Cerebellar defect associated with Schimke immuno-osseous dysplasia

Abstract  We report the finding of an absent cerebellar hemisphere and partial absence of the cerebellar vermis in a child with dysmorphic features, spondyloepiphyseal dysplasia, steroid resistant nephrotic syndrome secondary to focal segmental glomerulosclerosis and T-cell lymphopenia (Schimke immuno-osseous dysplasia). These findings have not, to our knowledge, been described before and are likely to represent the consequence of a vascular event either in-utero or in early infancy.

Conclusion  Cerebral imaging should be performed early in the course of the disease and should be repeated if further neurological events develop.

Key words  Cerebellar malformations · Nephrotic syndrome · Schimke immuno-osseous dysplasia

Abbreviations  FSGS focal segmental glomerulosclerosis · SED spondyloepiphyseal dysplasia · SIOD Schimke immuno-osseous dysplasia

Introduction

Schimke et al. [7] reported an association between spondyloepiphyseal dysplasia (SED), nephrotic syndrome with progressive renal insufficiency, and cyclical lymphopenia which they termed chondroitin-6-sulphate mucopolysaccharidosis. Later studies excluded mucopolysaccharidosis and Spranger et al. [9] proposed the eponymous name Schimke immuno-osseous dysplasia (SIOD). This is a multi-system disorder affecting chondrocytes and lymphocytes and is now recognised to be characterised by the combination of SED, cutaneous macules, proteinuria in all cases [2] and progressive renal insufficiency due to focal segmental glomerulosclerosis (FSGS), bone marrow failure and progressive arteriosclerotic disease with cerebral infarction. Most reported cases are sporadic but the inheritance is thought to be autosomal recessive [9]. An infantile form, with an unfavourable prognosis [4, 6], and a juvenile form [5] with a better prognosis have been described.

We describe a girl with SIOD who presented with a head tilt due to a lesion not previously described in this disorder.

Case report

The child was born at 31 weeks gestation by emergency caesarian section for premature labour and fetal distress. The birth weight, length and occipito-frontal circumference were on or below the 3rd percentile. She was briefly ventilated for hyaline membrane disease and made an unremarkable recovery. She was the 4th child of consanguineous Pakistani parents and there were three other well children; there was no family history of renal disease. At 6 months of age she was noted to be failing to thrive but was taken to Pakistan for a protracted period despite concerns about her progress. On her return, at 16 months of age, growth failure was noted to have persisted and there was global developmental delay. She was also noted to keep her head tilted to the right side and suffer...
from marked photophobia. Fundoscopy and an electroretinogram were normal.

She presented to this Department at 5 years of age with hypertension, heavy proteinuria, hypoalbuminaemia, and peripheral oedema. On examination she was noted to have: disproportionate truncal shortening, standing height 18 cm below the 3rd percentile, pigmented macules especially over the trunk and back and head tilt to the right side. She was noted to have dysmorphic facies with a broad, low nasal bridge, a bulbous nasal tip, and a short neck. An early morning urine protein/creatinine ratio was 2936 mg/mmol (normal < 20 mg/mmol), the serum albumin was 24 g/l (normal 35–52 g/l) and cholesterol 7.1 mmol/l (normal 2.9–6.4 mmol/l). The glomerular filtration rate estimated from height and plasma creatinine was 55 ml/min per 1.73 m². A percutaneous renal biopsy was undertaken. Seventeen glomeruli were obtained and FSGS was diagnosed. Renal function deteriorated rapidly and she progressed to end stage renal disease requiring haemodialysis by the age of 7 years. The skeletal abnormalities included abnormal vertebrae, pelvis, femoral heads, and dislocation of the hips requiring open reduction and acetabuloplasty.

Total white cell and lymphocyte counts were normal at birth but CD4 and CD8 lymphopenia developed from the age of 2 years. Anaemia unresponsive to erythropoietin therapy was noted from 6 years of age and thrombocytopenia associated with epistaxis and haemoptysis developed at 7 years of age.

A cranial MRI scan at 7 years of age showed an absent left cerebellar hemisphere and partial absence of the cerebellar vermis, with a CSF filled space in the left side of the posterior fossa at the site of the absent left cerebellar hemisphere (Fig. 1). The right cerebellar hemisphere and the ventricular system were normal. There was no cerebral atrophy. She subsequently suffered transient ischaemic attacks resulting in episodes of weakness in the left arm and repeat imaging at 7 years and 8 months of age demonstrated generalised atrophy of the cerebral hemispheres (Fig. 2).

**Discussion**

The severe disproportionate growth failure, SED, heavy proteinuria associated with FSGS, T-cell lymphopenia and cutaneous pigmented lesions confirmed the diagnosis of SIOD in this child. Neurological complications are common, the most frequent being cerebrovascular disease which was first noted by Spranger et al. [9] who reported four patients with cerebral ischaemia or atherosclerotic changes. Ehrich et al. [3] described three patients with SIOD and recurrent transient ischaemic attacks who had cerebral and cerebellar perfusion defects by positron emission tomography. The vascular disease is reported to progress at a variable rate and progression is unaffected by renal transplantation [1]. Schmidt et al. [8] described a patient with SIOD who suffered recurrent transient ischaemic attacks associated with white matter lesions on MRI and perfusion deficits on positron emission spectroscopy scans, and Boerkoel et al. [1] described two patients who had stenoses of cerebral arteries complicated by moyamoya phenomenon.

This child had no other signs of central nervous system disease but she has recently developed transient ischaemic attacks and weakness in the left arm and subsequent imaging demonstrated cerebral atrophy. The absent cerebellar hemisphere and partially absent cerebellar vermis in our patient has not, to our knowledge, been previously described in this condition and may well have been the likely cause of her head tilt. The early observation of head tilt suggests the cerebellar anomaly was present from infancy and may even have been present in-utero. It is, therefore, unclear if there are two pathological processes affecting her central nervous system, separately giving rise to the cerebellar malformation and the recent vascular events. Alternatively, this may represent the consequence of a vascular event either

![Fig. 1 MRI scan showing (a) axial T2-weighted and (b) coronal T2-weighted images depicting absence of the left cerebellar hemisphere and partial absence of the vermis](image-url)