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Langerhans' cell histiocytosis - A rare cause of sudden onset unilateral sensorineural hearing loss

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Abstract
Langerhans' cell histiocytosis is a rare disorder of unknown aetiology in which pathological Langerhans' cells accumulate and destroy local tissue. We report a 38-year-old female who presented with a sudden onset of left sensorineural hearing loss. Magnetic resonance imaging (MRI) revealed a contrast-enhancing lesion in the left mastoid and a second lesion in the hypothalamus. Following left mastoid exploration and biopsy a definitive diagnosis of Langerhans' cell histiocytosis was made and the patient was treated with external beam radiotherapy. Subsequent right femur and right mastoid involvement were successfully treated with steroids and cytotoxic chemotherapy. At one year follow-up the patient had residual left-sided sensorineural hearing loss with normal hearing in the right ear. To our knowledge, Langerhans' cell histiocytosis has not been previously reported as a cause of unilateral sudden onset sensorineural hearing loss. It should be considered in the differential diagnosis of this condition.

Key words: Hearing loss, sensorineural; Histiocytosis, Langerhans' cell

Introduction

Patients with unilateral hearing loss are frequently seen in otolaryngology departments. The causes of sensorineural hearing loss include trauma, infection, metabolic conditions and cerebello-pontine angle lesions (Brookhouser, 1996). It is important to exclude an acoustic neuroma and for this purpose the use of MRI is becoming increasingly widespread (Sheppard *et al.*, 1996).

Langerhans' cell histiocytosis (LCH) is a rare disease of unknown aetiology in which the accumulation of pathological Langerhans' cells leads to local tissue destruction. Langerhans' cells are normally found in the skin. When foreign antigens are encountered they move to the local lymph nodes and present these foreign antigens to T helper cells thus initiating an immune response. Pathological Langerhans' cells are distributed far more widely (Chu and Jaffe, 1994) and produce a greater range of cytokines (Kannourakis and Abbas, 1994) than normal Langerhans' cells. Almost any organ in the body can be involved (Broadbent *et al.*, 1994). Single system disease usually involving bone has a clinically benign course although it can lead to permanent disability. Multi-system LCH can involve the skin, the central nervous system (particularly the hypothalamus and pituitary), the bone marrow, lungs, liver and spleen. This is associated with a nine to 18 per cent mortality even with early detection and adequate treatment (McLelland *et al.*, 1990; Gadner *et al.*, 1994).

Sixty-two per cent of cases present with head and neck disease (Irving *et al.*, 1994) giving the Otolaryngologist a key role in establishing the diagnosis. The typical patient encountered is a young male child aged one to three years (Broadbent *et al.*, 1994). Common otological presentations include otorrhoea (from either external auditory meatal skin or temporal bone involvement) and post-auricular swelling from temporal bone involvement (Quraishi *et al.*, 1993). Painful localized swelling over the frontal bone due to an underlying osteolytic lesion, painless cervical lymphadenopathy, or an oral bony swelling arising from the alveolar margin, are less common, but possible presenting features of LCH (Irving *et al.*, 1994).

LCH, can rarely present with hearing problems. We describe a case of LCH presenting with a sudden onset of sensorineural hearing loss, tinnitus and vertigo. We discuss the diagnosis and management of this condition. To our knowledge this is the first case of LCH presenting in this way.

Case report

A 38-year-old female was referred three weeks following a sudden onset of left-sided hearing loss, tinnitus and rotatory vertigo. She had a past medical history of diabetes insipidus. This had been investigated four years earlier with a magnetic resonance image (MRI) of the hypothalamus and pituitary which was reported as normal. Tuning fork tests were consistent with sensorineural hearing loss on the left. The rest of the head, neck and neurological examinations were normal. A pure tone audiogram revealed sensorineural hearing loss averaging 80 dBs across 0.5, 1, 2 and 4 kHz with normal thresholds in the right ear. Full blood count was normal. A computed tomography (CT) scan showed abnormal soft tissue throughout the left petromastoid, sparing the middle-ear cleft. This was associated with bone erosion extending to the posterior part of the lateral semicircular canal but separate from the jugular foramen. MRI scan with

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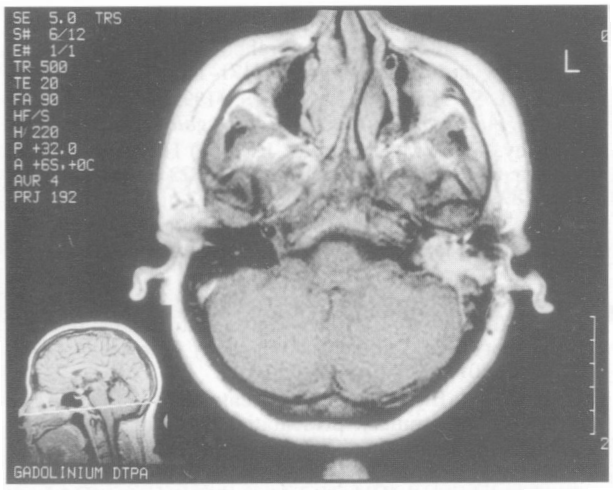

FIG. 1
MRI showing contrast enhancing mass within left mastoid.

gadolinium showed the petromastoid mass to be contrast enhancing (Figure 1). The internal auditory meatus was clear. A second contrast enhancing mass was seen in the hypothalamic/chiasmal region (Figure 2). The patient underwent a left mastoid exploration and biopsy. In addition to typical light microscopy features, pathognomonic intracellular Birbeck granules were identified on electron microscopy confirming a diagnosis of LCH. External beam radiotherapy of 40 Gy over 20 fractions was given to the left mastoid and hypothalamus. There was no change in the hearing thresholds on completion of treatment.

Three months later the patient developed pain around her right knee. An X-ray showed an osteolytic lesion which biopsy confirmed as a recurrence. Contrast-enhancing lesions were still present in the left mastoid and hypothalamus on a repeat scan. Prednisolone followed by vinblastine were given in 12 cycles. The knee pain resolved on completion of the course and minimal enhancement was seen in the left mastoid and hypothalamus on repeat MRI.

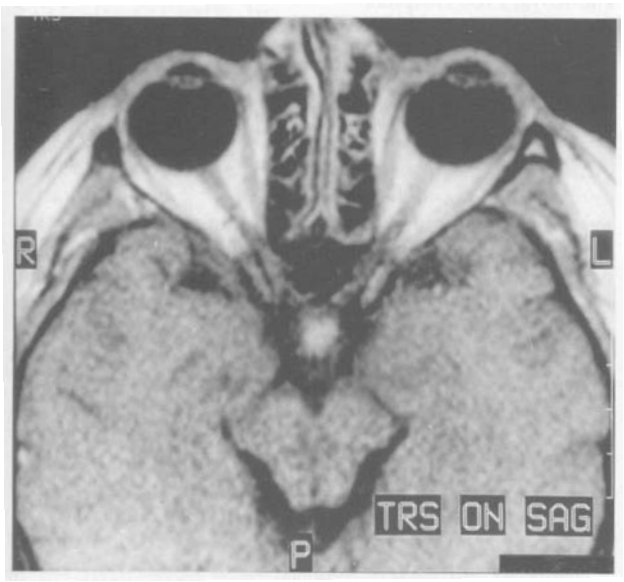

FIG. 2
MRI showing contrast enhancement of the hypothalamus.

Four months later she developed a hearing loss in the right ear. A pure tone audiogram confirmed a 40 dB conductive hearing loss averaged over 0.5, 1, 2 and 4 kHz. MRI showed a new contrast-enhancing mass in the right mastoid and the hypothalamus. Right mastoid exploration and biopsy confirmed LCH. Further prednisolone then cytotoxic chemotherapy of epirubicin, etoposide and isofamide was given in six cycles. After the fourth cycle her hearing returned to normal in the right ear and MRI after the final cycle showed only minimal enhancement at all sites of previous disease.

At one year follow-up, MRI scan of the head showed only minimal enhancement at sites of previous disease. A pure tone audiogram showed a left-sided sensorineural hearing loss of 80 dB across 0.5, 1, 2, and 4 kHz with normal thresholds in the right ear.

Discussion

This case demonstrates that LCH should be considered as a very rare cause of sudden sensorineural hearing loss, tinnitus and vertigo. Similar aural presentations were described in a review of 500 patients carried out by Tos in (1966) who reported four cases presenting with hearing loss (type not specified) and one presenting with vertigo. Eleven patients with otic capsule erosion due to LCH have previously been reported - three adults (Rosenwasser, 1940; Shuknecht and Perlman, 1948), seven children (Chisholm, 1954; Lopez-Ruis and Benitez, 1968; Cohen *et al.*, 1970; Smith and Evans, 1984; Irving *et al.*, 1994; Marion *et al.*, 1995) and two patients whose age was not specified (McCaffrey and McDonald, 1997). Tos (1966) pointed out that as LCH commonly presents in childhood, it is likely that auditory problems are under-reported.

The diagnosis may be suspected if the patient has otological symptoms as part of a multi-system disease. However, the temporal bone can be the only site involved. The diagnosis can be suspected on MRI. The lesions are contrast-enhancing differentiating them from cholesteatoma, and their position differentiates them from metastasis as they do not have a predilection for the petrous apex (Angeli *et al.*, 1996). However, a definitive diagnosis requires fresh tissue for histopathological analysis and this often necessitates a limited mastoidectomy and biopsy. Once the diagnosis is established mastoidectomy has no further role. Irving *et al.* (1994) found mastoidectomy as a treatment for temporal bone LCH to be associated with an unacceptably high morbidity and that it failed to render the disease inactive. Radiotherapy, intralesional steroids and systemic steroids as single agents or in combination have all been shown to be effective treatments for temporal bone disease. Cytotoxic chemotherapy and systemic steroids have been shown to be effective treatments for multisystem disease, as was demonstrated by the complete recovery in hearing in this patient's right ear.

Great progress in the management of LCH has been made in recent years. Strict criteria for classification and diagnosis have been laid down (Writing Group of the Histiocytosis Society, 1987). A 'definitive' diagnosis requires the demonstration of Birbeck granules within cells on electron microscopy, or for specific antigenic determinants (CD1a) on the surface of cells to be demonstrated by immune staining. Only a 'presumptive' diagnosis can be made on light microscopy. The first international prospective randomized controlled trial LCH-1 has been set up (comparing etoposide or vinblastine in newly diagnosed patients less than 18-years-old with multi-system involvement, Ladisch and Gadner, 1994). In addition new treatments such as the use of cytokine agonists (Kannourakis and Abbas, 1994) and monoclonal

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antibodies (Kelly and Pritchard, 1994) are being explored. Finally steps have been taken to determine the aetiology, that will lead the way to rational and systematic treatments. Whilst no evidence for a viral aetiology has been found (McClain and Weiss, 1994), clonality of lesional cells has been demonstrated (Willman *et al.*, 1994; Yu *et al.*, 1994) although the full significance of this is not yet established.

LCH is associated with significant morbidity and mortality. Whilst it is mainly a disease of young children it can occur at any age. Most patients present with head and neck disease making this an important disease to the otolaryngologist. This case demonstrates that the diagnosis should be considered in patients presenting with hearing loss and that once the diagnosis is established effective treatments can be given.

References

Angeli, S. I., Luxford, W. M., Lo, W. M. (1996) Magnetic resonance imaging in the evaluation of Langerhans' cell histiocytosis of the temporal bone: Case report. *Otolaryngology – Head and Neck Surgery* **114:** 120–124.

Broadbent, V., Egeler, R. M., Nesbit, Jr, E. (1994) Langerhans' cell histiocytosis - clinical and epidemiological aspects. *British Journal of Cancer* **70: (Suppl XXIII)** S11–S16.

Brookhouser, P. E. (1996) Sensorineural hearing loss in children. *Pediatric Clinics of North America* **43:** 1195–1216.

Cohn, A. M., Sataloff, J., Lindsay, J. R. (1970) Histiocytosis X (Letter-Swiwe Disease) with involvement of the inner ear. *Archives of Otolaryngology* **91:** 24–29.

Chisolm, J. J. (1954) Otorhinologic aspects of Hand-Schuller-Christian disease. *Laryngoscope* **64:** 486–496.

Chu, T., Jaffe, R. (1994) The normal Langerhans' cell and the LCH cell. *British Journal of Cancer* **70: (Suppl. XXIII)** S4–S10.

Gadner, H., Heitger, A., Grois, N., Gatterson-Menz, I., Ladisch, S. (1994) A treatment strategy for disseminated Langerhans cell histiocytosis. *Medical and Pediatric Oncology* **23:** 72–80.

Irving, R. M., Broadbent, V., Jones, N. S. (1994) Langerhans' cells histiocytosis in childhood: management of head and neck manifestations. *Laryngoscope* **104:** 64–70.

Kannourakis, G., Abbas, A. (1994) Monoclonal antibody therapy in Langerhans' cell histiocytosis – feasible and reasonable. *British Journal of Cancer* **70: (Suppl. XXIII)** S37–S40.

Kelly, K. M., Pritchard, J. (1994) Monoclonal antibody therapy in Langerhans' cell histiocytosis – feasible and reasonable? *British Journal of Cancer* **70: (Suppl. XXIII)** S54–S55.

Ladisch, S., Gadner, H. (1994) Treatment of Langerhans' cell histiocytosis – evolution and current approaches. *British Journal of Cancer* **70: (Suppl. XXIII)** S41–S46.

Lopez-Rois, G., Benitez, J. T. (1968) Histiocytosis; Histopathological study of the temporal bone. *Annals of Otology, Rhinology and Laryngology* **77:** 1171–1180.

Marion, M. S., Hinojosa, R., Libi, S. (1995) Histopathology update. *American Journal of Otolaryngology* **16:** 194–195.

McCaffrey, T. V., McDonald, T. J. (1979) Histiocytosis X of the ear and temporal bone: review of 22 cases. *Laryngoscope* **89:** 1735–1742.

McClain, K., Weiss, R. A. (1994) Viruses and Langerhans' cell histiocytosis: Is there a link? *British Journal of Cancer* **70:** S34–S36.

McClelland, J., Broadbent, V., Yeomans, E., Malone, M., Pritchard, J. (1990) Langerhans' cell histiocytosis; the case for conservative treatment. *Archives of Diseases in Childhood* **65:** 301–303.

Qurashi, M. S., Blayney, A. W., Breatnach, F. (1993) Aural symptoms as primary presentation of Langerhans' cell histiocytosis. *Clinical Otolaryngology* **18:** 317–323.

Rosenwasser, H. (1940) Lipoid granulomatosis (Hand-Schuller-Christian disease involving the middle ear and temporal bone. *Archives of Otolaryngology* **32:** 1045–1053.

Schuknecht, H. F., Perlman, H. B. (1948) Hand-Schuller-Christian disease and eosinophilic granuloma of the skull. *Annals of Otology, Rhinology and Laryngology* **57:** 643–674.

Sheppard, I. J., Milford, C. A. M., Anslow, P. (1996) MRI in the detection of acoustic neuromas – a suggested protocol for screening. *Clinical Otolaryngology* **21:** 301–304.

Smith, R. J. H., Evans, J. N. G. (1984) Head and neck manifestations of histiocytosis-X. *Laryngoscope* **94:** 395–399.

The Writing Group of the Histiocytosis Society (Chu, T., D'Angio, G. J., Favara, B., Ladisch, S., Nesbit, M., Pritchard, J.) (1987) Histiocytosis in children. *Lancet* **1:** 208–209.

Tos, M. (1966) A survey of Hand-Schuller-Christian's disease in otolaryngology. *Acta Oto-Laryngologica* **62:** 217–228.

Willman, C. L., Busque, L., Griffiths, B. B., Favara, B. E., McClain, K. L., Duncan, M. H., Gilliland, D. G. (1994) Langerhans cell histiocytosis – a clonal proliferative disease. *New England Journal of Medicine* **331:** 154–160.

Yu, R., Chu, C. E., Burwela, L., Chu, A. C. (1994) Langerhans' cell histiocytosis: a clonal proliferation of Langerhans' cells. *Lancet* **343:** 767–768.

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