Case Report

Squash Cytology of Langerhans Cell Histiocytosis of Sellar Region

Abstract

Langerhans cell histiocytosis (LCH) is a systemic disease, which usually involves the skeleton and skin of children with occasional involvement of the central nervous system (hypothalamo–pituitary axis). We report the case of a 16-year-old male with a space-occupying lesion (SOL) in the sellar region and diabetes insipidus. However, no systemic abnormality was noted. A clinical diagnosis of pituitary adenoma was given. However, on intraoperative consultation by squash smears, cells with nuclear grooves and few eosinophils were seen. Hence, a differential diagnosis of LCH was also given, which was confirmed by histopathology and immunohistochemistry. Hence, as a matter of fact, LCH should be considered as one of the rare differential diagnoses of SOL of sellar region.

Keywords: *Langerhans cell histiocytosis, sellar region, squash cytology*

Supriya Verma, Parinitha S. Sangam, Ravikala V. Rao

Department of Pathology, Shri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Sattur, Dharwad, Karnataka, India

Introduction

Langerhans cell histiocytosis (LCH) is a systemic disease, which mainly affects children and young adults. LCH commonly involves the skeleton (80%) and skin (50%) but also occurs in the hypothalamic–pituitary axis in the central nervous system (CNS). CNS involvement usually comes under systemic disease, and LCH limited to only CNS is rare.[1] Here, we report a case of isolated LCH of the sellar region in a 16-year-old male presenting with diabetes insipidus. Pituitary hormones were within normal limits. Intraoperative squash smears showed characteristic Langerhans cells with few eosinophils. LCH involving only the CNS is rare and is associated with poor prognosis and adverse outcome.[2] It mostly involves hypothalamic–pituitary region and manifests with granulomas followed by neurodegenerative changes.[2] Histological examination and immunohistochemistry is helpful in confirming the diagnosis in such cases.

Case Report

A 16-year-old male presented with frontal headache of 1-year duration with polydipsia and polyuria. Magnetic resonance imaging (MRI) of the brain demonstrated a space-occupying lesion (SOL) of 2 cm × 1.8 cm × 1.4 cm in the sellar region with suprasellar extension and was reported as pituitary adenoma [Figure 1]. Serum sodium levels increased suggestive of diabetes insipidus. Pituitary hormones were within normal limits. Systemic examination revealed no abnormality. The patient underwent endoscopic transphenoidal excision of the lesion, and biopsy was sent for intraoperative consultation. Squash smears showed cells having eccentrically placed nuclei, nuclear grooves, and abundant eosinophilic cytoplasm. Occasional eosinophils were seen [Figures 2 and 3]. A differential diagnosis of pituitary adenoma and a rare possibility of LCH were considered. A final diagnosis of LCH was done on histopathology [Figure 4] and confirmed by immunohistochemistry [Figure 5].

Discussion

LCH encompasses several disorders, previously known as histiocytosis X, Letterer–Siwe disease, Hand–Schuller–Christian syndrome, eosinophilic granuloma of bone, and self-healing reticulohistiocytosis.[3] It is a rare disease characterized by aberrant proliferation of specific immature dendritic (Langerhans) cells belonging to monocyte–macrophage system.[4]

Langerhans cells were first recognized as a component of the normal skin by Paul Langerhans in 1865; they are originally derived from the bone marrow. Their

How to cite this article: Verma S, Sangam PS, Rao RV. Squash cytology of Langerhans cell histiocytosis of sellar region. Clin Cancer Investig J 2019;8:257-60.

Address for correspondence:
Dr. Supriya Verma, Officers' Mess, MH Shimla, Jutogh Cantt, Shimla - 171 008, Himachal Pradesh, India.
E-mail: supriyaverma31@gmail.com

Access this article online

Website: www.ccij-online.org

DOI: 10.4103/ccij.ccij_66_19

Quick Response Code:

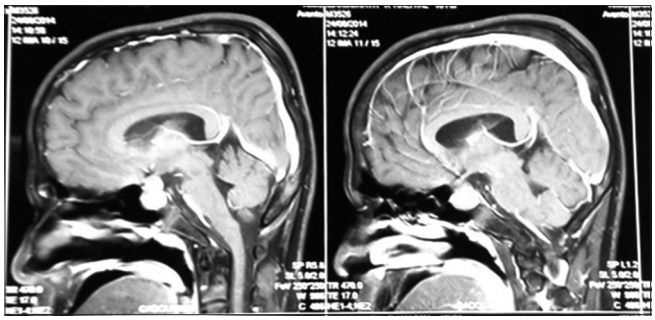

Figure 1: Magnetic resonance imaging brain – dumbbell-shaped lesion in the sella collapsing into the sphenoid sinus

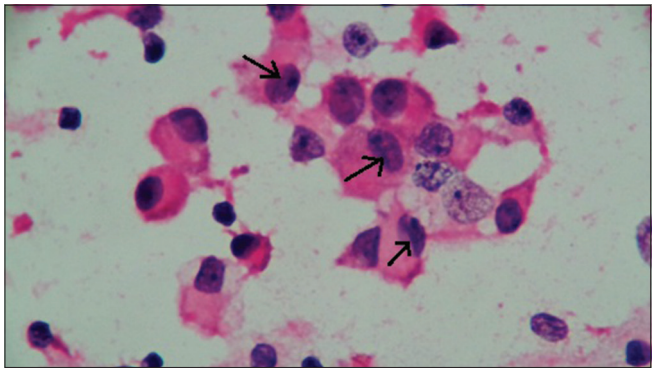

Figure 3: Squash cytology showing histiocytes with eccentrically placed nuclei with grooves (arrows) (H and E, ×40)

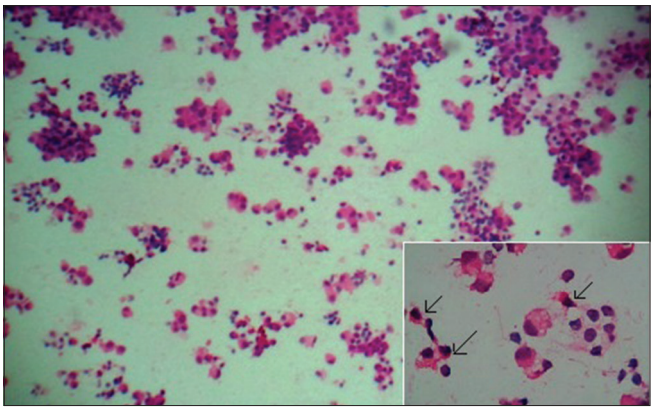

Figure 2: Squash cytology showing histiocytes in loose cohesive clusters (H and E, ×4). Right lower inset shows occasional eosinophils (arrows) amidst histiocytes (H and E, ×40)

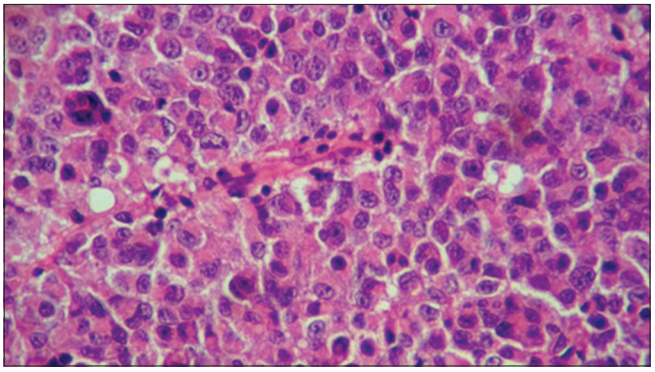

Figure 4: Paraffin section showing histiocytes with folded nuclei and giant cell (H and E, ×10)

immunologic role is now well established. They can detect foreign antigens entering the body through the skin and then migrate from the skin to the lymph nodes.[5] The incidence of LCH is five per million individuals according to the Surveillance, Epidemiology, and End Results Program database.[6] Males are more affected than females.[5] There is a wide spectrum of clinical manifestations of LCH that depends on the location and extent of proliferation of Langerhans cells. This leads to their high rate of misdiagnosis and missed diagnosis. Treatment also range from observation alone to systematic medication.[6]

CNS involvement in LCH is a rare but potentially devastating disease. Different types of involvement have been described by MRI.[2]

Squash cytology is of great value in intraoperative pathologic consultation. It provides rapid and reliable intraoperative diagnosis and guidance to the surgeon during surgical resection and lesion targeting. It also helps the surgeon to monitor and modify the surgical approach. By using scanty material, this technique makes it possible to detect cellular details and establish a provisional pathologic diagnosis.[7]

Single systemic disease and multisystemic disease are two kinds of LCH based on the extent of involvement at diagnosis.[6] CNS involvement in LCH is rare and is mainly diagnosed as multisystemic disease. The most common CNS manifestation is infiltration of the hypothalamic–pituitary region by LCH granuloma, frequently leading to diabetes insipidus and anterior pituitary hormone deficiency, most commonly growth hormone deficiency.[2,8] Neurodegenerative changes, the second-most frequent pattern, comprise mostly bilateral symmetric lesions in the cerebellum and basal ganglia.[8] LCH can also involve cerebellum, pons, and cerebral hemispheres. Investigators have identified three discrete pathologic lesions of LCH in the CNS. The first are well-circumscribed granulomas within the brain connective tissue space (meninges and choroid plexus), the second involves granulomas in the brain tissue with partial extension into the surrounding parenchyma, and the third are neurodegenerative lesions in the cerebellum and brainstem.[9,10]

The neurodegeneration in the vicinity of granulomas located in extra-axial spaces, meninges, and infundibulum is an important finding. The pathogenesis of diabetes insipidus and anterior pituitary hormone deficiencies may be explained by these neurodegenerative changes in the infundibulum, which may interfere with the axonal transfer of vasopressin or hormones from the hypothalamic nuclei to the pituitary, in addition to possible direct damage by the granuloma itself.[8]

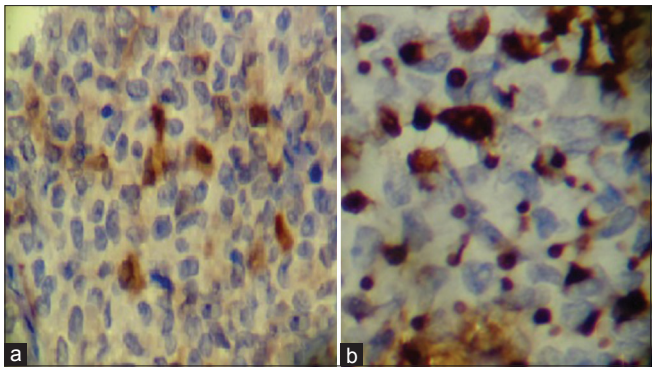

Figure 5: Immunohistochemistry: Tumor positivity for (a) S-100 (b) vimentin

LCH limited to the pituitary–hypothalamic axis is practically indistinguishable from suprasellar germinoma. Histological examination of the tissue and immunohistochemistry can aid in the diagnosis.

Cytological smears of LCH are cellular and show numerous atypical histiocytes singly and in loose cohesive clusters. These histiocytes are binucleate, multinucleate with abundant dense cytoplasm, and eccentric vesicular nuclei with characteristic intranuclear pseudoinclusions, prominent indentations, and grooves (with a kidney or coffee bean appearance). The background shows lymphocytes, neutrophils, and few eosinophils.[11] Immunohistochemical staining is positive for CD1a, S100, and CD 207 (Langerin).[6]

Clonal proliferative disorder via BRAF V600E mutation, MAP2K1 mutation, or activation of MAPK/ERK has been considered as a possible pathogenesis for LCH.[6] Treatment consists of topical or systemic steroids, chemotherapy with alkylating agents or vinca alkaloids, and intravenous immunoglobulin or plasmapheresis.[2]

There is a well-characterized histological appearance of the LCH lesions on hematoxylin and eosin-stained sections, but positive CD1a and/or CD207 (Langerin) staining of the lesional cells is required for a definitive diagnosis.[12] Paraffin sections show proliferation of Langerhans cells with moderate amount of eosinophilic cytoplasm, elongated kidney-shaped nuclei, and a nuclear groove. Background shows macrophages, lymphocytes, and many eosinophils.[5] However, CD1a positivity may be occasionally seen in other histiocytes, such as juvenile xanthogranuloma and Rosai–Dorfman disease.[5] It has to be emphasized that with the exception of LCH, dendritic cells within the brain compartment do not express CD1a and so are not derived from the pool of Langerhans cells.[13]

Electron microscopy is no longer needed because it has been shown that the expression of Langerin correlates with the ultrastructural presence of Birbeck granules.[13] Birbeck granules are rigid tubular structures of variable length that specifically possess a striated or zipper-like central core. They may originate as invaginations of the cell membrane.[5]

Kobayashi *et al.*[14] diagnosed a case of LCH in a 25-year-old male who presented with raised intracranial pressure and decreased visual acuity by squash cytology. Hence, whenever squash smears yield mixed populations of mature lymphocytes, eosinophils, and histiocytes, the cytologists should be aware and consider LCH as a diagnostic possibility. Similar findings were noted in this case also. A case of vertebral histiocytosis X was also diagnosed on squash cytology according to Gandolfi.[15]

Conclusion

LCH, an enigmatic disease, has been variously classified as a neoplastic process, a reactive disorder, or an aberrant immune response. LCH should be considered one of the rare differential diagnoses of SOL of the sellar region. Cytological features of LCH are highly characteristic to suggest a diagnosis in an appropriate clinical setting with classical radiological findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Isoo A, Ueki K, Ishida T, Yoshikawa T, Fujimaki T, Suzuki I, *et al.* Langerhans cell histiocytosis limited to the pituitary-hypothalamic axis – Two case reports. Neurol Med Chir (Tokyo) 2000;40:532-5.
2. Turner S, Kazmi S, Lacroix M. Intra-axial CNS involvement of Langerhans cell histiocytosis. Neurology 2018;90 Suppl 15:6-103.
3. Willman CL, Busque L, Griffith BB, Favara BE, McClain KL, Duncan MH, *et al.* Langerhans'-cell histiocytosis (histiocytosis X) – A clonal proliferative disease. N Engl J Med 1994;331:154-60.
4. Kaltsas GA, Powles TB, Evanson J, Plowman PN, Drinkwater JE, Jenkins PJ, *et al.* Hypothalamo-pituitary abnormalities in adult patients with Langerhans cell histiocytosis: Clinical, endocrinological, and radiological features and response to treatment. J Clin Endocrinol Metab 2000;85:1370-6.
5. Schmidt S, Eich G, Geoffray A, Hanquinet S, Waibel P, Wolf R, *et al.* Extraosseous Langerhans cell histiocytosis in children. Radiographics 2008;28:707-26.
6. Tan H, Yu K, Yu Y, An Z, Li J. Isolated hypothalamic-pituitary Langerhans' cell histiocytosis in female adult: A case report. Medicine (Baltimore) 2019;98:e13853.

7. Nahm JH, Yoon G, Do SI, Kim HS. Squash smear cytology of Langerhans cell histiocytosis. Int J Clin Exp Pathol 2015;8:7998-8007.
8. Grois N, Fahrner B, Arceci RJ, Henter JI, McClain K, Lassmann H, *et al*. Central nervous system disease in Langerhans cell histiocytosis. J Pediatr 2010;156:873-81.e1.
9. Grois N, Prayer D, Prosch H, Lassmann H, CNS LCH Co-operative Group. Neuropathology of CNS disease in Langerhans cell histiocytosis. Brain 2005;128:829-38.
10. Jubran RF, Finlay J. Langerhans cell histiocytosis of the central nervous system. In: Raghavan D, Brecher ML, Johnson DH, Meropol NJ, Moots PL, Rose PG, *et al*., editors. Textbook of Uncommon Cancer. Hoboken NJ: John Wiley & Sons, Ltd.; 2006.
11. Chandekar SA, Shah VB, Kavishwar V. Cytological diagnosis of Langerhans cell histiocytosis with cutaneous involvement. J Cytol 2013;30:81-3.
12. Haupt R, Minkov M, Astigarraga I, Schäfer E, Nanduri V, Jubran R, *et al.* Langerhans cell histiocytosis (LCH): Guidelines for diagnosis, clinical work-up, and treatment for patients till the age of 18 years. Pediatr Blood Cancer 2013;60:175-84.
13. Plumb J, Armstrong MA, Duddy M, Mirakhur M, McQuaid S. CD83-positive dendritic cells are present in occasional perivascular cuffs in multiple sclerosis lesions. Mult Scler 2003;9:142-7.
14. Kobayashi TK, Ueda M, Nishino T, Bamba M, Echigo T, Oka H, *et al.* Langerhans cell histiocytosis of the skull on cytologic squash preparations. Diagn Cytopathol 2007;35:154-7.
15. Gandolfi A. Vertebral histiocytosis-X causing spinal cord compression. Surg Neurol 1983;19:369-72.