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Clinical Record

Cerebrospinal fluid otorrhoea: a rare presentation of Langerhans' cell histiocytosis of the temporal bone

J-P Vezina, N Audet, G Fradet

Abstract

Objective: To report a case of Langerhans cell histiocytosis of the temporal bone presenting with cerebrospinal fluid fistula.

Patient: A Caucasian woman presented to a tertiary care centre in Quebec, Canada, with a new onset of cerebrospinal fluid fistula. She had a significant destructive lesion of the temporal bone, and was diagnosed with Langerhans cell histiocytosis on biopsy.

Interventions: The patient underwent surgical resection with reconstruction of the posterior fossa and tegmen. She suffered a relapse less than one year after surgery, and was finally treated with chemotherapy.

Main outcome and results: The patient was free of disease at three-year follow up. No recurrence of the cerebrospinal fluid leak was observed after treatment.

Conclusion: Langerhans cell histiocytosis of the temporal bone with intra-cranial involvement is rare in adults, with only two cases previously reported. Eleven paediatric cases have been reported. To our knowledge, this patient represents the first report of cerebrospinal fluid fistula as the initial presentation of the disease.

Key words: Temporal Bone; Histiocytosis; Langerhans Cell; Cerebrospinal Fluid Otorrhea

Introduction

Langerhans cell histiocytosis is a spectrum of diseases defined by the infiltration of pathological Langerhans cells.[1] The clinical pattern may encompass localised forms, termed 'eosinophilic granulomas', and multi-system forms, including Hand–Schüller–Christian disease and Letterer–Siwe disease. Skull lesions are frequent, and otological manifestations occur in 15 to 61 per cent of cases.[2–4] Few cases of intra-cranial extension secondary to temporal bone erosion have been reported. Furthermore, the disease has never been reported to violate the dura.[5]

We report the first case of Langerhans cell histiocytosis of the temporal bone presenting with cerebrospinal fluid (CSF) fistula, and we review the relevant literature.

Case report

A 38-year-old Caucasian woman presented to the otolaryngologists with left otitis media with effusion.

A ventilation tube was installed, resulting in drainage of abundant clear fluid and the onset of vertigo; thus, a CSF fistula was diagnosed.

Computed tomography (CT) and magnetic resonance imaging (MRI) scans showed a significant destructive bone lesion involving the left posterior external auditory canal, middle and posterior cranial fossa, and lateral semicircular canal (Figures 1 and 2). The audiogram was normal. The differential diagnosis at that time included Langerhans cell histiocytosis, fibrous dysplasia, skull base malformation and endolymphatic sac carcinoma.

Surgical biopsies were taken via a mastoidectomy approach. Histological analysis revealed an eosinophil-rich cellular proliferation, and immunohistochemical staining was positive for cluster of differentiation 1a glycoprotein and S-100 protein (Figure 3). This confirmed the diagnosis of Langerhans cell histiocytosis.

The patient was recalled to the operating theatre. The resection was completed, and the posterior fossa and tegmen were reconstructed with a titanium plate. The mastoid cavity was obliterated with temporalis fascia and abdominal fat in a watertight fashion.

During the initial investigation, panoramic dental radiography of the mandible had shown bone rarefaction in the left parasymphyseal area. This lesion was confirmed with bone scintigraphy, and the patient underwent curettage.

During the following years, the disease recurred in the patient's left mastoid and mandible, and new lesions appeared in the maxilla and lung. The patient later developed severe hearing loss on the affected side. She was treated with vinblastine.

Three years after surgery, follow-up MRI scanning showed no disease, and the patient had suffered no recurrence of her CSF leak.

Discussion

Lichtenstein and Jaffe introduced the term eosinophilic granuloma in 1940.[6] In 1953, Lichtenstein linked this disease with Hand–Schüller–Christian disease and Letterer–Siwe disease, and proposed to combine these three

From the Department of Otolaryngology and Maxillofacial Surgery, Centre Hospitalier Affilie Universitaire de Quebec, Laval University, Quebec, Canada.
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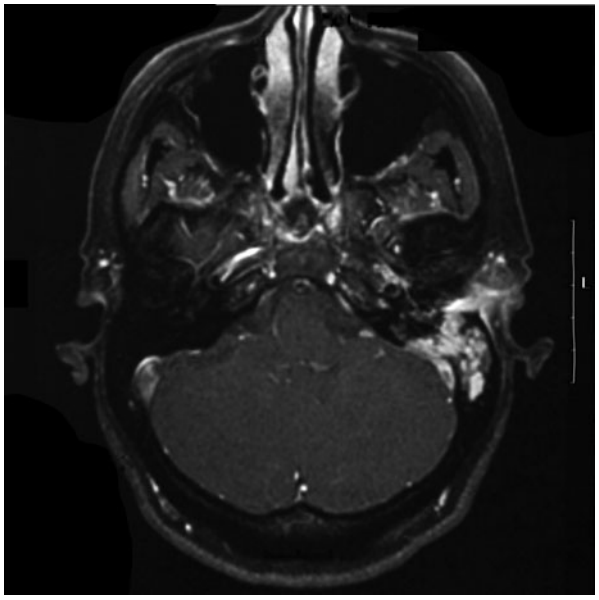

FIG. 1

Axial, fat suppression, T1-weighted magnetic resonance imaging scan with gadolinium contrast, showing an enhancing lesion in the left mastoid. Note the involvement of the dura and sigmoid sinus. L = left

entities under the name 'histiocytosis X', on the basis of their similar histopathological findings.[7] In 1973, Nezelof described a cytoplasmic structure visible on electron microscopy in all cases of histiocytosis X, which he termed an 'X-body'.[8] He also noted that these bodies were similar to those described by Birbeck in Langerhans cells. He proposed that histiocytosis X was in fact a proliferation of Langerhans cells, and that the term should be changed to 'Langerhans cell histiocytosis'. This

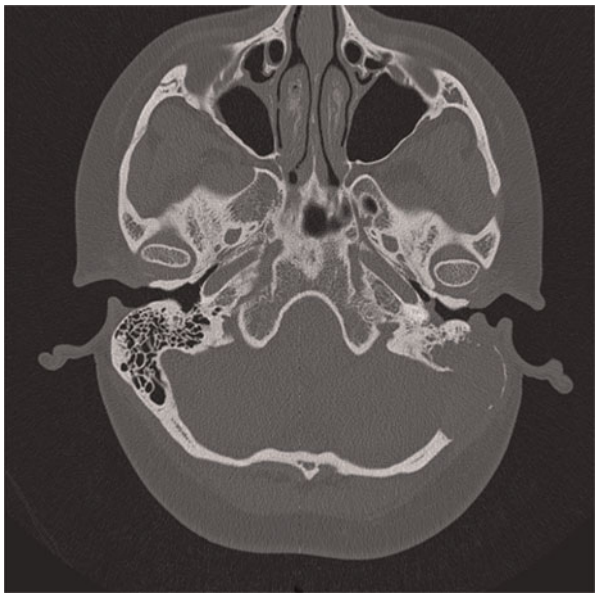

FIG. 2

Axial computed tomography scan of mastoid, showing destruction of the posterior wall of the left external auditory canal and extension to the left sigmoid sinus and anterior cerebellar cisterna.

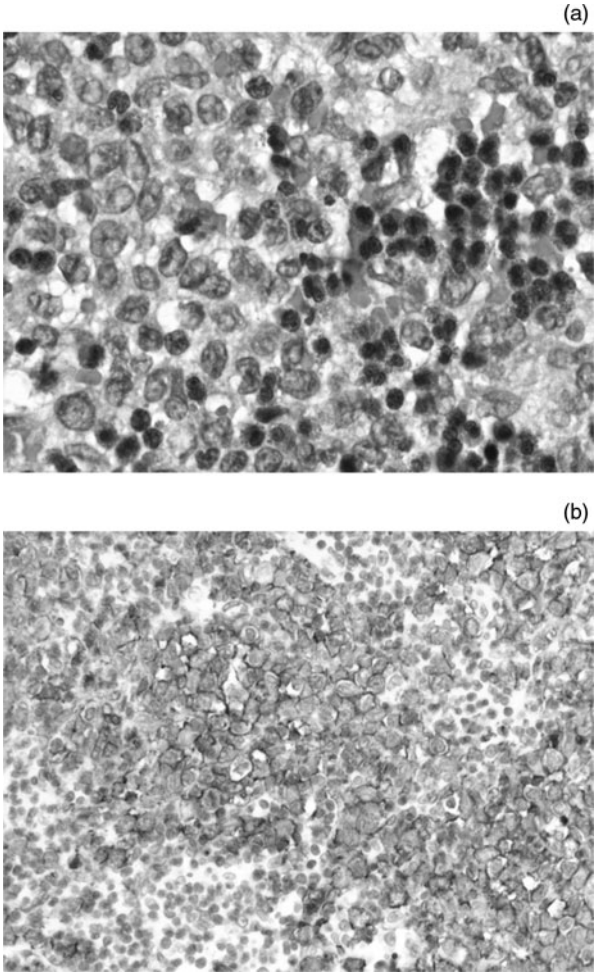

FIG. 3

(a) Photomicrograph of surgical biopsy material, showing eosinophils and histiocytes (H&E; ×400). (b) Immunohistochemical staining showing positivity for cluster of differentiation 1a glycoprotein (×200).

term was officially adopted in 1986 during the Workshop on Childhood Histiocytoses.[9]

Langerhans cell histiocytosis primarily affects children, but can manifest as late as the eighth decade.[1] In the paediatric population, its incidence ranges from 2 to 5 cases per million per year.[10,11] Most cases are diagnosed before the age of 20 years.[3,12] The disease affects Caucasians more than Afro-Caribbeans, and males slightly more than females.[1,2,10,12,13] Langerhans cell histiocytosis is more often seen in flat bones, with the skull, ribs and pelvis being the most frequently involved.[2,11,14,15] Otological involvement occurs in 15 to 61 per cent of cases, and is the first manifestation in up to 25 per cent.[2–4] The otological form seems to be more prevalent in multi-system Langerhans cell histiocytosis.[3] Middle and posterior fossa involvement have been documented in a few cases, but violation of the dura has not previously been reported.[5]

The aetiology of Langerhans cell histiocytosis is unknown. It is still debated whether the proliferation of Langerhans cells is of neoplastic or reactive (e.g. due to viral infection) origin.[16–18] Many classifications have been proposed over the years. With regard to treatment and prognosis, patients are best categorised as having either restricted or extensive disease.[18] Restricted disease consists of monostotic and polyostotic eosinophilic granulomas of the bone or skin. Extensive forms include

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TABLE I

PREVIOUSLY REPORTED CASES OF LANGERHANS CELL HISTIOCYTOSIS WITH INTRA-CRANIAL INVOLVEMENT

Study	Pts (*n*)	Age* (y)	Presenting symptoms	Anatomical site	Treatment
Arcand *et al.*[27]	1	4	Otitis media	Mastoid	Surgery + RT
Brisman *et al.*[14]	1	4	Headache, diplopia	Clivus	Stereotactic RT
Cataltepe *et al.*[28]	1	14	Diplopia	Petrous apex	Surgery + RT
Goldsmith *et al.*[29]	1	8	Facial palsy	Petrous apex	RT
Hadjigeorgi *et al.*[30]	3	6, 5, 2	Deafness, post-auricular swelling	Petrous apex, mastoid	Not stated
Leiberman *et al.*[31]	1	5	Intra-cranial hypertension	Mastoid	Surgery
Miller *et al.*[32]	1	15	Facial numbness	Foramen rotundum	Surgery
Rosenfeld *et al.*[33]	1	12	Diplopia	Clivus	Biopsy only
Sampson *et al.*[34]	1	41	Diplopia	Clivus	Surgery
Krishna *et al.*[35]	1	15	Diplopia	Petrous apex	Surgery + RT
Mihova *et al.*[36]	1	53	Visual disturbance	Anterior fossa	RT + CT

*At diagnosis. Pts = patients; y = years; RT = radiotherapy; CT = chemotherapy

Hand–Schüller–Christian disease and Letterer–Siwe disease. The former is defined by a chronic or subchronic course, with the classic triad of diabetes insipidus, exophthalmos and bone lesion present in only 10 per cent of patients.[2] The latter is an acute or subacute, disseminated form which mostly affects children younger than two years and carries a much poorer prognosis.[2,15]

Temporal bone involvement occurs in up to 63.2 per cent of multi-system Langerhans cell histiocytosis cases.[3] These patients most commonly present with purulent aural discharge.[2–4,12] Post-auricular swelling, vertigo, hearing loss and otalgia are also frequent. Facial palsy is a rare finding (less than 5 per cent).[12] Physical examination shows otitis media or an external auditory canal polyp and granulation tissue. An assessment of cranial nerves, orbits and cerebellar function should be performed in all cases.[19]

Head and neck lesions should first be investigated radiologically.[12] Bone lesions typically show a 'punched-out' appearance, with no reactive sclerosis, although a local periosteal reaction can occur.[20–22] In the mastoid, CT scanning reveals a coalescence of cells with extension to the surrounding structures (bony canal walls, tegmentum and posterior fossa) which can appear similar to cholesteatoma. Soft tissue lesions are best characterised with MRI.

Histopathological findings include eosinophils, T-cells and 'foamy' macrophages on light microscopy.[15,22] Macroscopically, the lesion is often reddish or brown.[22] Immunohistochemical staining includes S-100 protein, cluster of differentiation 1a glycoprotein antigen, peanut lectin, adenosine triphosphatase and α-D-mannosidase.[11,16,17] Electron microscopy shows classic Birbeck granules, although this technique is less often used nowadays.[8] In 1987, the Writing Group of the Histiocyte Society published diagnostic criteria for Langerhans cell histiocytosis. A presumptive diagnosis is warranted when only the light microscopic appearance is consistent with the disease. A 'designated diagnosis' is defined by the presence of positive staining for two or more of the following: adenosine triphosphatase, S-100 protein, α-D-mannosidase or peanut lectin. A definitive diagnosis requires the demonstration of cluster of differentiation 1a glycoprotein antigens or Birbeck granules on electron microscopy.[23]

The treatment of patients with Langerhans cell histiocytosis varies widely according to the extent of the disease. Isolated bony lesions can often be observed, unless there is pain or deformity, because of a high rate of spontaneous remission.[24] Restricted disease can be treated by curettage or intralesional corticosteroids. The latter is less useful in skull lesions. Low dose radiotherapy is also effective and can be combined with surgery.[1,3,5,17,18] Extensive disease requires a systemic approach comprising chemotherapy often combined with corticosteroids. The principal agents used are vinblastine and etoposide.[1,17,24] 2-CdA can be administered in refractory cases.[1]

Factors indicating a poor prognosis include an age of less than two years, multiple organ involvement and organ failure (i.e. liver, lungs and haematopoietic system).[3,4,18,24,25] The patient's initial response to therapy has also proven to be a prognostic factor.[26] Otological involvement seems to predict a poorer outcome. In their series of 251 paediatric Langerhans cell histiocytosis patients, Surico *et al.* found that 93.8 per cent of cases with otological involvement had multi-system disease, and that they also had a younger age at diagnosis.[4]

- **Langerhans cell histiocytosis can present in three different forms: eosinophilic granuloma, Hand–Schüller–Christian disease and Letterer–Siwe disease**
- **Temporal bone involvement occurs in 67 per cent of multi-system forms**
- **Involvement of the middle and posterior fossae is rare, and violation of the dura has not previously been reported**
- **We report a case of Langerhans cell histiocytosis of the temporal bone which presented with cerebrospinal fluid fistula, showing that the disease can penetrate the dura**

Thirteen cases of skull base Langerhans cell histiocytosis with intra-cranial involvement have previously been reported (Table I).[14,27–36] Of those, three had lesions in the mastoid, five in the petrous apex, three in the clivus, one in the floor of the anterior fossa and one near the foramen rotundum. The mean age at diagnosis was 14 years, with only two adults. Visual symptoms (mostly diplopia) were the most frequent complaints at presentation (six of 13 cases); others included intra-cranial hypertension, facial numbness, hearing loss, post-auricular swelling, refractory otitis media and facial palsy. Treatment modalities consisted of radiotherapy alone in two cases, surgery alone in three, combined surgery and radiotherapy in three, biopsy alone in one, and chemoradiotherapy in one. Treatment was not described for three cases.

Conclusion

Langerhans cell histiocytosis of the temporal bone rarely extends intra-cranially. Only 13 cases of skull base Langerhans cell histiocytosis with intra-cranial involvement have previously been reported, with only two involving adult

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patients. Our patient originally presented with violation of the dura and CSF otorrhoea; to our knowledge, such a manifestation of Langerhans cell histiocytosis had not previously been reported. Her fistula was successfully treated by mastoid obliteration, but the disease recurred locally and systemically, requiring chemotherapy for control. Although rare, Langerhans cell histiocytosis should be included in the differential diagnosis of any refractory otological disease.

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Address for correspondence:
Jean-Philippe Vezina,
Department at Laval University
Faculty of Medicine,
Ferdinand-Vandry Pavilion #3222, Laval University,
Québec, G1K 7P4, Canada.

Fax: 418 656 5071
E-mail: jean-philippe.vezina.2@ulaval.ca

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