Langerhans cell histiocytosis

Langerhans cell histiocytosis (LCH) is a rare disease involving clonal proliferation of Langerhans cells, abnormal cells deriving from bone marrow and capable of migrating from skin to lymph nodes. Clinically, its manifestations range from isolated bone lesions to multisystem disease. LCH is part of a group of clinical syndromes called histiocytoses, which are characterized by an abnormal proliferation of histiocytes (an archaic term for activated dendritic cells and macrophages). These diseases are related to other forms of abnormal proliferation of white blood cells, such as leukemias and lymphomas.

Eosinophilic granuloma is a rare disease belonging to the Langerhans cell histiocytosis group.

Hand Schüller Christian disease

Abt Letterer Siwe disease

see Skull Langerhans cell histiocytosis.

see Langerhans cell histiocytosis of the clivus.

Pathogenesis

The pathogenesis of Langerhans cell histiocytosis (LCH) is a matter of debate. There are ongoing investigations to determine whether LCH is a reactive or neoplastic process. Arguments supporting the reactive nature of LCH include the occurrence of spontaneous remissions, the extensive secretion of multiple cytokines by dendritic cells and bystander-cells (a phenomenon known as cytokine storm) in the lesional tissue, favorable prognosis and relatively good survival rate in patients without organ dysfunction or risk organ involvement.

On the other hand, the infiltration of organs by monoclonal population of pathologic cells, and the successful treatment of subset of disseminated disease using chemotherapeutic regimens are all consistent with a neoplastic process.

In addition, a demonstration, using X chromosome–linked DNA probes, of LCH as a monoclonal proliferation provided additional support for the neoplastic origin of this disease.[16] While clonality is an important attribute of cancer, its presence does not prove that a proliferative process is neoplastic. Recurrent cytogenetic or genomic abnormalities would also be required to demonstrate convincingly that LCH is a malignancy.

Activating mutation of a protooncogen in the Raf family, the BRAF gene, was detected in 35 of 61 (57%) LCH biopsy samples with mutations being more common in patients younger than 10 years (76%) than in patients aged 10 years and older (44%).[17] This study documented the first recurrent mutation in LCH samples. Two independent studies have confirmed this finding.

Presence of this activating mutation could support the notion to characterize LCH as myeloproliferative disorder.

Diagnosis

Diagnosis is confirmed histologically by tissue biopsy. Hematoxylin-eosin stain of biopsy slide will show features of Langerhans Cell e.g. distinct cell margin, pink granular cytoplasm. Presence of Birbeck granules on electron microscopy and immuno-cytochemical features e. g. CD1 positivity are more specific. Initially routine blood tests e.g. full blood count, liver function test, U&Es, bone profile are done to determine disease extent and rule out other causes. Radiology will show osteolytic bone lesions and damage to the lung. The latter may be evident in chest X-rays with micronodular and interstitial infiltrate in the mid and lower zone of lung, with sparing of the Costophrenic angle or honeycomb appearance in older lesions. MRI and CT may show infiltration in sella turcica. Assessment of endocrine function and bonemarrow biopsy are also performed when indicated.

S-100 protein is expressed in a cytoplasmic pattern peanut agglutinin (PNA) is expressed on the cell surface and perinuclearly major histocompatibility (MHC) class II is expressed (because histiocytes are macrophages) CD1a langerin (CD207), a Langerhans Cell–restricted protein that induces the formation of Birbeck granules and is constitutively associated with them, is a highly specific marker.

Literature reviews

A comprehensive literature_review presents an updated synthesis of clinical, pathological, and therapeutic insights into orbital tumor and ocular adnexal histiocytic neoplasms, including LCH, JXG, AOXG, ECD, RDD, and HS. A total of 73 studies, selected from 263 screened publications up to January 2024, were analyzed [1].

The strength of this review lies in its diagnostic and therapeutic clarity. It establishes the role of surgical_debulking as both a diagnostic and therapeutic cornerstone in most histiocytic tumors, especially LCH and XG variants. The review underscores the shift toward systemic_chemotherapy and the emerging role of targeted_therapy in systemic or refractory disease, a particularly relevant advancement in the management of multi_organ_involvement.

However, while the article successfully compiles a diverse range of histiocytic disorders, the heterogeneity of the included studies (in terms of sample size, methodology, and reporting) may limit the generalizability of certain conclusions. The review would have benefited from a standardized quality assessment of the individual studies included.

The recommendation for follow-up — imaging every 3–6 months for 2 years, then annually — is clinically practical but may need individual adaptation based on tumor type and systemic burden.

Overall, this work is a valuable resource for ophthalmologists, oncologists, and pathologists involved in the management of orbital histiocytic lesions. It bridges multiple specialties and provides a roadmap for both current management and future directions such as molecular profiling and targeted treatment approaches.

Key points:

- Histology and immunohistochemistry remain the gold standard for diagnosis.
- Surgery is the first-line treatment in LCH and XG; chemotherapy is essential in systemic disease.
- Targeted therapies hold promise but are not yet standard of care.

- Multidisciplinary management is essential for optimal outcomes.

For clinicians and researchers interested in rare orbital tumors, this review offers a robust framework for understanding and treating these challenging conditions.

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Let me know if you want a Spanish version, summary slide, or if you're thinking of integrating it into your own clinical wiki.

Case reports

Langerhans cell histiocytosis (LCH) localised in the hypothalamic-pituitary region (HPR) is very rare, especially in adults. Diabetes insipidus (DI) is considered to be a hallmark of HPR LCH, while anterior pituitary abnormalities are usually seen as consequences of surgery, radiotherapy or chemotherapy.

CASE DESCRIPTION: We present a patient with localised HPR LCH with dominant anterior pituitary dysfunction and tumour mass effects but without DI. Seven years after surgery and local radiotherapy, she is stable. Control MRI shows no residual tumour growth and thorough physical examination is still without any signs of disease spread.

CONCLUSIONS: Anterior pituitary deficiency can appear without DI and not only as a consequence of LCH treatment. All patients with LCH should be screened for this endocrine abnormality so that appropriate substitution therapy may be provided [2)].

Case reports

Bärtschi et al. report a case of a 42-years-old male complaining of a right side hemicranial pain and left arm minor paresis due to a right insular lobe heterogeneous enhancing lesion associated with extensive vasogenic edema. The first diagnostic impression suggested a glioblastoma multiforme or a localized metastasis. The thoracic-abdominal-pelvic CT only detected small upper lungs inactive nodules suggesting a silent focal LHC. A very hard consistency lesion was almost completely removed through a pterional craniotomy approach, with no fluorescence after aminolevulinic acid (5-ALA) infusion. The intraoperative biopsy ruled out a glioma but could not confirm a lymphoma. Definitive cerebral biopsy reported lymphocytes and histiocytes (CD1a+, S1001+). This gave rise to the diagnosis of an intracerebral parenchymal LCH. The treatment with fractioned radiotherapy maintained a clinical and radiological remission.

This case is so rare that it cannot be used as a guide and we probably will never see again a single intraparenchymal supratentorial CNS LHC in a neurosurgery ward, but we hope that it might help colleagues in the future with the thought process [3)].

A 36-year-old man was diagnosed with Langerhans cell histiocytosis (LCH) of the cervical spine with a unifocal expansive osteolytic lesion of C4. The surgical management with a 2-year follow-up and a review of the literature on LCH of the cervical spine are presented. Although a rare condition, LCH is

an important differential diagnosis of any osteolytic lesion in the cervical spine with localized pain in a young adult patient. Review of the literature suggests a higher prevalence of LCH lesions affecting the cervical spine as compared with the thoracic or lumbar spine than historically reported [4].

1)
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