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Case study

Classic Hodgkin lymphoma with osseous involvement mimicking Langerhans cell histiocytosis in a child☆

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Summary Hodgkin lymphoma (HL) commonly presents superficial lymphadenopathy. In addition, HL cells can arise in various organs including the liver and spleen as an extranodal lymphoma. HL in bone is unusual at the initial diagnosis, although some cases show late-stage localization of lymphoma cells to bone. We report the rare case of a young patient with cranial bone classic HL, presumably originating from the skull without any involvement of lymph nodes. As the main clinical manifestation was only tumor mass in the skull without osteoscopic pain, the tentative diagnosis of Langerhans cell histiocytosis was histologically confirmed by an excisional biopsy. Before the final pathological diagnosis as classic HL, we noticed several small lesions in extranodal regions through systemic surveys, suggesting that the cranial lesion appeared antecedent to those lesions. This is a rare and instructive case of cranial bone HL for which a histological diagnosis has been meticulously made.

1. Introduction

Although Hodgkin lymphoma (HL) can develop almost anywhere in the body, it frequently starts in lymph nodes, especially lymph nodes of the neck, chest, and under the arms. Primary onset in bone is extremely rare, although HL in bone has been implicated in the late stage. A few case reports of primary bone HL at the initial diagnosis mainly mentioned the origins in the humerus, femur, and vertebra, so-called long bones [1,2]. Moreover, in cases involving young patients, the lack of typical clinical and radiological findings is problematic. We report here the rare case of a child with classic

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Hodgkin lymphoma (cHL) accompanied by cranial bone involvement. Preoperative diagnosis based on the clinical features and the radiological findings strongly indicated Langerhans cell histiocytosis (LCH), a group of idiopathic of disorders accompanied by various hematopoietic cells. Intraoperative frozen-section analysis using the surrounding connective tissue of the skull was not inconsistent with LCH; however, further analysis using permanent sections of the surgical material by detailed immunohistochemistry revealed cHL with Reed-Sternberg cells showing $CD30^{+}$, $CD15^{+}$, $Pax\text{-}5^{+}$, $CD1a^{-}$, and $Langerin^{-}$. Based on the clinical manifestations, radiological findings, and histological studies, we diagnosed an atypical onset of cranial bone HL.

2. Materials and methods

Bone tissue resected from the skull was fixed in 10% buffered formalin and subjected to decalcification prior to paraffin embedding. Soft granulation tissues firmly attached to the skull were separated and fixed in 10% buffered formalin. Hematoxylin and eosin (H-E) staining and Papanicolaou staining were performed according to routine laboratory methods. Immunohistochemical studies were performed using a Ventana Benchmark Ultra Autostainer (Ventana Medical Systems, Tucson, AZ) after antigen retrieval on 4-μm–thick formalin-fixed, paraffin-embedded tissue for the following antibodies: CD1a (clone 010, 1:50; Dako, Santa Clara, CA), CD68 (clone KP1, 1:200; Dako), S100 (polyclonal, 1:3000; Dako), Langerin (clone 12D6, 1:200; Abcam, Cambridge, UK), CD30 (clone Ber-H2, diluted; Ventana), CD15 (clone MCS-1, 1:50; Nichirei, Tokyo, Japan), Pax-5 (clone SP34, diluted; Ventana), CD20 (clone L26, diluted; Nichirei), CD79a (clone JCB117, diluted; Nichirei), Bob1 (polyclonal, 1:500, Santa Cruz, Dallas, TX), and Oct-2 (polyclonal, 1:2000, Santa Cruz). Ventana's Cell Conditioning 1 (CC1), a Tris-based buffer with pH8.5, and Protease 1 were used for antigen retrieval. The conditions were as follows: 36 minutes at 100°C in CC1 (for CD1a); 8 minutes in Protease 1, (for CD68); 4 minutes in Protease 1 (for S100); 64 minutes at 100°C in CC1 (for all other antibodies).

Intraoperative cytology (IC) was performed on imprint specimens prepared from the surrounding connective tissue of skull. Samples underwent wet fixation for 1 minute in 95% ethanol, followed by convenient and rapid H-E staining and cytological examination with a light microscope [3].

3. Case report

A 9-year-old Japanese girl presented with an asymptomatic growing mass in the left temporoparietal area. Skull radiographs demonstrated round foamy shadows indicating osteolytic changes. Concordantly, computed tomography (CT) and magnetic resonance imaging showed a tumor mass in the skull destroying normal bone (Fig. 1). A whole-body

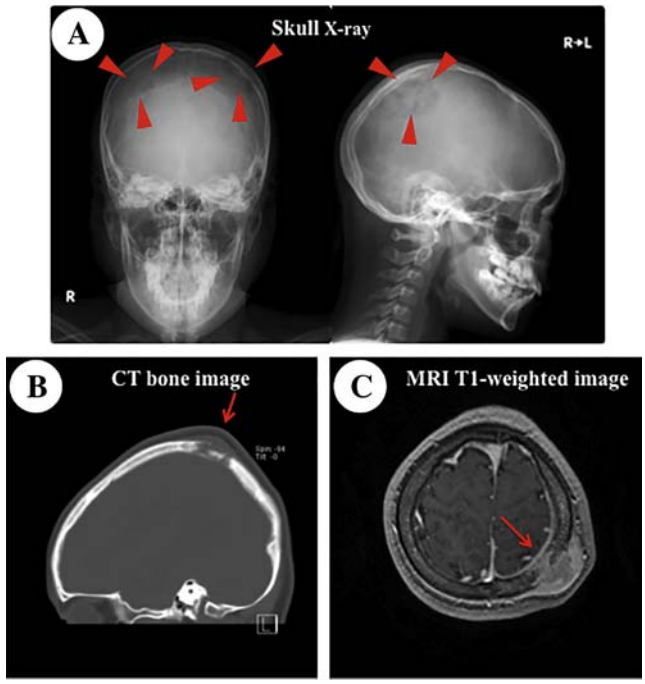

Fig. 1 Radiological examinations of the skull-associated mass lesion. A, Skull radiographs showed round foamy shadows indicated by arrowheads. B and C, A sagittal bone image by CT and a horizontal image by T1-weighted magnetic resonance imaging are shown. Arrows indicate the growing tumor mass accompanied by destruction of the cranial bone.

physical examination revealed no other lesions including lymphadenopathy. Preoperative diagnosis based on the clinical features and the radiological findings of the skull strongly indicated LCH. Three months later, she was hospitalized in the university hospital. The results of hematologic tests were as follows: red blood cell count $4.75 \times 10^{6}/\mu$L, hemoglobin 12.1 g/dL, white blood cell count $13.6 \times 10^{3}/\mu$L, and platelet count $508 \times 10^{3}/\mu$L. Blood biochemistry data were within the normal range, except for elevated C-reactive protein (6.275 mg/dL). A preoperative biopsy was not performed. The lesion of the skull was surgically resected to prevent progressive bone destruction. Intraoperative frozen-section analysis using the surrounding connective tissue of the skull was performed, revealing massive infiltration by neutrophils and eosinophils and scattered atypical histiocyte-like cells with large nuclei, which were not inconsistent with LCH.

The resected skull bone with surrounding soft tissues was submitted for pathological examination. The skull specimen revealed that granulation tissue with massive inflammatory cells developed while destroying the bone trabeculae and extending to the subcutaneous tissue (Fig. 2A). Inflammatory cells consisted of lymphocytes, eosinophils, histiocytes, and neutrophils (Fig. 2B). In the mixture of these inflammatory cells were scattered atypical larger cells with light eosinophilic cytoplasm and irregularly lobular nuclei (Fig. 2C; arrows). These atypical cells possessed one or a few conspicuous eosinophilic nucleoli. A small number of these atypical cells