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Case report

Labyrinthine involvement in Langerhans' cell histiocytosis

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Abstract

Background: Langerhans' cell histiocytosis, a rare condition caused by the proliferation of abnormal Langerhans' cells ('LCH cells') and an accompanying granulomatous infiltrate, can affect several organs including the ear. External and middle ear involvement are common with a reported incidence as high as 61%. The bony labyrinth is resistant to erosion by the granulation tissue, thereby protecting the cochlea and vestibular structures. Probably for this reason, involvement of the inner ear is rare, with few case reports in the literature. *Patients*: We report two girls, one with bilateral and the other with unilateral mastoid involvement, in whom there was invasion of the labyrinth. The first girl had 'single system' LCH affecting only bone and developed an acute hearing loss due to invasion of the cochlea, while the second had both bone and skin involvement and labyrinthine involvement was diagnosed on imaging prior to the onset of labyrinthine symptoms. *Conclusion*: Inner ear involvement can lead to permanent deafness, which may be prevented by early institution of treatment. Threatened inner ear involvement requires urgent systemic medical therapy with steroids, possibly combined with chemotherapy.

Keywords: Langerhans' cell histiocytosis; Inner ear; Sensorineural hearing loss; Labyrinth; Cochlea; Semi-circular canals

1. Introduction

Langerhans' cell histiocytosis is a rare disorder of unknown cause associated with proliferation of

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pathological Langerhans cells ('LCH cells') leading to infiltration of one or more organs/organ systems [1]. In 1953, Lichtenstein coined the term Histiocytosis X, to cover the group of conditions previously termed Hand–Schüller–Christian disease, lipoid granulomatosis, Abt–Letterer–Siwe disease and eosinophilic granuloma. Since 1987, the 'LCH cell' has been recognised as the sine qua non of the disease and the description Langerhans' cell histiocytosis (LCH) has been widely accepted and used [2]. As well as 'LCH cells', the LCH lesions contain neutrophils, lymphocytes, 'ordinary' phagocytic histiocytes and eosinophils, together forming a 'granulomatous' infiltrate.

Involvement of the ears is relatively common in patients with LCH, the reported incidence ranging from 15 to 61% [3–9]. This variation probably reflects the use of different diagnostic criteria and the different specialities reporting the problem, with resultant selection bias. The most common symptoms are aural discharge, swelling behind the ear due to mastoid involvement and conductive hearing loss due to middle ear involvement. Sensorineural defects, sometimes associated with vertigo, are rarer.

There are only a few reports of involvement of the inner ear by LCH [3,6,10–13]. The dense bone of the otic capsule appears to be particularly resistant to destruction by granulomatous tissue and is often intact even when there is gross destruction of the surrounding temporal bone. The cochlea and semi-circular canals are often spared and the granulomas tend to spread around them, rather than invading directly. It has been suggested that the hearing loss and associated disturbance of balance may sometimes be due to interference with the blood flow, secondary to pressure from granulation tissue, rather than to actual involvement of vestibular structures.

Between 1965 and 1998, a total of 275 patients with LCH have been seen at Great Ormond Street Hospital for Children. Of the 58 patients (21%) with ear involvement, 18 patients had documented evidence of mastoid disease, but we have identified only one child ($<0.5\%$, Case 1) with involvement of the inner ear. The other child (Case 2) was referred to us for an opinion.

2. Case 1

This young girl first presented to an otolaryngologist at the age of 2.5 years with a 4-month history of discharge from the right ear, with swelling just above the pinna. She was noted to have a swelling arising from the roof of the external auditory canal, completely occluding the meatus. Granulation tissue and pus were present. The left ear was also involved, but to a lesser extent. Initial meatal biopsies were reported as showing non-specific inflammation. She was commenced on steroid and antibiotic ear drops and there was some improvement. Swelling then recurred in both ears with occlusion of the right meatus. A right post-aural exploration revealed a defect in the mastoid bone, just above the canal, filled with granulation tissue. Histopathology confirmed the diagnosis of LCH—the sections from the mastoid showed sheets of large cells with cleft nuclei, admixed with eosinophils. Immunocytochemistry demonstrated S100 positivity indicating 'LCH' cells.

A computed tomography (CT) scan revealed bilateral petrous bone destruction, with soft tissue masses extending into both external auditory meatuses. The middle ear cavities contained soft tissue. Part of the ossicular chain could be identified on the left, but appeared to be disrupted on the right. The lateral part of the vestibular labyrinth was demineralised on both sides, but the cochleas and internal auditory meatuses appeared to be intact. There was destruction of the upper part of the mastoid on both sides and of the squamous temporal bone on the right. The tegmen was breached bilaterally and the masses were encroaching on the floor of the middle cranial fossa, especially on the right. There was no obvious extension through the dura mater.

Further investigations showed no evidence of disease elsewhere, i.e. the child had 'single system' skeletal LCH confined to both temporal bones. In an attempt to avoid systemic therapy, she was treated with intralesional steroid injections into both mastoids, following clearance of both ears by microsuction. There was clinical improvement, but an occasional scanty aural discharge persisted. The procedure was repeated a few weeks later with dramatic improvement.

She remained well and asymptomatic for about 9 months, but then developed some discharge from the left ear. It was also felt that her hearing was impaired. Tympanograms were flat suggesting the presence of bilateral middle ear effusions and she underwent bilateral grommet insertion and further steroid injection into the left mastoid. A short-lived improvement in hearing was followed by rapid progression of hearing loss, accompanied by severe behavioural disturbance with grinding of teeth, lack of concentration and temper tantrums. Pure tone audiometry indicated a severe degree of mixed hearing loss in the right ear. Unmasked thresholds of around 110dB on the left were interpreted as a 'shadow' threshold from the right ear, indicating profound loss on the left.

A repeat CT scan showed bone destruction in both petrous bones encroaching on the left cochlea and both left and right semi-circular canals (Fig. 1). A magnetic resonance imaging (MRI) scan of the brain was performed as there was some concern that she was drinking excessively. There was no evidence of thickening of the stalk of the pituitary and, in the T1 weighted sequences, the posterior pituitary 'bright spot', which probably represents Vasopressin production, was present. The urinary osmolality was also within normal limits.

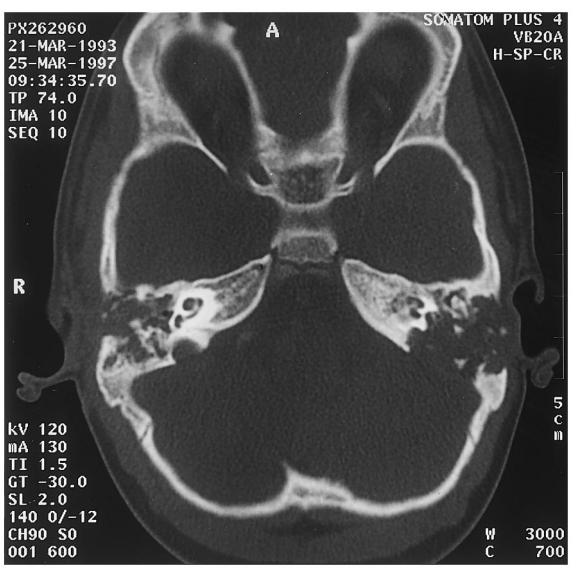

Fig. 1. Transverse CT scan with bone windows. Bilateral destruction of the petrous temporal bones with opacification of both middle ear cavities and the external auditory canal on the left.

The MRI scan also showed extensive soft tissue abnormality adjacent to the mastoid portions of both temporal bones.

She was commenced on oral steroids (prednisolone, 2 mg/kg/day) and had bilateral hearing aids fitted. She showed a rapid improvement, both in her hearing and behaviour and went back to being the happy, friendly child she had been before this episode. Masked auditory brain stem evoked responses, using clicks, showed a threshold of 100dB in the left ear. Regular, fortnightly audiograms showed a steady improvement in her hearing in the right ear, which stabilised after 12 weeks, with a mild to moderate, predominantly sensorineural hearing loss on the right, but a profound hearing loss on the left. The air–bone gap in the right ear had reduced markedly (Fig. 2). The steroid dose was subsequently weaned gradually, to a low dose, alternate day regime without any deterioration, as monitored by continued serial audiometry. A CT scan showed evidence of healing of the petrous bone, but there was still some persistent soft tissue in the mastoid region. After 6 months, she is well, off steroids, with improved hearing in the right ear and remineralisation of the bone of the otic capsule on CT scan.

3. Case 2

This girl presented at the age of 2 years with a history of a seborrheic rash on her scalp and behind the ears and nappy region with inguinal lymphadenopathy. In addition, she was lethargic and failed to thrive. Inguinal lymph node biopsy showed an infiltrate of large histiocytic cells with grooved and cleft nuclei and eosinophilic cytoplasm. Immunohistochemistry showed strong positive staining with antisera to S100 protein. Full staging showed no evidence of other organ involvement, or of diabetes insipidus. She was treated with a 3-day pulse of methyl prednisolone and a 6-month course of weekly vinblastine with great improvement.

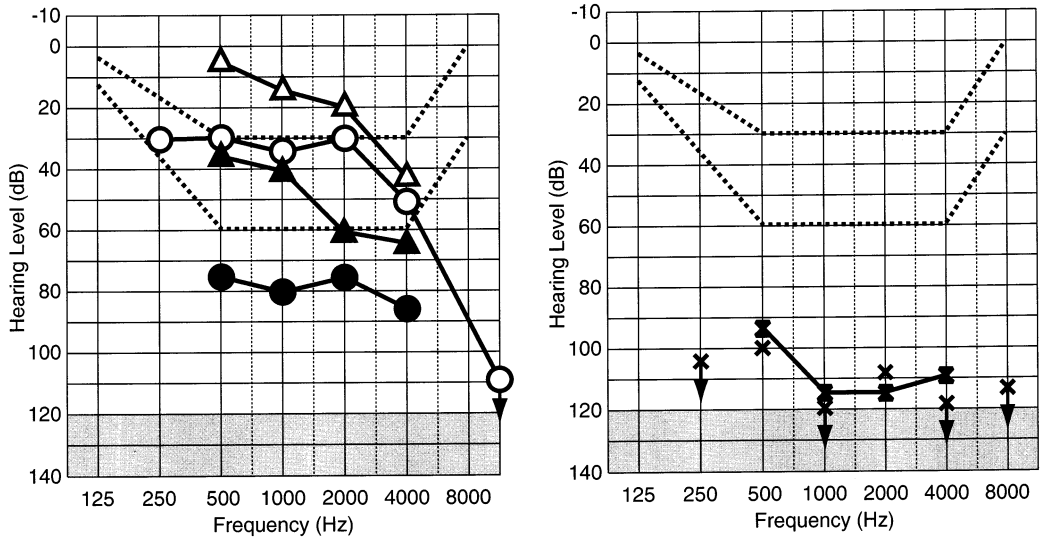

Fig. 2. Pure tone audiometry. Right ear: ▲, unmasked bone conduction—initial; •, air conduction—initial; △, unmasked bone conduction—4 months later; ○, air conduction—4 months later. Left ear: ×, masked air conduction—initial; ▼, masked air conduction—4 months later. There is improvement in the hearing in the right ear in both air and bone conduction with narrowing of the air–bone gap. There is no change in the left ear, with a profound hearing loss.

A recurrence of the weeping rash behind the ears was managed successfully with topical 20% aqueous mustine [14].

Eight months after diagnosis, she developed polyuria and polydipsia. A diagnosis of diabetes insipidus was made and DDAVP replacement was commenced.

One month later she developed a chronic discharging left ear with earache and was found to have a polyp in the left ear canal, which was removed under general anaesthesia. Histopathology of the polyp showed an infiltrate of pleomorphic histiocytic cells, with Birbeck granules identified on an electron microscope, confirming the diagnosis of LCH. A CT scan of the petrous bones showed a large lytic lesion of the left mastoid eroding the tegmen and the lateral semi-circular canal. The right petrous bone was normal (Fig. 3). A MRI scan of the head showed a large enhancing lesion of the left mastoid, invading the labyrinth (Fig. 4).

A left mastoid exploration was carried out via a post-auricular incision. The posterior canal wall was destroyed and the mastoid was filled with granulation tissue. The bone overlying the sigmoid venous sinus and the posterior fossa had been eroded and there were visible granulations, adherent to the dura. The disease had also eroded

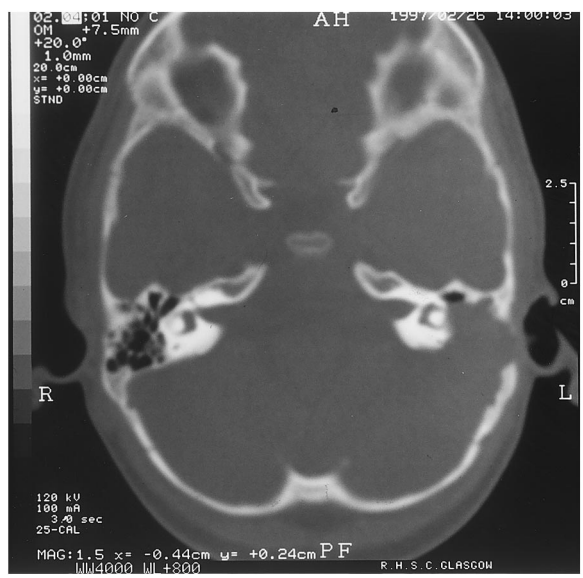

Fig. 3. Transverse CT scan with bone windows. Lytic lesion in the left petrous temporal bone with extension into the lateral semi-circular canal.

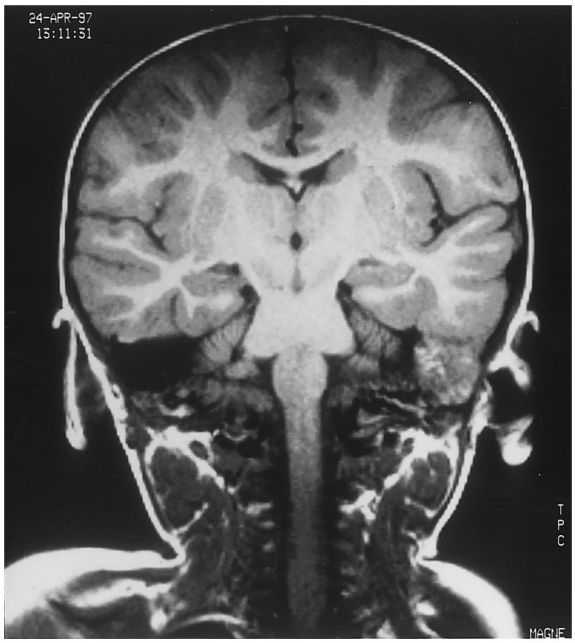

Fig. 4. Coronal T1 weighted MRI scan. Abnormal soft tissue in the left mastoid region.

the lateral semi-circular canal with formation of a fistula. The granulation tissue was cleared and the fistula in the semi-circular canal was capped. Postoperatively she recovered well with no evidence of facial nerve involvement. On distraction testing, her hearing was normal bilaterally and she had no ataxia or nystagmus. She is currently well, 6 months after surgery, and the LCH is inactive.

4. Discussion

Involvement of the ear by histiocytosis is relatively common. The original patients described by Schüller [15] and Letterer [16] had clinical evidence of ear involvement and the first report of otologic manifestations by 'histiocytosis X' by Lederer et al. appeared in 1935 [17]. Since then, there have been several reviews of aural involvement, its incidence ranging from 15 to 61% [3–5,7–9,18]. LCH involving the skin of the auricle and meatus leads to otitis externa. Middle ear disease can cause otitis media, destruction of the ossicles and mastoiditis. Inner ear involvement, however, is rare and is mentioned only in a few individual case reports [3,10–13].

Although temporal bone involvement by LCH is often reported, its frequency may be underestimated because it is overlooked in patients with multisystem LCH who are ill and have several other systemic manifestations. As they expand, these lesions may erode the posterior bony canal wall, the mastoid cortex, the tegmen and sigmoid sinus plate and, albeit rarely, invade the labyrinth.

In 1968, Lopez-Rios et al. [13] reported the autopsy findings in a 23-month-old baby with multisystem involvement by 'histiocytosis'. These authors noted severe destruction of the otic capsule involving the semi-circular canals, but the membranous labyrinth was well preserved. Histiocytes were identified within the perilymphatic and endolymphatic fluids of the cochlea. In 1970, Cohn et al. [10] reported a 6-year-old boy with 'histiocytosis X' who developed vertigo. X-rays showed extensive, bilateral temporal bone destruction. He later died of multisystem disease with central nervous system infiltration. The entire temporal bone was examined post-mortem; there was extensive bone destruction, and, except for part of the shell of the cochlea, the bone surrounding the inner ear was destroyed. The vestibular labyrinth was replaced by granulomatous tissue and the cochlea was directly invaded. There was evidence of labyrinthitis ossificans and hydrops of the coils of the cochlea. The invading mass had areas of dense fibrous tissue and scattered islands of large histiocytes with a foamy cytoplasm. Collections of eosinophils were not noted.

In 1979, McCaffrey and McDonald [3] reported the findings in 22 patients with ear involvement. Two had unilateral sensorineural hearing loss with erosion of the bony labyrinth, and in one, it was accompanied by vertigo. In 1989, Cunningham et al. [6] reviewed 62 children with both single system and multisystem LCH, 18 of whom had ear involvement. One patient had sensorineural hearing loss, vertigo and nystagmus due to inner ear involvement. In 1993, Goldsmith et al. [12] reported an 8-year-old girl with unifocal LCH of the petrous apex, who developed sensorineural hearing loss due to destruction of the labyrinth,

with bony erosion extending to involve the region of the cochlea.

5. Conclusions

Invasion of the labyrinth, therefore, appears to be rare but should be suspected in any child with LCH who has sensorineural hearing loss, nystagmus, vertigo or behavioural change. Children with severe mastoid involvement should be imaged to identify or exclude inner ear involvement before symptoms appear. CT scanning with fine cuts through the mastoid region provides a detailed view of the anatomy of the inner ear and the labyrinthine structures and MRI scans are helpful in elucidating the extent of associated soft tissue changes. Early treatment may prevent permanent damage and reduce the long-term morbidity due to deafness.

The main role of surgery in patients with ear involvement is (a) for performing diagnostic biopsy, and (b) to gain access for intralesional steroid injection. Occasionally, debridement may be required to relieve pain and inflammation. Temporal bone surgery for LCH carries a high risk of complications and should be avoided if possible, and undertaken in a highly conservative fashion if considered unavoidable, as in Case 2 [4]. The surgeon should be aware of the possibility of creating a fistula into the labyrinth and of damaging the facial nerve.

Alternatives for systemic therapy include corticosteroids alone, or combined with chemotherapy according to one of the schedules recommended by the Trials Committee of the Histiocyte Society. Vinblastine, etoposide, methotrexate and 6-mercaptopurine are the most effective agents. Both because of the rare, but treatable, manifestations of this complex disease, and the favourable overall prognosis, all patients with ear involvement by LCH should be managed jointly by paediatric oncologists and otolaryngologists.

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