

## Langerhans Cell Histiocytosis: A Case Report

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**Objective:** Langerhans Cell Histiocytosis (LCH) is a rare proliferative disorder of a distinct cell type that is similar to Langerhans cell. Prevalence is estimated at 1:200.000/year in children. Clinical presentations are variable, ranging from a single location in the bone to severe multivisceral involvement leading to dysfunction of vital organs. Therefore, objective of this study was to explore LCH based on clinical findings, skull x-ray, head CT-Scan, cytology, histopathology. and Immunohistochemistry.

**Method:** We report a case of Langerhans Cell Histiocytosis of a 3-year-old boy. Fine needle aspiration biopsy was performed from a nodule in parietal area on the scalp; dry fixation was made and stained with Giemsa. Immunohistochemistry examination was performed with CD1a and S100. Histopathology examination was done post-operatively and cytology examination were consistent with LCH, composing Langerhans cells with complex, clefted, grooved, irregular or convoluted nuclei with fine chromatin and one or more small nucleoli and moderate to abundant quantities of eosinophilic cytoplasm, mixed with multinucleated eosinophils.

**Results:** The finding of pentalaminar Birbeck granules by electron microscope is diagnostic of LCH, but this examination cannot be performed in our institution, so diagnosis was supported by immunohistochemistry with CD1a and S 100.

**Conclusions:** Based on clinical findings, skull x ray, Head CT-Scan, cytology, histopathology and Immunohistochemistry, this case was concluded as a Langerhans Cell Histiocytosis.

**Keywords:** Langerhans cell histiocytosis, Histiocytosis X, CD1a, S-100.

### PRESENTATION, HISTORY, AND EXAMINATION

A 3-year-old boy with a history of a scalp mass that had been experienced for 6 months being brought to neurosurgery service. Skull X-ray showed multiple punched out lesions and lymph node enlargement was found on chest X-ray (Figure1).

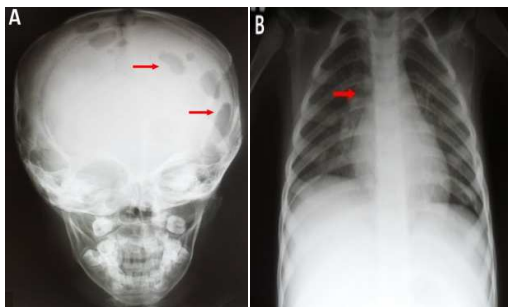


Figure 1 A. Multiple punch out lesion indicated osteolytic lesion  
B. Lymph node enlargement

Contrast head CT scan reveals multiple osteolytic lesions with no intracranial involvement (Figure 2).

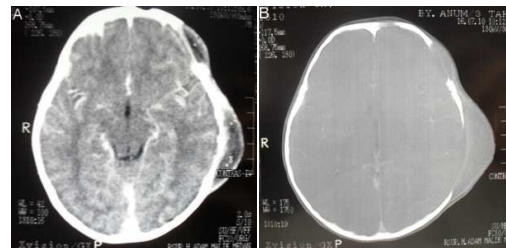


Figure 2 A. Contrast head CT scan: no intracranial involvement  
B. Bone window: multiple osteolytic lesions

Cytological examination concluded this case as Langerhans Cell Histiocytosis, Hand-Schuller-Christian Type (Figure 3).

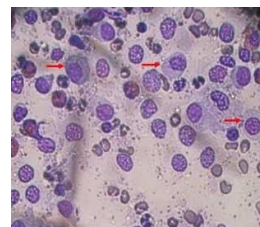


Figure 3. Langerhans cell: irregular and groove nuclei, soft chromatin, one or more nucleoli, abundant eosinophilic cytoplasm, and scattered eosinophil.

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The patient underwent operation, and the mass was completely removed as depicted in Figure 4. Yellowish solid masses were found. Sample of the calvarium was also taken for histopathology examination. The dura was intact.

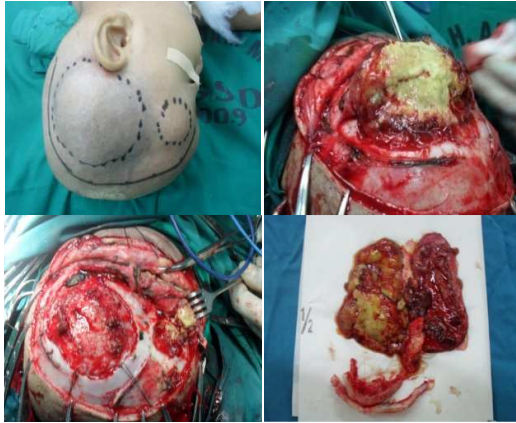
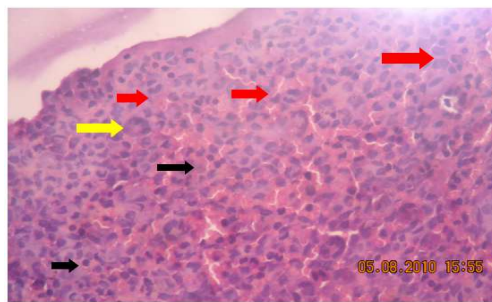


Figure 4 Tumor Removal

Because of the limitation of facilities in our institution, we could not perform electron microscope examination for identification of the Birbeck's granule that is the gold standard examination in diagnosing. Therefore, we performed S100 and CD1a immunohistochemistry examination that strongly expressed the histiocytosis process (Figure 5).



■ LC    ■ : multinucleated giant cell    ■ : eosinophil  
Figure 5 Histopathologic Examination

Accordingly to these findings, the histopathology examination also proved the diagnosis as Langerhans cell histiocytosis (Figure 6).

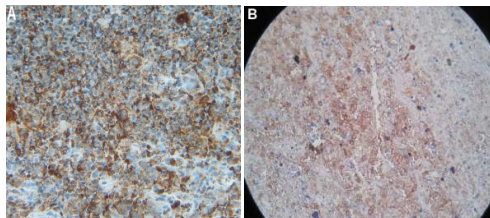


Figure 6 Dark Brown Stain Indicated Strongly Process of LCH (A. S100; B. CD1a).

## DISCUSSION

Langerhans Cell Histiocytosis is a rare disease.<sup>1</sup> This disease has annual incidence 5,4 million children per year, has slightly male predominance, 50% of them were diagnosed between the ages of 1 and 15. The peak incidence was between ages of 1 and 4.<sup>2</sup>

Cases of this disease have been written from early of 20<sup>th</sup> century. At first Lichtenstein coined Histiocytosis-X in 1953 to explain a spectrum of clinical syndromes with a lesion caused by clonal proliferation of histiocytes.<sup>3</sup> Different terminology have been suggested to define the disease: Histiocytosis X, eosinophilic granuloma, Letterer-Sewe disease, Hand-Schuller Christian syndrome, Hashimoto-Pritzker syndrome, self healing histiocytosis, pure cutaneous histiocytosis, Langerhans cell granulomatosis, eosinophilic granulomatosis, type II histiocytosis, and non-lipid reticuloendotheliosis. The disease is now termed Langerhans cell histiocytosis (LCH), a term that has been agreed by the Histiocyte Society in 1987.<sup>4</sup> The clinical landmark to Langerhans cell histiocytosis is the identification of Langerhans cells with varying proportions. Langerhans cells were first described in 1868 using a gold chloride staining technique with identification of nonpigmented dendritic appearing cell in epidermis.<sup>4</sup> Langerhans cells appear abundantly in the stratum spinosum of the skin and lymph nodes. They act as antigen-presenting cells with the process of microbial antigens.<sup>3</sup> Langerhans cells also can be found in lymph nodes, thymus, oral mucosa, esophagus, main bronchi, and distal colon.<sup>4</sup> Langerhans Cell Histiocytosis can proliferate in 1 discrete location to multi organ involvement.<sup>3</sup>

Our case involved histiocytosis process on the calvarium, temporoparietal region, and enlargement of parahylar lymphnodes without involvement of any visceral organ. Fine needle aspiration biopsy showed numerous Langerhans cells.

Histiocytes are antigen-processing cells of the monocyte-macrophage lineage, from CD34+ precursor cells. Some investigators still consider this lesion to be a disorder of altered immunity, analogous to sarcoidosis, and prefer the term Langerhans cell granulomatosis.<sup>4</sup>

The etiology and pathogenesis of LCH have remained an enigma despite continuous research. Current theories: a role for environmental, infectious, immunologic, and genetic causes. Others believe that LCH is a neoplastic process.<sup>2</sup> It has been postulated also that HHV-6 (Human Herpes Virus 6) has been implicated as a potential trigger, and a viral infection is now been considered as the underlying etiology.<sup>2</sup>

There are three well recognized spectrums in LCH: Eosinophilic granuloma, Letterer-Siwe

disease, and Hand-Schuller-Christian disease.<sup>3</sup> In Hand-Schuller Christian disease there are cranial involvement (Skull lesions, diabetes insipidus, exophthalmos), other bones, oral cavity, skin, lymph nodes, brain, lungs, and liver.<sup>2</sup> Other known spectrum is Hashimoto-Pritzker syndrome (skin eruption in the first months or days after birth that spontaneously resolve).<sup>5</sup> In some cases the disease cannot be applied into aforementioned spectrums

There are 3 types of histiocytoses: malignant or true histiocytosis, benign or reactive histiocytosis, and LCH. LCH divided into three subgroups: disseminated, multifocal, and unifocal LCH. Then disseminated LCH categorized as Letterer-Siwe disease and Hand-Schuller Christian disease (Eosinophilic Granulomatosis).<sup>3</sup>

Histiocyte Society recommended a classification of histiocytes. Langerhans histiocytosis (Class I), Non-LC histiocytosis (Class II), and malignant histiocytosis (Class III).<sup>6</sup>

The common phenotype of LCH, which affects children under 15 years of age, is the eosinophilic granulomatosis. It present as "punched out" lesions as lytic processes on plain radiography that is believed as a result from bone metabolism upregulation.<sup>3</sup>

The manifestations of pituitary hormone deficiency are caused by infiltration of LCH granuloma into hypothalamic pituitary region and pronounced inflammation was noted in all types of CNS disease in early and late forms of LCH, as well as in granular or diffuse lesions<sup>1</sup>. It also has been reported an incidence LCH to the optic nerve.<sup>3</sup> No CNS manifestation found on our case.

With the presence of typical cutaneous, osseous, or pulmonary lesions or evidence of diabetes insipidus or pituitary insufficiency, investigations for hepatic lesions must be considered; because hepatic involvement is associated with a high mortality rate in patients with Langerhans cell histiocytosis.<sup>7</sup> Systemic involvement of bones, lungs, liver, lymph nodes, hypothalamic pituitary axis or central nervous system can occur several years following initial skin lesions.<sup>8</sup>

Immunohistochemistry examination could reconfirm the diagnosis of LCH using Fascin, CD1a, Langerin and S-100 protein. Fascin, a 55-kD actin-bundling protein, represents a highly selective marker for dendritic cells of lymphoid tissues and peripheral blood and is involved in the formation of dendritic processes in maturing epidermal Langerhans cells. However, this protein is not a feature of normal epidermal Langerhans cells and lacks the specificity of CD1a as a marker for the lesional cells of LCH.<sup>4</sup> Langerin (CD207) is a relative new monoclonal protein associated with Birbeck granules. It appears more sensitive and specific for LC than CD1a, and in the future it may be a key component of an immunocytochemistry panel to diagnose LCH.<sup>6</sup>

Electron microscopy to identify Birbeck granules is rarely performed today<sup>6</sup> despite the most specific markers for LCH are Birbeck granules and CD1a.<sup>4</sup> In this case, electron microscopy cannot be done in our institution, therefore the diagnosis was being made by using clinical findings, cytology, histopathology, immunohistochemistry staining.

Current recommended therapy for LCH has been noted. LCH with limited cutaneous disease: no therapy; can be given steroids, nitrogen mustard or PUVA (second line options). LCH with localized bone lesions: curettage, intralesional steroids or low dose radiation. LCH with multi organ: therapy is still controversial, can be considered using high dose prednisone or single agent chemotherapy or multi agent chemotherapy.<sup>6</sup>

In our case, with localized bone lesions and lymph node involvement, we have done bone curettage and chemotherapy with vincristine, MTX, cyclophosphamide and prednisone with complete respond.

The single best prognostic indicator is a patient's response to chemotherapy during the 6-week induction phase. Patients who respond to chemotherapy have a 88% to 91% survival rate. With non-responder to induction phase, the survival rate drops to 17% to 34%, mandating more aggressive therapy be given.<sup>6</sup>

## CONCLUSION

It has been reported a case of a 3-year-old boy with a scalp mass. Fine needle aspiration biopsy showed numerous Langerhans cells. Skull X-ray showed multiple punched out lesion and lytic processes on CT-scan. The diagnosis of Langerhans cell histiocytosis was made and the therapy of operative curettage and chemotherapy with vincristine, MTX, cyclophosphamide and prednisone showed good result, a complete response. The diagnosis was confirmed with immunohistochemistry test of protein CD1a and S-100. Electron microscopy was not being done because of limitations of resources and there is a trend that it is not being done nowadays.

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