

A rare case of Langerhans cell histiocytosis of the skull in an adult: a systematic review

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Abstract

We report a 41-year old male who presented to the Emergency Department after falling while water-skiing. He had a previous medical history included chronic headaches, which had persisted for the last 2-3 months prior to presentation. Computed tomography of the head showed a small hypersensitivity with a small extra axial collection with a maximum thickness of 1mm. Differential diagnoses included an arachnoid cyst, haemangioma, meningioma or a secondary lesion. A diagnosis of Langerhans Cell Histiocytosis was made based on the histopathology examination and the immunoperoxidase staining.

Introduction

Langerhans cell histiocytosis (LCH) is a rare condition that usually affects the pediatric population. The condition can affect almost any organ in the body. It is a rare condition with an estimated annual incidence between 1-7 cases per million of the population.¹ More than 50% of patients are less than two-years of age have disseminated LCH with organ dysfunction and die of the disease.² The prevalence of LCH seems to be higher among whites



Figure 1. X-ray showing lesion on skull.

than other races. The incidence of LCH is greater in males than in females, with a male-to-female ratio of 2:1. Recent early data from the U.K. suggest that just as many cases of LCH present in adult life as in childhood.¹ However, it should be noted that at present it remains unclear if these *adult* cases are de novo or if they are occult cases from childhood.³ We report a case of adult LCH with his presentation, medical history, clinical characteristics, and radiological findings as well as the success of the surgical intervention.

Literature search

The search strategy involved the major electronic databases MEDLINE, EMBASE, PubMed and Current Contents (1950-2013) to find all available articles on Langerhans cell histiocytosis affecting the skull specifically in adults. Additional manual searches were made using the reference lists from the selected articles to retrieve other papers relevant to the topic. No language restriction was placed on any of the literature searches. The keywords used, alone and in combination, were *Langerhans cell histiocytosis, histiocytosis X, eosinophilic granuloma, Letterer-Siwe disease, Hand-Schuller-Christian syndrome, Histomoto-Prizker syndrome, self-healing histiocytosis, Langerhans cell granulomatosis, Type II histiocytosis and non-lipid reticuloendotheliosis*. Articles with cases involving both adults and children were excluded. In addition, foreign language papers identified in the search that were not translatable to English were excluded.

Case Report

A 41-year old male who presented to the Emergency Department after falling while water-skiing at 40-50 km/hr. He landed face first onto the water but did not lose consciousness and remembered that he was *in trouble*.

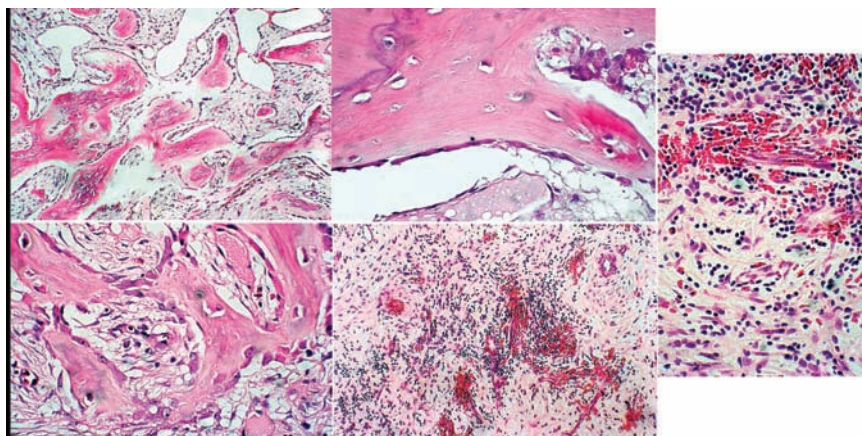


Figure 2. Histopathology of lesion removed from skull.

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Key words: Langerhans cell histiocytosis, skull, adult.

Acknowledgements: we would like to thank Mr Peter Paton of the Anatomical Pathology Department and Mr Chris Henwood of the Audiovisual Department, Nepean Hospital for their assistance with the X-ray.

Contributions: CC, GDE analysed the case, organised the radiographic figures, and co-wrote and edited the manuscript; SJ conducted the systematic review and literature search and co-wrote the manuscript; VC, DAK diagnosed and treated the patient.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 21 September 2012.

Revision received: 29 May 2013.

Accepted for publication: 29 May 2013.

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Rare Tumors 2013; 5:e38

doi:10.4081/rt.2013.e38

The patient recalls his face feeling puffy for 10-15 min but then settled and both his eyes were bleeding for approximately 30 min. He complained of neck and right shoulder pain and a frontal headache. His previous medical history included surgery for lumbar disc prolapse and chronic headaches, which had persisted for

the last 2-3 months prior to presentation. Medications included Dothiepin (TCA) and Salazopyrin (Sulfasalazine). On assessment, the patient was conscious (GCS 15), had a BP of 123/92, pulse of 72, and an oxygen saturation of 95%. There was periorbital bruising and swelling with a laceration of the right inner aspect of the upper eye-lid which was bleeding and blood was present in both eyes. A full ophthalmology assessment found no abnormalities. Radiological assessment included X-rays of the head (Figure 1), pelvis, C-spine, right shoulder, lumbar spine, and a CT of the head. The radiographs showed no evidence of acute fractures/dislocations. The head CT showed a small hypersensitivity with a small extra axial collection with a maximum thickness of 1mm. Differential diagnoses included an arachnoid cyst, haemangioma, meningioma or a secondary lesion. Due to the possibility of a malignant lesion a bone scan was also undertaken and subsequently showed an active lesion. The patient was admitted and had a craniotomy to excise the skull tumor. The excised lesion consisted on bone with soft tissue (30x20x7 mm). Histopathological examination of the specimen, which included immunoperoxidase studies revealed a rounded defect of the bone which consisted of a proliferation of fibrous stroma within which can be seen *inflammation foci* (Figure 2).

Immunoperoxidase studies were positive for S100 and CD68 and negative for HMB45 and Cam 5.2. The patient is currently well.

Discussion and Conclusions

Langerhans cell histiocytosis is a clonal proliferative disorder of the antigen presenting Langerhans' cell and refers collectively to a group of diseases previously known as histiocytosis X, eosinophilic granuloma, Letterer-Siwe disease, Hand-Schuller-Christian syndrome, Hashimoto-Prizker syndrome, self-healing histiocytosis, pure cutaneous histiocytosis, Langerhans cell granulomatosis, Type II histiocytosis and non-lipid reticuloendotheliosis.^{4,5} Langerhans cell histiocytosis usually affects patients under 10 years of age, however, studies have reported that the average age for presentation is 25 years.⁵ Patients mainly present with localized bone pain, dyspnea and malaise, and 75% have non-disseminated disease. The skull, femur, pelvis and ribs are most commonly involved.⁵ With skull lesions, the orbit and the cranial base are frequently involved and produce the classic triad of bony defects, exophthalmos and diabetes insipidus.⁵

Our adult case exemplifies an uncommon presentation of LCH which more commonly occurs in pediatric populations. However, this case illustrates a classic presentation of LCH

Table 1. Case reports of Langerhans cell histiocytosis with skull lesions in adults.

Study (ref)	Age/sex	Symptoms and signs	Investigations	Lesions	Histological findings	Management	Outcome
Suzuki <i>et al.</i> , 2008 ¹⁰	47/F	Hip pain, diabetes insipidus, forehead bone defect	Skull XR, whole body CT, bone scintigram scan	Multifocal	Accumulation of Langerhans cells expressing CD1a and S100 antigens, with scattered eosinophils and lymphocytes	Chemotherapy: 6-weeks of PSL + VLB, then 6-mercaptopurine, PSL + VLB for 1year	Clinical improvement traced for over 12 months
Fung <i>et al.</i> , 2002 ¹¹	29/F	Progressive non-tender left frontal head swelling over 2 months	CT head	Unifocal	Round cells expressing CD1a and S100 admixed with osteoclast-like giant cells expressing CD68, Birbeck granules and inflammatory cells	Craniotomy and resection of lesion	
Suzuki <i>et al.</i> , 2010 ⁷	56/F	Sudden sensorineural hearing loss and vertigo	CT head, MRI head	Unifocal	Histiocytic cells expressing CD1a and S100 with eosinophilic cytoplasm, inflammatory and giant cells	Excision of lesion and post-operative chemotherapy with VLB, PSL, 6-mercaptopurine	Disease free 2 years post-surgery although hearing not fully recovered
Kobayashi <i>et al.</i> , 2007 ⁸	25/M	Raised intracranial pressure and reduced visual acuity	CT head, MRI head, squash preparation from lesion specimens	Unifocal	Admixture of small, mature lymphocytes, eosinophils and Langerhans cells expressing CD1a & S100	Surgical resection	
Murayama <i>et al.</i> , 1988 ⁸	39/M	Tenderness in right posterior parietal region	CT head and T2-weighted MRI head	Unifocal			
Makras <i>et al.</i> , 2004 ⁶	57/F	Right scalp pan, nodular lesion in right parietal bone, diabetes insipidus 3 months post commencement of treatment	MRI head	Multifocal	Characteristic Langerhans cells with prominent nuclear groove exhibiting positive immunohistochemistry to S-100 protein and CD1a antibody	Local excision and chemotherapy with methotrexate and azathioprine	Improvement reported at 9 months post-treatment initiation

CT, computed tomography; MRI, magnetic resonance imaging; PSL, prednisolone; VLB, vinblastine.

in adults. Osteolytic bone lesions are a common manifestation of single system LCH in adults. These lesions tend to be unifocal rather than multifocal, often involving the skull or axial skeleton,⁴ such as in our patient. Our review of skull vault lesions in adults (Table 1) has confirmed this observation with 4 out of 6 cases of LCH involving the skull having unifocal lesions.⁶⁻¹¹ Calvarial lesions are normally found incidentally as was the case with our patient. However they may also present with bone pain, soft-tissue swelling, hearing loss, vertigo and visual disturbances.⁶⁻¹¹ Histologically, proliferation of Langerhans cells expressing CD1a and S100 admixed with acute and chronic inflammatory cells are consistently reported.⁶⁻¹¹ Immunohistochemical findings in our patient were consistent with these features. This report is interesting and adds valuable information to limited literature available on unifocal skull vault lesions in adults with LCH. Local treatment with excision, systemic chemotherapy and corticosteroid injection is highly successful in treating this disease and patients have excellent prognosis.⁵ Over 90% of patients survive 3 to 5 years post diagnosis.^{5,12,13} Age at diagnosis and initial response to therapy affect the prognosis and rate of recurrence of disease.⁵

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