) inhibitor, acts by preventing cell-cycle progression; it prolongs delayed graft function (DGF) and decreases repair of tubular cells [1]. There are reports of thrombotic microangiopathy when rapamycin is used with calcineurin inhibitors [2]. We hereby report a man who developed hypokalaemic nephropathy secondary to rapamycin.

A 31-year-old male with end-stage renal disease (ESRD) underwent a renal transplantation on 4 May 2005, the donor being his mother. He was induced with dacluzimab 20 mg and immunosuppressed with ciclosporin 275 mgBD, prednisolone 35 mgOD and sodium salt of mycophenylate, 360 mgBD. He weighed 68 kgs. He had a biopsy-proven graft injury. This case highlights the profound hypokalaemic response to minimal maintenance dose of rapamycin in the absence of diarrhoea, vomiting or medications causing hypokalaemia.

due to hypokalaemia secondary to rapamycin use and the drug was withheld. Two weeks later his creatinine declined to 2.1 mg/dl with serum potassium 4.1 mmol/l. His immunosuppressants were tacrolimus 3 mgBD and prednisolone 12.5 mgOD.

At the molecular level, MTOR is necessary for maintaining the integrity and regeneration of tubular epithelial cells, which account for the majority of potassium reabsorption [1]. The sustained improvement in creatinine and potassium following discontinuation of rapamycin strongly implicates this agent in the development of hypokalaemic nephropathy. Though the incidence of hypokalaemia on rapamycin is 34%, profound hypokalaemia is very rare [3]. The temporal relationship of recovery of renal function following discontinuation of rapamycin and correction of hypokalaemia suggests rapamycin as the inciting agent for acute kidney injury. This case highlights the profound hypokalaemic response to minimal maintenance dose of rapamycin in the absence of diarrhoea, vomiting or medications causing hypokalaemia.

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