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Case Report

Recurrent multifocal Langerhans cell histiocytosis of the mandible and maxilla in a 46-year-old man: a pathologic case report

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Abstract: A 46-year-old man consulted to a private dental clinic for tooth extraction, where he was indicated to have abnormal shadow in the right mandible. The patient was referred to our clinic hospital. X-ray examination revealed an osteolytic lesion (3 x 2 x 1 cm), and tumor excision was performed. Pathological diagnosis was difficult. The tumor consisted of round cells with moderate atypia. Nuclear grooves were recognized. Immunohistochemistry showed positive CD1a and S100 protein. The Ki67 labeling was 16%. The author diagnosed the lesion as Langerhans cell histiocytosis (LCH). The patient became free of tumor, and discharged. However, the tumor recurred 5 years later. Two osteolytic lesions were found: one is mandible (3 x 1 x 1 cm), and another was maxilla (0.5 x 0.5 x 0.4 cm). Tumorectomy with wide margins were performed. The pathological diagnosis was LCH in both lesions. Whole body CT, MRI and PET were performed, but revealed no tumors. The patient is now free from tumor, and is followed up 7 years after the first presentation.

Keywords: Langerhans cell histiocytosis (LCH), mandible, pathology, therapy

Introduction

Langerhans cell histiocytosis (LCH) is defined as a neoplastic proliferation of Langerhans cells, with expression of CD1a and S100 protein, and the presence of Birbeck granules by ultrastructural examination [1]. LCH is also called histiocytosis X, Langerhans cell granulomatosis, and eosinophilic granuloma. The incidence of LCH is about 5 per million, with most cases occurring in childhood [2]. LCH may be associated with malignant lymphoma [3]. LCH is classified into unifocal disease of one organ, multifocal disease of one organ, and multisystem disease involving more than two organs, depending on the extent of involvement of LCH [1]. The sites of involvement are bones (skull, femur, pelvis, ribs, and other bones), lymph nodes, skin, lung, and other organs. The mandible is also involved by LCH, and there have been several case reports of mandibular LCH [4-10].

The author herein reports a multifocal LCH involving the mandible in a 46-year-old man, with a special emphasis on pathologic findings.

Case report

A 46-year-old man consulted to a private dental clinic for tooth extraction, where he was indicated to have abnormal shadow in the right mandible. Then, the patient was referred to oral surgery division of our hospital. X-ray examination revealed a small osteolytic lesion (3 x 2 x 1 cm) (**Figure 1**), and tumor excision was performed with a frozen section. In frozen section, the author identified atypical cells with hypercellularity; the frozen section diagnosis was low grade malignant tumor suggestive of plasmacytoma. In permanent sections, pathological diagnosis was difficult. The tumor consisted of round cells with moderate cellular atypia (**Figure 2**). Nuclear grooves were recognized (**Figure 3**). No eosinophilic abscess was recognized. There was much inflammatory infiltration.

The author performed an immunohistochemical study was performed, with the use of Dako Envision method (Dako, Glostrup, Denmark), as described previously [11-13]. The antibodies used were as follows: pancytokeratin (AE 1/3, Dako), pancytokeratin (polyclonal wide, Dako),

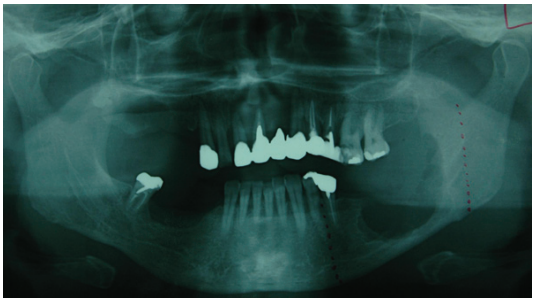

Figure 1. X-ray appearances at recurrence. Vague tumor formation is seen in the mandible.

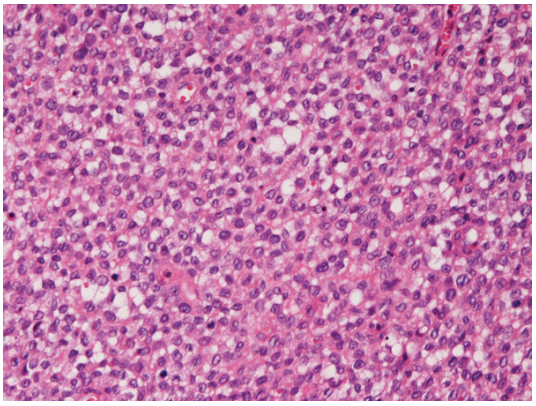

Figure 2. The tumor cells show hyperchromatic nuclei. HE, x100.

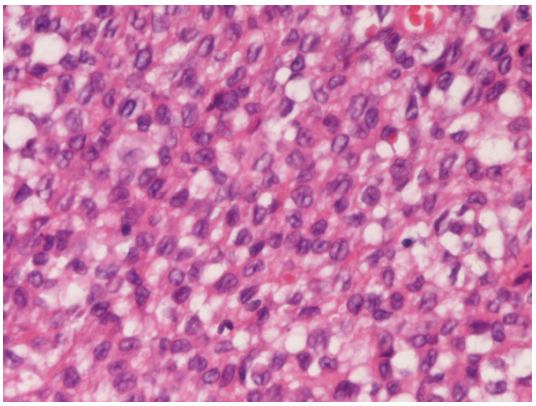

Figure 3. Higher power view. The tumor cells show vesicular nuclei and nuclear grooves. Nucleoli are not prominent. HE, x200.

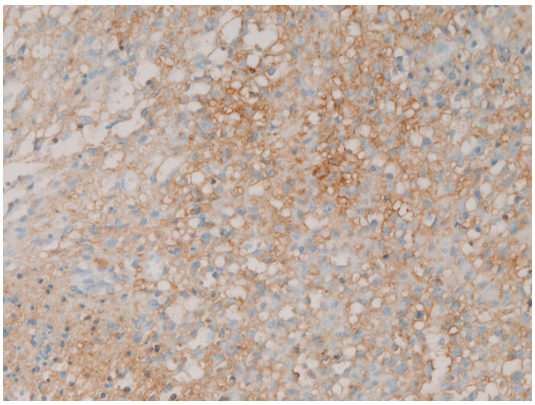

Figure 4. The tumor cells are positive for S100 protein. X200.

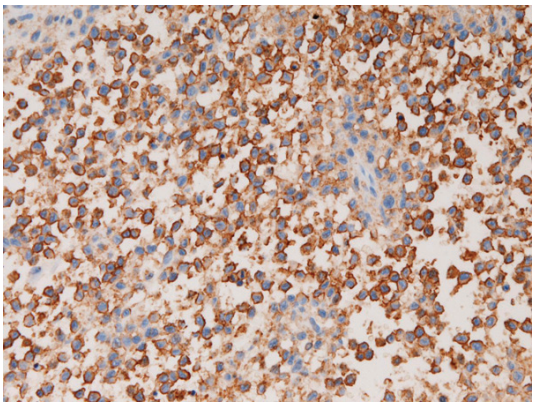

Figure 5. The tumor cells are positive for CD1a. x200.

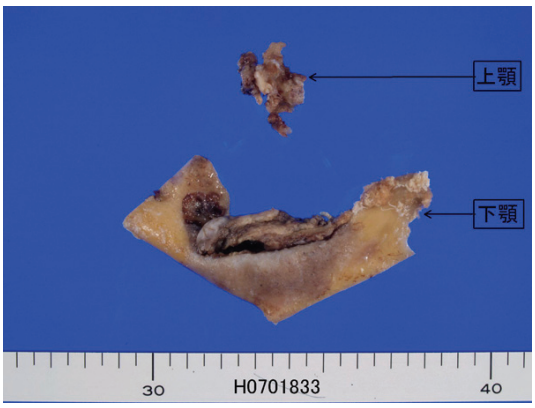

Figure 6. Resected mandible (lower) and a part of maxilla (upper). Tumor formation in the mandible is apparent.

pancytokeratin (CAM5.2, Beckton-Dickinson, CA, USA), epithelial membrane antigen (E29, Dako), CD45 (LCA, Dako), CD20 (L26, Dako), CD45RO (UCHL-1, Dako), κ-light chain (polyclonal, Dako), λ-light chain (polyclonal, Dako), α-heavy chain (polyclonal, Dako), λ-heavy chain (polyclonal, Dako), μ-heavy chain (polyclonal, Dako), δ-heavy chain (polyclonal, Dako), ε-heavy

chain (polyclonal, Dako), IgA (polyclonal, Dako), IgG (polyclonal, Dako), IgM (polyclonal, Dako), IgD (polyclonal, Dako), CD68 (KP-1, Dako), vimentin (Vim3B4, Dako), synaptophysin (polyclonal Dako), chromogranin (DAK-A3, Dako), S100 protein (polyclonal, Dako), CD1a, (O10, Dako), desmin (D33, Dako), α-smooth muscle antigen (1A4, Dako), myoglobin (polyclonal. Dako), p53 protein (D07, Dako), and Ki-67 antigen (MIB-I, Dako). Immunohistochemically, the tumor cells were positive for vimentin, S100 protein (**Figure 4**), and CD1a (**Figure 5**), but negative for cytokeratins, epithelial membrane antigen, vimentin, CD45, CD20, CD45RO, κ-light chain, λ-light chain, α-heavy chain, λ-heavy chain, μ-heavy chain, δ-heavy chain, ε-heavy chain, IgA, IgG, IgM, IgD, synaptophysin, chromogranin, desmin, α-smooth muscle antigen, myoglobin, and p53 protein. The Ki-67 labeling was 16%. The author diagnosed the tumor as LCH.

The patient became free of tumor, and discharged. However, the tumor recurred 5 years later, when two osteolytic lesions were found: one is mandible (3 x 1 x 1 cm), and another was maxilla (0.5 x 0.5 x 0.4 cm). Tumorectomy with wide margins were performed. Grossly, the tumors were seen in the bones near the gum (**Figure 6**). The pathological diagnosis was LCH in both lesions. Whole body CT, MRI and PET were performed, but revealed no tumors. The patient is now free from tumor, and is followed up 7 years after the first presentation.

Discussion

In the present case, pathological diagnosis was difficult. No eosinophilic abscess was present. The nature of tumor cells was uncertain on HE sections. However, nuclear grooves were recognized, so the author included in S100 protein and CD1a in the immunohistochemical study. Immunohistochemically, the tumor cells were positive for vimentin, S100 protein, and CD1a, but negative for other antigens examined. Thus, the diagnosis of LCH was obtained. Regrettably, no ultrastructural study was performed in the present case. The pathological diagnosis of the recurrent tumors were relatively easy, because they were similar to the diagnosis of the original tumor.

Clinically, LCH is a disease of childhood or young adult [2]. Review of the literature of the mandibular LCH identified that the oldest patient was 43-year-old (6). The present patient was 46-year-old man, suggesting that mandibular LCH may occur in middle aged persons.

In the present study, the tumor recurred and new maxillary tumor emerged (multifocal disease), suggesting that unifocal LCH may progress into multifocal disease. The LCH recurrence in the present case is also reported in the mandibular LCH [4, 8]. The rare of recurrence is 60% [10]. The clinical course of LCH is related to the number of organs affected at presentation. Bone LCH shows better prognosis than visceral organ LCH (1). There is a progression of unifocal LCH into multisystem disease in about 10% of patients [1]. The overall survival of patient with unifocal disease is higher than 95%. In unilocular LCH, the treatment of choice is surgical curettage. In recurrent and multisystem disease, chemoradiation should be considered [10].

Conflict of interest statement

The author has no conflict of interest.

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