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No eye for ears

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Case

A 50-year-old man was seen for chronic renal failure of unknown origin. He had been diagnosed in 1981 and monitored continuously while his renal functions had deteriorated slowly; his current glomerular filtration rate was 17 ml/min. On this occasion, he was seen by a new doctor who observed that he was hard of hearing. The day was unusually bright and sunny; hence lateral cervical scars, 3 cm in length, were noted bilaterally (Figure 1). The patient recalled that these were from surgery in childhood. On even closer examination, bilateral pre-auricular pits were also found, and the patient could express some whitish material from one of these (Figure 2). Further history taking revealed that his father and grandmother had similar pits, and that his father had died with renal failure of unknown cause. The patient had four children: three of whom had pre-auricular pits and branchial sinuses but no known renal problems. One of his daughters had died in a car accident, and her kidneys had been 'unsuitable' for transplantation although details were unavailable (Figure 3).

Question

What is the diagnosis?

Answer

The diagnosis is branchio-oto-renal (BOR) syndrome [1]. The patient was referred for genetic counselling and hearing assessment. Investigation of his children was arranged.

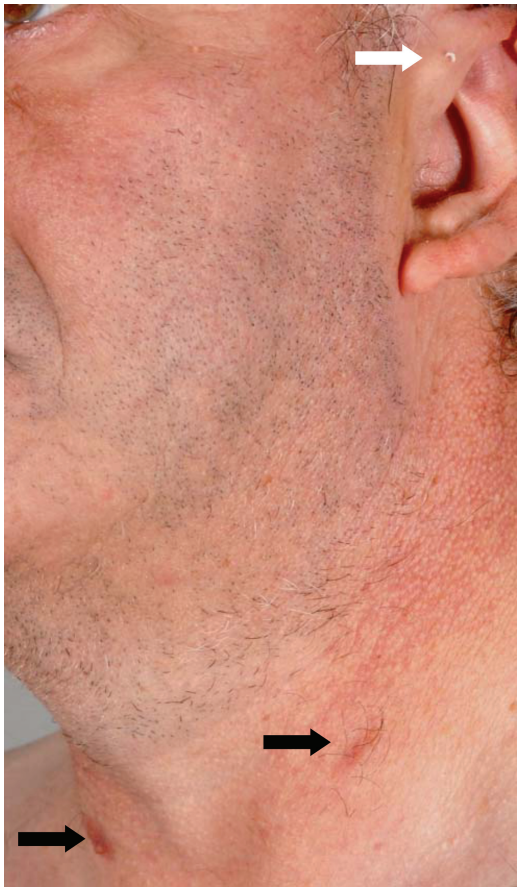

Fig. 1. Cervical scars (black arrows) and pre-auricular pit (white arrow).

Discussion

BOR syndrome [Online Mendelian Inheritance in Man (OMIM) 113 650, 610 896] is a developmental disorder mainly of the second branchial arch. It is characterized by sensori-neural, conductive or mixed hearing loss, structural defects of the inner and middle ear and branchial fistulas or cysts. Other manifestations are cleft palate, gustatory lacrimation and euthyroid goitre. Renal abnormalities vary in severity, may affect one or both kidneys and include renal

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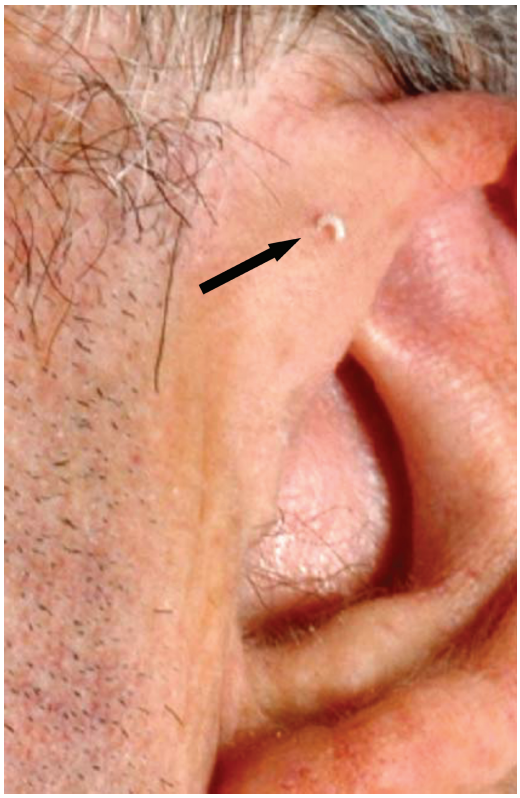

Fig. 2. Pre-auricular pit with whitish discharge.

hypoplasia or agenesis, pelvi-ureteric junction obstruction, vesicoureteric reflux and hydronephrosis.

BOR syndrome is autosomal dominant and genetically heterogeneous [2]. Disruption of genes that are crucial to the vertebrate development is the common theme: BOR1 syndrome (OMIM 113 650) is due to mutations in the EYA1 gene, the human homologue to the Drosophila *eyes absent* gene [3]. The SIX gene family, a human homologue to the Drosophila *sine oculis*, is affected in BOR2 syndrome (OMIM 610896) [4]. Interestingly, SIX and EYA1 interact during embryonic development [5]. This may provide a clue as to why BOR 1 and 2, although genetically different, cause a similar phenotype.

A clinical diagnosis of BOR syndrome can be established if an affected individual meets at least three major, or two major and two minor criteria, or one major criteria and an affected first-degree relative (Table 1) [1]. Our patient had three major criteria and affected relatives; hence a clinical diagnosis could be made with confidence. Unfortunately, the BOR syndrome is relatively unknown in adult nephrology. The neck of patients with vesicoureteral reflux should be examined for signs of BOR syndrome. This case and a sunny day (unusual in the North West of England) provided an interesting detour into the *eyes absent* and *sine oculis* genes in Drosophila. Previous doctors literally had no eye for the very subtle pre-auricular pits and the tell-tale cervical scars.

Conflict of interest statement. None declared.

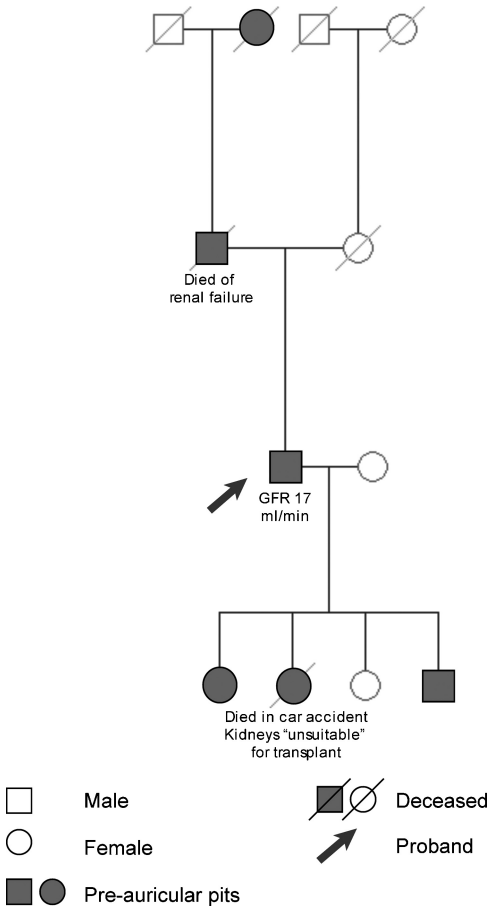

Fig. 3. Pedigree of the patient (drawn with the Pedidraw™ online tool, http://pedidraw.gcnet.org.cn/, accessed 16 December 2008).

Table 1. Diagnostic criteria for BOR syndrome [1]

Major criteria	Minor criteria
Pre-auricular pits	External auditory canal anomalies
Deafness	Middle ear anomalies
Branchial sinuses/cysts/fistulas	Inner ear anomalies
Auricular deformity	Pre-auricular tags
Renal anomalies	Facial asymmetry or cleft palate

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