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A Case Report: Langerhans Cell Histiocytosis of bone mimicking a Chronic Osteomyelitis

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Abstrak

Latar belakang: *Langerhans cell histiocytosis* adalah suatu lesi jinak pada tulang yang biasanya mengenai populasi anak dan dewasa muda. Penegakan diagnosis *langerhans cell histiocytosis* memiliki tantangan tersendiri karena selain kasus yang jarang, secara histopatologi *langerhans cell histiocytosis* memiliki gambaran seperti proses inflamasi lainnya. Kami melaporkan kasus pada anak laki-laki berusia 4 tahun dengan keluhan benjolan yang tumbuh lambat, konsistensi kenyal padat di area kepala. Hasil CT scan kepala menunjukkan *Space Occupying Lesion* (SOL) multipel dengan destruksi tulang os parietal kanan dan kiri. Pada gambaran histopatologi didapatkan kesan granuloma eosinofilik. Adanya dominasi sel eosinofilik, sel limfosit, sel plasma, serta sel inflamasi lainnya di tulang dapat menyebabkan misdiagnosis sebagai suatu osteomielitis kronik. Kemiripan tampilan histopatologi ini, selain meninjau kembali manifestasi klinis dan lokasi lesi maka analisis morfologi sel yang didukung oleh pemeriksaan imunohistokimia penting untuk membedakan sel histiosit Langerhans dengan sel histiosit normal lainnya. Pendekatan multidisiplin ini sangat penting untuk membuat diagnosis yang tepat sehingga dapat mengoptimalkan terapi yang diberikan.

Katakunci : Chronic osteomyelitis, Langerhans cell histiocytosis

Abstract

Background*: Langerhans cell histiocytosis is a benign bone lesion that usually affects children and young adults. Established the diagnosis of Langerhans cell histiocytosis has its own challenges because in addition to being a rare case, histopathologically Langerhans cell histiocytosis has an image like other inflammatory processes. We report a case in a 4-year-old boy with complaints of a slow-growing lump, a dense, elastic consistency in the head area. The results of A contrast-enhanced head CT scan revealed multiple space-occupying lesions with bilateral parietal bone destruction. The histopathological image showed an impression of eosinophilic granuloma. The dominance of eosinophilic cells, lymphocytes, plasma cells, and other inflammatory cells in the bone can cause misdiagnosis as chronic osteomyelitis. The similarity of this histopathological appearance, in addition to reviewing the clinical manifestations and location of the lesion, analysis of cell morphology supported by immunohistochemistry is important to differentiated Langerhans histiocyte cells from other normal histiocyte cells. This multidisciplinary approach is very important to make a correct diagnosis so that the therapy given can be optimized.*

Keywords : *Chronic osteomyelitis, Langerhans cell histiocytosis*

I. INTRODUCTION

Langerhans cell histiocytosis (LCH) is an uncommon disease with an unknown cause; it is featured by exceeding and acute proliferation of Langerhans cells derived from bone marrow and mature eosinophils. The diagnosis of Langerhans cell histiocytosis has its own challenges, besides a rare case, histopathologically Langerhans cell histiocytosis has an image like other inflammatory processes, and it is often delayed because it resembles chronic osteomyelitis clinically and microscopically.[1] The cell origin of langerhans cell histiocytosis is closer to a myeloid dendritic cell than to an epidermal langerhans cell.[2] Its clinical manifestations vary and can involve a variety of organs.[3] The disease can form in any part of the body. The most affected organ is bone, especially the skull followed by the femur, mandible, and pelvis. The usual manifestations in the skull are pain and tumor formation.[4]

The spectrum includes localized-to-bone eosinophilic granuloma, and the rare multisystem syndromes Hand-Schu¨ller– Christian disease and Abt– Letterer– Siwe disease; the manifestations range from isolated bone lesions to multisystem disease.[5]

Eosinophilic granuloma (EG) is the mildest of localized LCH, and there are 2 common clinical forms: a single bone lesion (solitary) or multiple bone lesions (multiple). Eosinophilic granuloma (EG) mainly affects children, with the highest frequency in patients aged 5 to 10 years, and is most prevalent in males. Solitary EG comprises 70% of cases, with the most common site being the mandible (30%), followed by the skull (21%), vertebrae (13%), and extremities (13%), and rib and clavicle involvement are extremely rare (6%).[6]

The symptoms of LCH differ a lot depending on the location of the disease. They include otorrhea, mass in the temporal region, aural polyps, and deafness when LCH is located in the petrous ridge and mastoid of the temporal bone. Soft, tender, and painful mass is also a known manifestation in the skull .The histologic and immunophenotypic examination is the golden method in diagnosis. The critical importance of precise histopathological and IHC evaluation CD 1a and S-100 in distinguish between eosinophilic granuloma/ langerhans cell histiocytosis from other normal histiocytes entities. Early recognition and multidisciplinary management are essential to improve outcomes.[4,7]

II. CASE REPORT

A 4 year old boy was brought to the hospital with complaints of 2 lumps on his head the size of quail eggs, felt rubbery, grew slowly since 2 months before entered the hospital. A contrast-enhanced head CT scan showed multiple SOL, right and left os parietal bone destruction (Figure 1).

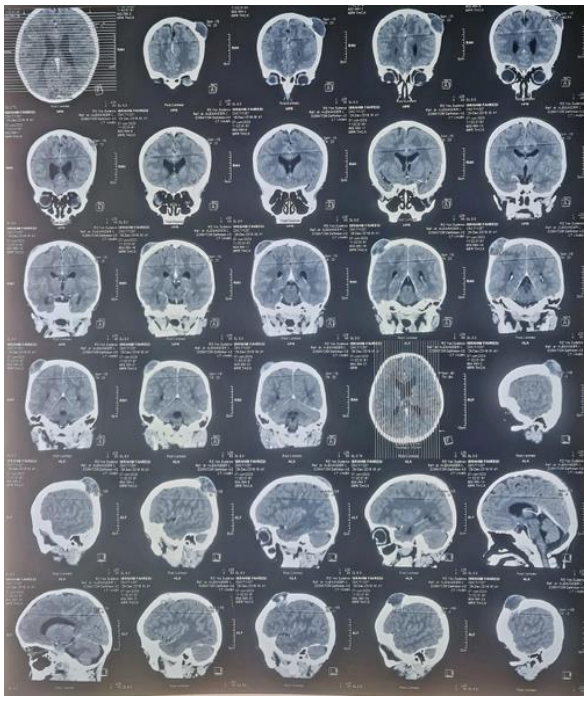

FIGURE 1. HEAD CT SCAN WITH CONTRAST SHOWED MULTIPLE SOL, RIGHT AND LEFT OS PARIETAL BONE DESTRUCTION

The results of the operation showed a reddish soft mass, destruction of the cranial bones, intact of duramater. Macroscopic the blackish brown mass measures 3.5x3x1 cm. Microscopic the tumor cells are arranged like sheets, round-oval cells, irregular nuclei, vesicular, grooved nuclei, pale cytoplasm, nucleoli present, numerous eosinophils, osteoclast-like multinucleated giant cells (Figure 2).

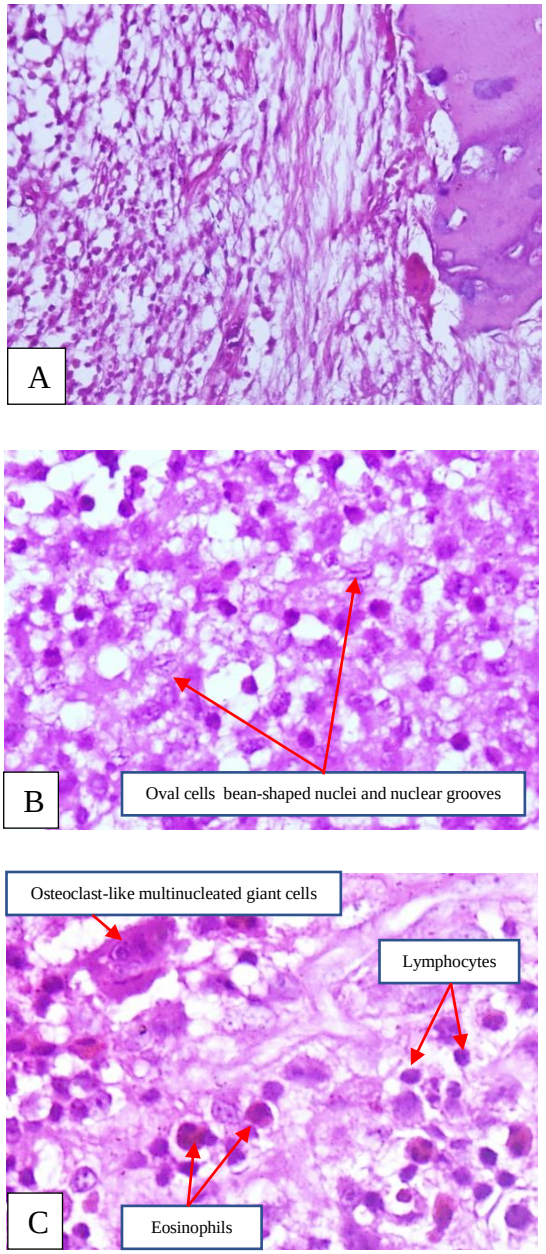

FIGURE.2. MICROSCOPICALLY. A. LANGERHANS CELL HISTIOCYTOSIS WITH MANY INTERMIXED LYMPHOCYTES AND EOSINOPHILS (HE, 100X). B, C. THE TUMOR CELLS ARE ARRANGED LIKE SHEETS, ROUND-OVAL CELLS, PALE CYTOPLASM WITH INDENTED BEAN-SHAPED NUCLEI AND NUCLEAR GROOVES, NUMEROUS EOSINOPHILS, OSTEOCLAST-LIKE MULTINUCLEATED GIANT CELLS (HE, 400 X).

Immunohistochemistry staining in langerhans cell histiocytosis, the histiocytes showed strongly and diffusely positive for S100 protein and positive express for CD 1a (Figure 3). Diagnosis of Langerhans cell histiocytosis was made based on histopathological and immunohistochemical examination.

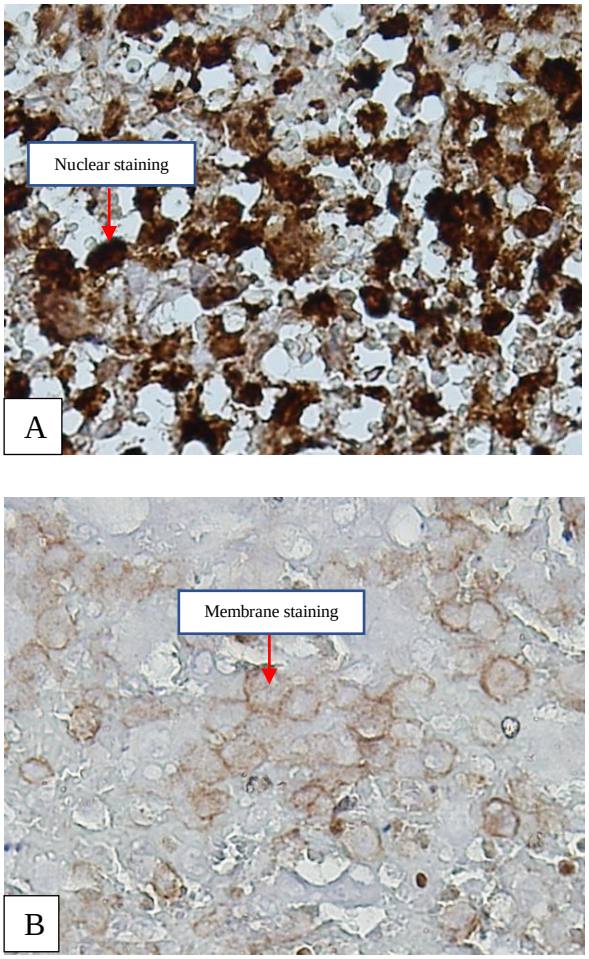

FIGURE.3. IMMUNOHISTOCHEMICAL STAIN. A.THE HISTIOCYTES SHOWED NUCLEAR AND CYTOPLASMIC STAINING FOR S100 PROTEIN. B. CELL MEMBRANE STAINING FOR CD 1A (400 X).

III. DISCUSSION

LCH most commonly affects the bone, although it may also affect the skin and lymph nodes. In LCH of the bone, common sites were vertebral bodies, long bones, and mandibles in children patients and the cranium and ribs in adults,[11] which is consistent with our findings.

The etiology of this disease is controversial, but several theories have suggested the relation of infection (e.g., with the Epstein– Barr virus), environment, immunology, genetics (gene mutation and chromosomal instability), smoking (especially for isolated pulmonary LCH), and neoplastic process with LCH. In this disease, lesional tissue cells have clonal proliferative characteristics, which may indicate that the innate lesion of LCH involving the patient is a tumor. Some scholars have considered LCH as a reactive and hyperplastic disorder; whereas, others have mentioned that LCH can be related to cytokine mediation, immunologic derangement, and viral infections.[3]

Some authors suggesting that LCH is an immune system disorder that manifests with hypersensitivity to unknown antigens and stimulation of the histiocyte-macrophage system. The clonal proliferation of Langerhans cells and the increased expression of several tumor-associated factors have resulted in speculations that LCH is a tumor. In addition, although the specific pathogenic microorganism has not been identified due to its self-limitation and response to steroids and antibiotics, some researchers suspect the disease' s origin is an inflammatory response.[9] It is not clear etiology was found in this patient.

Depending on the different clinical manifestations, LCH had been classified conventionally by the International Histiocyte Society into three different types: type I-Eosinophilic granuloma (chronic focal LCH), type II—Hand- Schüller- Christian disease (chronic disseminated LCH), and type III—Letterer– Siwe disease (acute disseminated LCH).[6] However, because clinical findings are widely manifested, the disease has also been classified into unifocal and multifocal forms; depending on the extent of its spread throughout the body. The unifocal form presents only one destructive lesion in an organ, affecting bones or skin (80% of cases), liver, spleen, brain, and lymph nodes more frequently.[6] The disease manifests itself in a variety of ways, from isolated disease that resolves on its own to life-threatening multisystem disease, with a 20% mortality rate. In this patient were found osteolytic bone lesion in temporal region.

LCH is a rare disease; thus, it may be at a high risk of being under or misdiagnosed. Kim et al. reports LCH of the jaw, a mimicker of osteomyelitis on CT and MRI. Claire et al. reports LCH as a great imitator because affects many organs. Histologic evaluation of LCH is often enough to differentiate it from the many clinical mimickers.[11,12] Although cases showed mimicker based on radioclinical findings, the present case showed mimicker with other inflammation in pathological findings. Previous study have been described LCH as giant granuloma because there are granulomatous reaction shows extensive aggregates of histiocytes and clusters of eosinophils. [13]

Another pathological findings were characterized by the infiltration of involved tissues with large number of unusual histiocytes. Subsequently, these histiocytes were found similar to Langerhans cells normally present in the skin and other epithelia.[14] Royasa Shakya et al. revealed a case of LCH in hard palate with histopathological examination, a highly cellular connective tissue stroma with numerous scattered round to polygonal-shaped cells with pale cytoplasm was evident. On higher magnification a characteristic coffee bean-shaped and oval nuclei which were folded or indented with some cells having grooved nuclei were observed. Background stroma was abundant with eosinophils. The histopathological features along with clinical findings and altered serum biochemical parameters were suggestive for Langerhans cell histiocytosis.[10]

LCH is mostly diagnosed by biopsy and microscopic examination of the lesion. Histological sampling should be performed after adequate local imaging, an essential step in diagnosing and treating bone lesions. Definitive diagnosis of LCH based on its histopathology needs S100 and CD1a positive immunohistochemistry or the presence of Birbeck granules under electron microscopy. Other indicating factors that can lead to a specific diagnosis of LCH are: Langerin (CD207), Vimentin, CD45, ecto-ATPase, and simultaneous expression of CD68, MIB-1, peanut agglutinin, and placental-like alkaline phosphatase.[3,9] This case, immunohistochemistry was performed using monoclonal antibodies against S-100 (Dako) and CD1a (Abcam) using a streptavidin-biotin method. This case found expression S100 protein positive in the nucleus and cytoplasm and CD1a positive in the cell membrane.

The differential diagnosis for LCH is other cutaneous histiocytosis, Ewing sarcoma, tuberculosis, multiple myeloma, lymphoma, primary bone malignancy and other osteolytic lesions.[3,9] When an unclear osteolytic bone lesion is presented, LCH must be kept in mind.

The prognosis of this disease can be based on the age of the patient, the number of organs that are involved, and the stage of the functional lesion. The prognosis of a single organ is proven to be better than multiorgans. Adult LCH has mostly shown a better prognosis; although, the prognosis in patients with lung, liver, spleen, and bone marrow involvement is poor; in these cases, the response to early treatment is relatively poor as well.[3] This patient have favorable prognosis because involved single organ.

III. CONCLUSION

In this case, due to the resemble of histopathology feature, it is important to differentiate langerhans cell histiocytosis from other normal histiocytes which are negative for all two stains. Therefore, a careful assessment must be made with consideration to the LCH. The clinical, radiological, histopathological and immunohistological are important for accurate diagnosis.

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