MULTISYSTEM LANGERHANS CELL HISTIOCYTOSIS: CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT
Langerhans cell histiocytosis (LCH) is a rare and heterogeneous disease of unknown etiopathogenesis caused by clonal proliferation of Langerhans cells. We report a case of an adult woman diagnosed with Langerhans cell histiocytosis with neurological, endocrine and bone involvement. Clinicians should consider Langerhans cell histiocytosis in combination of central diabetes insipidus and lytic bone lesions.

KEYWORDS: Langerhans Cell Histiocytosis, Bone, Central nervous system.

INTRODUCTION
Langerhans cell histiocytosis (LCH) is a rare and heterogeneous disease of unknown etiopathogenesis caused by clonal proliferation of Langerhans cells. LCH is generally considered to be a disease of childhood and adults are rarely affected. The clinical course of LCH is highly variable ranging from a self-healing solitary bone lesion to widely disseminated life-threatening disease.¹ In this paper a particular case of multisystem LCH presenting with bone and central nervous system (CNS) involvement is discussed with the existing literature.

CASE REPORT
A 60-year-old woman presented with a 2-month history of vomiting, dizziness, unsteady gait, polyuria and polydipsia. Physical examination revealed a skull mass with cerebellar ataxia. Laboratory tests revealed increased inflammatory parameters with hypernatremia and...
hypercalcemia. Bone X-rays graphs showed a round lytic skull defect (Fig.1A). Magnetic resonance imaging showed a mass like lesion of the parietal skull bone (Fig.1B), thickened enhancing pituitary stalk, left superior colliculus (Fig.1C) and multifocal cerebellar lesions (Fig.1D). Patient underwent a left parietal craniotomy to excise the skull tumor. When the scalp flap was reflected, an intradiploic tumor herniating through a bone defect was identified (Fig.2A). The tumor was resected within the apparently normal bone (Fig.2B) followed by skull bone reconstruction. Histopathology of the specimen was consistent with LCH based on the presence of characteristic Langerhans cells exhibiting positive immunohistochemistry to S-100 protein and CD1a antibody. Extra-cranial extension was evaluated by a positron emission tomography (PET) demonstrating intense F18 fluorodeoxyglucose (FDG) uptake in the hypothalamus (Fig.3A) and lower limb bones (Fig.3B). On the basis of these findings, diagnosis of multisystem Langerhans cell histiocytosis with bone and neuroendocrine involvement was made. The patient is currently being given oral prednisolone daily and intravenous vinblastine weekly with clinical course improvement after 6 weeks.

Figures

Figure 1 Radiological findings at presentation (white arrows) (A) Skull lytic bone lesion (B) T2 hyperintense lesion of parietal bone (C) Thickened enhancing pituitary stalk and left superior colliculus.
Figure 2 Per-operative findings with (A) Intradiploic tumor herniating through a bone defect (B) Resected bone tumor within normal limits.

Figure 3 PET/FDG scans showing intense uptake of hypothalamus (A) and lower limb bones (B).
DISCUSSION

LCH is a monoclonal disease with unknown etiology characterized by an abnormal proliferation of the Langerhans cells, which originate from bone marrow, derived dendritic cells. The immune mechanisms underlying LCH are still not fully understood, although many hypotheses exist. LCH has been diagnosed in all age groups, but are most common in children. The incidence appears one to two cases per million adults. The clinical course and biological behavior of LCH varies depending upon the sites and extent of involvement.\(^1\)

LCH is traditionally divided into two major categories; single system LCH and multisystem LCH defined as involvement of two or more organs at diagnosis with or without organ dysfunction. Bones are the most frequent site of this disorder, the flat bones are involved most frequently and among them the skull is commonest.\(^2\) Skull lesions are often painless and found only because a soft tissue mass over the bone defect is detected such as in our patient. CNS involvement in LCH has been recognized since the early reports of the disease. The most common CNS manifestation in LCH is infiltration of the hypothalamic pituitary region by LCH granuloma, frequently leading to diabetes insipidus and anterior pituitary hormone deficiency. Neurodegenerative changes, the second most frequent pattern, comprise mostly bilateral symmetric lesions in the cerebellum and basal ganglia of variable signal quality on MRI, depending on site and stage of the lesion.\(^3\) Polyuria, polydipsia and cerebellar ataxia revealed the disease in our patient with cranial and intracranial changes in MR imaging. Because of nonspecific clinical presentation, histopathology plays a crucial role in the diagnosis of LCH. The diagnosis is based on histological and immunophenotypical examination of involved tissue showing Langerhans cell proliferation expressing CD1a and S100 admixed with acute and chronic inflammatory cells.\(^1,2\) Immunohistochemical findings in our patient were consistent with these features. FDG PET/CT is a powerful tool for making an early diagnosis; it allows higher diagnostic confidence with regard to lesions, measuring the extent of disease and assessing disease activity and is consequently useful for evaluating the response to therapy in patients with Langerhans cell histiocytosis.\(^4\) The treatment of LCH is still controversial. Treatment decisions are based on whether the disease is single system or multisystem. Combination prednisone/vinblastine has been proven to be an effective treatment with minimal toxicity; therefore, it is the standard initial therapy for patients in whom systemic therapy is indicated.\(^5\) Rapid response to initial therapy and risk organ involvement are the most important predictors of outcome. Early intensification of therapy is justified for patients who do not respond to initial therapy. Our patient is currently
being given oral prednisolone daily and intravenous vinblastine weekly with clinical course improvement after 6 weeks.

CONCLUSION

This multisystem presentation of Langerhans cell histiocytosis with central nervous system and bone involvement suggests variation in the clinical manifestations of the disease. Our report adds valuable information to limited literature available on adult multisystem Langerhans histiocytosis.

Conflict of interest: None.

REFERENCES