Ear and kidney malformations with renal failure in an infant: what is the link?

Case

A male term newborn was admitted because of neonatal renal failure leading to the diagnosis of left hypodysplastic kidney and aplasia of the right kidney on ultrasound. The serum creatinine was 500 μmol/l. There was no history of fetal urological malformation. He also presented other congenital malformations, i.e. bilateral pre-auricular pits and a right branchial fistula (Figure 1). He had no hearing impairment. The parents were healthy and there was no significant family history. Renal impairment was then rapidly progressive and led to terminal renal failure at 2 years of age, while the patient was treated by peritoneal dialysis (PD). A few months later, a renal transplantation was performed. Acute steroid resistant graft rejection occurred on day 27 and led to graft loss, so that PD was again performed, followed by haemodialysis at 4 years of age. At age 6, a second renal transplantation was successfully performed.

Question

Is this case report suggestive of any known malformative syndrome?

Fig. 1. Pre-auricular pit and branchial fistula.
Answer to the quiz on the preceding page

This child presents with a phenotype of branchio-oto-renal (BOR) syndrome.

BOR syndrome is an autosomal dominant disorder with incomplete penetrance and extremely variable phenotypic expressivity. However, it has been established that such variable phenotypic expression was related to the same disease [1,2].

The prevalence of BOR syndrome approximates 1:40 000.

The main clinical features are due to congenital abnormal development of the first and second branchial arches and urinary tract. Other subsequent anomalies can be found, some of them are classified as major (hearing impairment, preauricular pits, pinnae deformities, external auditory canal stenosis, branchial fistulae and renal anomalies), others are minor (preauricular tags, lacrimal duct aplasia, short/cleft palate, retrognathia, benign intracranial tumour, congenital hip dysplasia, euthyroid goiter, facial nerve paresis, gustatory lacrimation, non-rotation of the gastrointestinal tract, pancreatic duplication cyst, temporo-parietal linear nevus) [1–3]. Such minor anomalies are particularly relevant as they allow expanding phenotypic heterogeneity of BOR syndrome [4]. Renal anomalies are almost always present and consist mainly of agenesis and hypoplasia/dysplasia; however, ureteropelvic junction stenosis, vesicoureteric reflux and calyceal diverticula have also been described [1].

The BOR gene maps to chromosome 8q13.3. This gene has sequence homology with the Drosophila (eyes absent) gene and was therefore called EYA1 [5]. The function of the EYA1 gene is unknown; it seems to act as a transcriptional activator [5]. Another gene was recently identified to be possibly associated with BOR syndrome on chromosome 1q31 [6]. Such a molecular diversity may partly explain the clinical heterogeneity of the syndrome.

References


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