Dentistry, neurology and nephrology—what is the connection?

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Case report

A 28-year-old female patient was admitted because of painless macroscopic haematuria. Past history included severe mental retardation and nystagmus. At age 17, a computed tomography (CT) scan of the brain showed an absent cerebellar vermis and cerebellar hypoplasia. There was no family history of neurological or renal disease.

On examination, the patient was hypertensive, did not communicate verbally, was hypotonic and had nystagmus. Laboratory investigation revealed severe kidney disease [serum blood urea nitrogen (BUN) 70 mg/dl, serum creatinine 6.0 mg/dl]. Urinalysis revealed haematuria and proteinuria. A renal ultrasound showed two small, echogenic kidneys with multiple bilateral cysts. The patient was felt to have chronic renal disease and is currently being seen in the pre-dialysis clinic. A magnetic resonance imaging (MRI) scan of the brain was performed (Figure 1).

What is the diagnosis?

Discussion

This MRI is pathognomonic of Joubert syndrome. It shows cerebellar vermal hypoplasia, thickened superior cerebellar peduncles and an interpeduncular fossa, which together constitute the ‘molar tooth sign’ [1–3].

Joubert syndrome was first described in 1968 as a syndrome of familial dysgenesis of the vermis accompanied by hyperventilation, abnormal eye movements and retardation. Today, at least two phenotypic variants of Joubert syndrome are accepted: Joubert syndrome type A with urological manifestations only and Joubert syndrome type B (CORS: cerebello-ocular-renal syndrome), in which retinal dysplasia and renal cystic/nephronophthisis disease, leading to renal failure in adolescence, are present [2–4].

Most patients with Joubert syndrome are sporadic, but the syndrome can also be inherited. Genetic mapping studies in two Middle-Eastern families have identified one locus from classical Joubert syndrome type A on chromosome 9q34.3, while in three families with Joubert syndrome type B, a novel locus on chromosome 11p12–q13.3 has been identified [2,3].

The association of Joubert syndrome with multicystic kidney/nephronophthisis raises the question of whether there is a developmental link between the malformation of the kidneys and the central nervous system. One explanation is the proximity in time of the embryonic development of these two systems. Also, development of the kidneys and the central nervous system depends upon inductive intercellular reactions. The observation that contact with embryonic spinal cord induces early differentiation of the metanephrogenic mesenchyme has prompted investigation into the likelihood that specific factors in the central nervous system (e.g. glial-derived nerve factor) may stimulate mesenchymal differentiation.

Conflict of interest statement. None declared.

References


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**Fig. 1.** Axial T2-weighted image with umbrella-like fourth ventricle (asterisk) and elongated superior cerebellar peduncles (arrow) giving the impression of the ‘molar tooth sign’.