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Bilateral congenital cholesteatoma in branchio-oto-renal syndrome

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Abstract
Branchio-oto-renal syndrome is a rare autosomal dominant condition characterized by hearing loss, branchial arch abnormalities and renal tract malformations. We present the first reported case of branchio-oto-renal syndrome associated with bilateral congenital cholesteatoma and ossicular chain abnormalities. The pathogenesis of this syndrome is described and the literature is reviewed.

Key words: Urinary tract; Cholesteatoma, middle ear; Ear ossicles, abnormalities; Hearing loss, bilateral

Case report

The proband, a white female, is the first child of non-consanguineous, phenotypically normal parents. She was born at 41 weeks of gestation following an uneventful pregnancy but at 17 months she required paediatric assessment for failure to thrive, mild developmental delay, hypotonia and congenital ligamentous laxity. No specific syndrome was recognized at this stage.

At three years of age she underwent ENT assessment at another hospital because of concerns about her hearing. Distraction testing suggested a bilateral moderate hearing loss. She was noted to have bilateral preauricular sinuses, a right grade 1 microtia and a 'mild' right lower motor neurone facial weakness, which had apparently been present since birth. Bilateral otitis media with effusion was also noted and she went on to have bilateral grommets inserted.

Almost immediately both ears began to discharge, with loss of ventilation tubes and development of active chronic otitis media. The left ear eventually dried up and the perforation healed, but on the right side the perforation persisted, with associated offensive discharge.

By the age of eight years her care had been transferred to Great Ormond Street Hospital for Children. Her bilateral hearing loss had been identified as mainly conductive, with an associated mild high frequency sensorineural loss and she was prescribed bilateral air conduction hearing aids. Her right ear continued to be active most of the time, so she was admitted for a middle ear exploration. A post-auricular approach was used and almost immediately a cholesteatoma was identified which seemed to be in continuity with a fistula in the retro-auricular skin crease. The sac extended from the anterior attic, posteriorly over a dehiscent facial nerve. The ossicles were all abnormal, with a fused malleus and incus and a dysplastic but mobile stapes. In view of the findings a radical mastoidectomy was performed with no attempt at reconstruction at this stage. Facial nerve function, post-operatively, was unchanged. The cavity healed well, although the meatus became rather stenosed and required a revision and use of a stent for a number of months.

In view of the findings a computed tomography (CT) scan was organized which did not show any other cholesteatomatous masses within the right temporal bone. The scan did show, however, a soft tissue mass in the antrum of the left temporal bone, consistent with a congenital cholesteatoma (Figure 1). In addition the left malleus and incus were fused and both middle-ear cavities

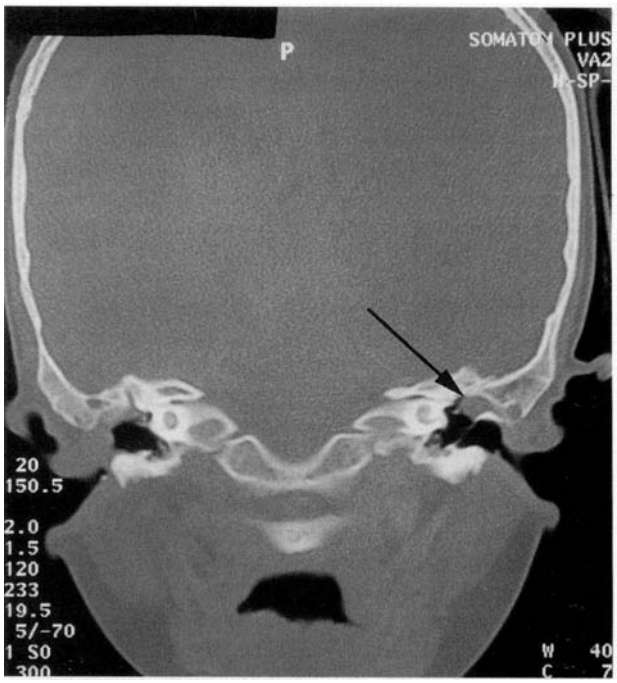

FIG. 1
CT scan showing a soft tissue mass (arrow) in the left antrum, consistent with a congenital cholesteatoma.

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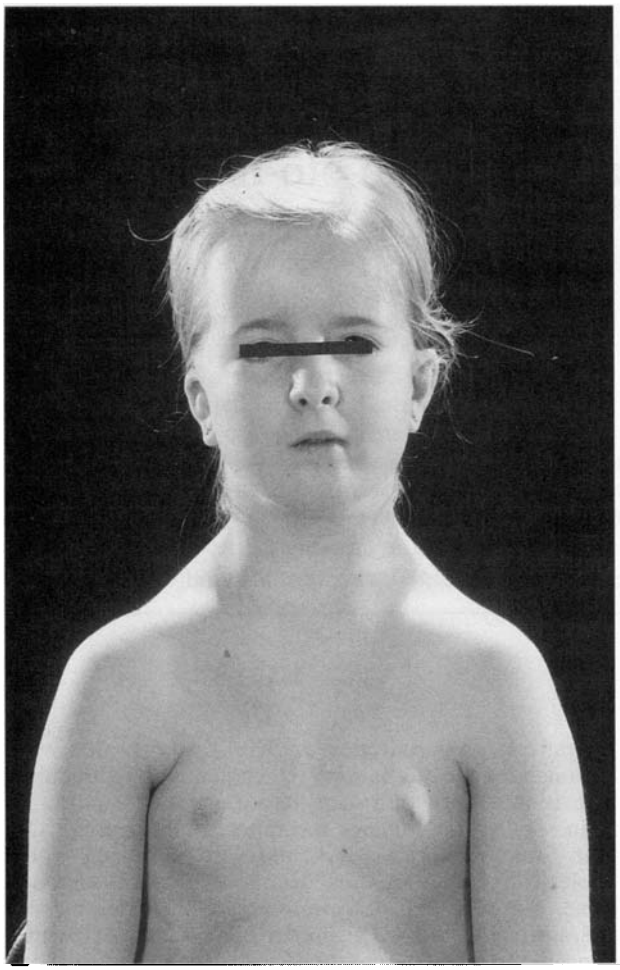

FIG. 2
Patient exhibits mild dysmorphism, right microtia, short neck and sloping shoulders.

were deformed with some bony obliteration of the attic and antrum. The cochleae were small with a reduced number of turns and both lateral semicircular canals were hypoplastic and pointing superiorly. Since the left ear was, subjectively, the better hearing ear and the disease was inactive, a decision was made not to operate on that side.

At this stage the Professor of Genetics, at Great Ormond Street Hospital for Children, undertook a detailed review of the case. In addition to the findings previously described the child was found to be mildly dysmorphic with a high arched palate and left lacrimal pit. The neck was short with sloping shoulders (Figure 2) and there was limitation of shoulder abduction.

This association of facial, neck and ear findings pointed towards a diagnosis of oto-facio-cervical syndrome, but because of the marked overlap between this syndrome and branchio-oto-renal syndrome, renal investigations were performed. Intravenous urography showed a right-sided bifid pelvis and a small left kidney. Blood biochemistry was within normal limits but DMSA scans showed 45 per cent uptake on the left and 55 per cent uptake on the right, indicating some degree of renal impairment. This helped to establish the diagnosis of branchio-oto-renal syndrome.

The child is now 11 years old and continues to manage well with bilateral aids. She attends a mainstream school but has input from a teacher for the deaf. The left ear has remained inactive and a recent follow-up CT scan has not showed any change in the radiological appearance.

Discussion

Branchio-oto-renal syndrome is a rare (1 in 40 000) autosomal dominant condition (Fraser *et al.*, 1980) with near 100 per cent gene penetrance but variable expressivity (Chen *et al.*, 1995). It is a disorder of the renal tract and first and second branchial arches and is characterized by hearing impairment (73 per cent); preauricular pits (70 per cent); renal abnormalities (67 per cent); branchial cleft fistulae/sinuses (60 per cent) and pinna abnormalities (37 per cent) (Cremers and Fikkers-Van Noord, 1980; Chen *et al.*, 1995). The hearing impairment may be conductive (30 per cent), sensorineural (20 per cent) or mixed (50 per cent) (Gorlin *et al.*, 1990), and Fraser *et al.* (1980) found that the incidence and severity of the loss increased as the number of branchial cleft anomalies increased. Of note, no evidence of branchial cleft fistula was found in our case. Other less common anomalies have been reported, including pre-auricular tags; lacrimal duct obstruction/stenosis; facial nerve palsy; palatoschisis and meatal atresia. Shoulder abnormalities and joint laxity have been reported on only one other occasion and demonstrate the significant overlap between branchio-oto-renal syndrome and oto-cervico-facial syndrome.

Temporal bone abnormalities are found in a high proportion of those patients undergoing CT scanning. The most common outer ear anomalies are stenosis and atresia of the external auditory canal (Chen *et al.*, 1995). Middle ear anomalies include fusion of the ossicles; absence of the long process of the incus; absence of the stapes superstructure; congenital fixation of the stapes foot plate and malformation of the middle ear cavity (Smith *et al.*, 1984). Several types of inner ear pathology are also described including cochlear hypoplasia (four-fifths of normal size with only two turns); enlargement of the vestibular aqueduct and dysplasia of the semi-circular canals (Fitch *et al.*, 1976).

The connection between renal and inner ear development is poorly understood, but there is evidence for a shared antigen between glomeruli and the stria vascularis (Quick *et al.*, 1973; Arnold *et al.*, 1976). Dysmorphogenesis of the external or middle ear is caused, by aberrant differentiation of the first and second branchial arches and it is thought that the pathogenesis of congenital cholesteatomas, associated with ossicular abnormalities, is also due to this developmental abnormality (Suetake *et al.*, 1991). However an association between branchio-oto-renal syndrome and congenital cholesteatoma has never been documented. Three other cases of bilateral congenital cholesteatoma associated with ossicular chain abnormalities have been reported in the world literature, but none of these were associated with a syndrome (Peron and Schuknecht, 1975; Wang *et al.*, 1984; Suetake *et al.*, 1991).

In summary, branchio-oto-renal syndrome is a rare autosomal dominant condition with high penetrance but variable expression. Hearing loss is common and clinicians should be aware of this newly documented association with congenital cholesteatoma. If there is otoscopic suspicion of cholesteatoma behind an intact tympanic membrane, active chronic otitis media or unexplained conductive hearing loss then CT scanning of the temporal bones should be considered.

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