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MULTISYSTEM LANGERHANS CELL HISTIOCYTOSIS WITH ADVANCED ORBITAL INVOLVEMENT: CASE REPORT
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J. McCAFFREY and C. RAWLINGSON

ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease occurring most frequently in infancy or early childhood. The aetiology is still not completely understood, although some form of immunologic dysfunction has been implicated. Clinically, the disease may either be localised or present with multisystem involvement. Here we discuss the case of a seven year old boy presenting with advanced proptosis. To the best of our knowledge, proptosis of this extent has not been reported previously in association with LCH.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disorder of uncertain aetiology. Debate continues as to whether it is primarily a malignant or reactive disease. The observation of high levels of several cytokines in lesions suggest immunologic dysfunction is involved, (l) although evidence exists to support the hypothesis of LCH as a clonal neoplastic disorder. (2) Additionally, studies examining a possible viral aetiology have had some limited success (3).

The disease displays considerable clinical heterogeneity, ranging from single system (55) to multisystem (M5) disease. Characteristic tissues involved in LCH are bone, skin, lung, liver, spleen, bone marrow, lymph nodes and the hypothalmic-pituitary system. In M5 disease, involvement of certain 'risk organs' (ie, bone marrow, liver, spleen and lungs) is a poor prognostic sign (4).

We report a case of multisystem LCH with rapidly progressive and extensive orbital involvement.

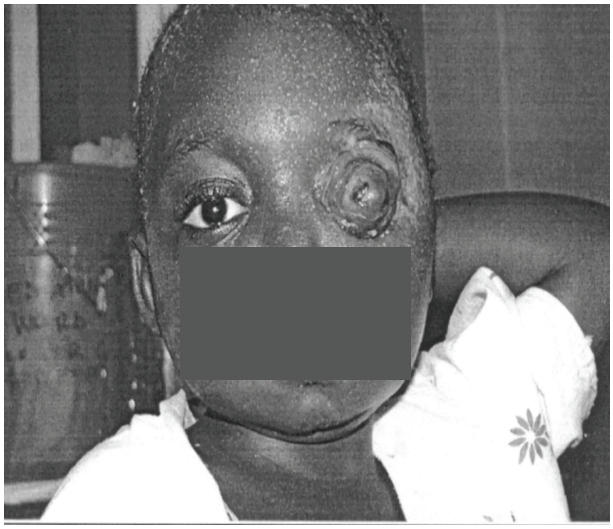
CASE REPORT

A seven year old boy presented to the outpatient clinic of Mbara University Teaching Hospital, Uganda, with severe painless proptosis of his left eye occurring in a period of three months. There was a history of a rash over the left face and scalp of five years duration and a chronic discharge from the left ear since the age of 3. There were no features in the history suggestive of diabetes inspidus.

On examination, the boy' s left eye had proptosed to the extent that his upper lid was everted and the cornea has become keratosed (see Figure1).

Figure 1

Advanced proptosis of the left eye



The boy was blind in his left eye, but visual acuity was normal in his right eye, and there was no visual field defect.

There was a raised, hypopigmented rash involving the whole of the scalp and extending to the left eye (see Figure 2). A dark green discharge was evident from the left auditory meatus consistent with chronic suppurative otitis media. Examination in the right ear was unremarkable.

Abdominal examination revealed grade 3 splenomegaly and a smooth liver edge 3 cm below the costal margin. There was no fever or clinically-detectable anaemia and chest was clear when auscultated. No focal pathology was detected on abdominal ultrasound scan.

Figure 2
Generalised scalp rash

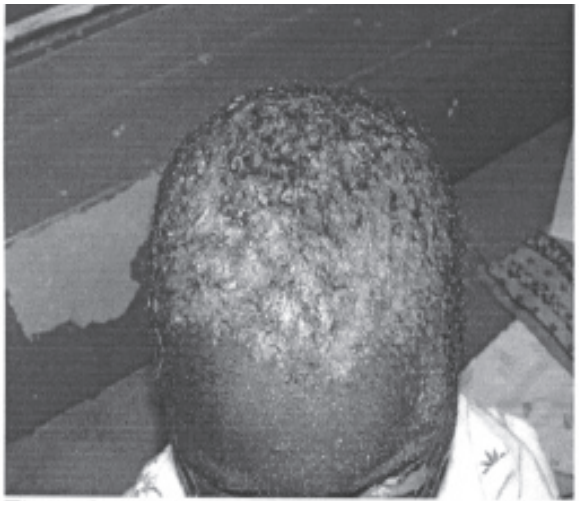
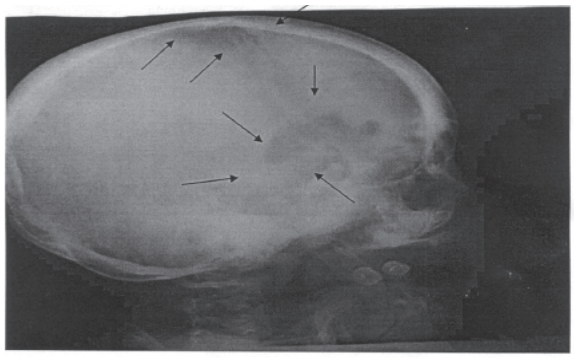


Figure 3
X-ray of the skull showed multiple ,lytic leisons



Computed tomography (CT) imaging and accurate blood testing facilities were not available at the time of presentation.

The proptosed left eye was surgically removed with no post-operative complications.
Immunohistochemistry on a 8mm punch biopsy taken from the skin rash and a tissue sample from orbital tissue taken revealed infiltrates were S100 and CD1a positive, confirming the diagnosis of LCH.

Although a diagnosis of LCH was strongly suspected clinically, a decision was made to await definitive histological confirmation before starting treatment. Appropriate testing facilities were not available in Uganda and so tissue samples were sent to a European centre. This process took several weeks due to a combination of difficulty in locating an appropriate centre to analyse the samples, and the actual transit time of samples and results. During this period, the boy and his father were forced to return to their village due to financial constraints. The delay in definitive diagnosis was a major reason why this boy never received appropriate treatment. When results were received, the boy and his family could not be located.

DISCUSSION

LCH is a rare disorder, with a recent study estimating an annual incidence of four per million (age 0-15 years) 5. The median age at diagnosis was 6.7 years in the SS cases, 3.2 years in the MS cases without risk-organ involvement (MSRO-), and 0.7 years in the MS cases with risk-organ involvement (MSRO+). Overall mortality was 3%, with all deaths occurring in the MSRO+ group.

LCH is characterised by abnormal proliferation of the Langerhans cell. The Langerhans cell is usually found as an epidermal histiocyte and functions as an antigen presenting cell. However, in LCH the cell seems to loose this ability (6).

Work by Willman (2), suggests that childhood LCH is a clonal disease; although the rarity of familial cases makes it unlikely that a predisposing mutation could be inherited. Egelerl, found higher levels of several cytokines in LCH lesions compared to unaffected areas, raising the possibility that LCH results from an aberrant immune response.

A viral cause has been suggested after studies identified Human herpes virus-6 (HHV- 6) in LCH lesions (3) although the significance of these findings has subsequently been questioned (7).

In order to reach a diagnosis of LCH, excision biopsy followed by histopathology and immunohistochemistry is vital. Definitive diagnosis requires ei ther expression of CD1a or the presence of Birbeck granules (8).

Treatment of multisystem LCH is a controversial area. The results of the LCH III trial, investigating potential benefit of combining methotrexate and vinblastine are eagerly awaited.

Proptosis is a recognised feature of LCH, and reports by Shetty (9) and Sarkar (l0) describe less advanced case of unifocal disease. However, nothing of this magnitude in the setting of multisystem involvement has been reported previously.

This case report shows for the first time the extent to which LCH can can affect the orbit if left untreated and highlights the difficulties of diagnosing and treating LCH in a developing country. Debate about establishing links to centres with access to relevant equipment and expertise to aid rapid diagnosis and instigation of treatment is required.

REFERENCES

1. Egeler, R.M., Favara, B.E., van Meurs, M., Laman, J.D. and Claassen, E. Differential In Situ cytokine profiles of Langerhans-like cells and T cells in Langerhans cell histiocytosis: abundant expression of cytokines relevant to disease and treatment. *Blood*. 1999; **94**:4195-4201.

2. Willman, C.L., Busque, L., Griffith, B.B., Favara, B.E.,*et al*.Langerhans'-cell)(histocytocis X) a clonal proliferative disease. *N Engl J Med*. 1994;**331**:154-160
3. Glotzbecker, M. P.,Carpentieri, D. F., Dormans,J.P.Langerhans cell histiocytsis:a primary viral infection of bone?Human herps virus 6 latent protein detected in lymphocytes from tissue of children. *J. Pediatr Orthop*. 2004; **24**:123-129.
4. Gadner, H. Grois, N.,Arico, M.,Broadbent, V., Ceci, A., Jakobson, A.,et al.A randomized trait of treatment for multisystem langerhans'cell histiocytosis.*J Pediatr*.2001;**138**: 728-734.
5 .Salotti, J. A.,Nanduri, V., Pearce, M. S.,Parker, L.Lyne, R. and Windebank, K. p.Incidence and clinical features of langerhans cell histiocytosis in the UK and Ireland. *Arch Dis Child*.2009; **94**:376-380.
6. Yu, R.C., Morris, J.F., Pritchard, J. and Chu, T.C. Defective alloantigen-presenting capacity of 'Langerhans cell histiocytosis cells'. *Arch Dis Child*. 1992; **67**: 1370-1372.
7. Glotzbecker, M.P., Dormans, J.P., Pawel, B.R., Wills, B.P, Joshi, Y., Elkan, M., *et al*. Langerhans cell histiocytosis and human herpes virus 6 (HHV -6), an analysis by realtime polymerase chain reaction. *J Orthop Res*. 2006; **24**: 313-320.
8. Mazal, P.R., Hainfellner, J.A., Preiser, J.,*et al*. Langerhans cell histiocytosis of the hypothalamus: diagnostic value of immunohistochemistry. *Clin Neuropathol*. 1996; **15**:87-91.
9. Shetty, S.B. and Mehta, C. Langerhans cell histiocytosis of the orbit. Indian *J Ophthalmol*. 2001; **49**:267-268.
10. Sarkar, S., Singh, M., Nag, D.,*et al*. A case report of unifocal Langerhans' cell histiocytosis or eosinophilic granuloma. *J Indian Med Assoc*. 2007; **105**:218- 220.