Langerhans cell histiocytosis of the jaw, a mimicker of osteomyelitis on CT and MR images

A retrospective analysis

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Abstract

Differential diagnosis of Langerhans Cell Histiocytosis (LCH) in the jaw is essential for early treatment including systemic therapy. Records of 17 patients (6 men and 11 women; mean age, 14 years) with histologically confirmed LCH were reviewed. All the lesions occurred in the mandible. Most of the cases (n=12) were intraosseous type LCH, only 5 patients had alveolar type LCH. Patients complained of facial swelling and pain most likely. In the 14 patients who underwent CT and/or MR imaging, all LCH lesions were osteolytic, with a mean size of 23 mm. LCH presented as expansile lesions with periosteal new bone formation, perilesional sclerosis, fluid attenuation/signal within the lesion, and inflammatory changes in adjacent soft tissues on CT/MR images. Considering the major symptoms of LCH were swelling and pain, the differential diagnosis of LCH from osteomyelitis might be more difficult. The differential diagnosis for osteolytic lesions of the jaw with surrounding inflammatory changes should include LCH, especially in young patients.

Abbreviations: CT = computed tomography, LCH = Langerhans cell histiocytosis, MR = magnetic resonance.

Keywords: histiocytosis, jaw, Langerhans-cell, magnetic resonance imaging, tomography, X-ray computed

1. Introduction

Langerhans cell histiocytosis (LCH) is a rare disease characterized by the proliferation of Langerhans cells. Formerly known as histiocytosis X, LCH includes Letterer-Siwe disease, Hand-Schuller-Christian disease, and eosinophilic granuloma. Although LCH could affect any organ, bones were most affected, especially vertebral bodies, long bones, and jaw.1,2 Patients with LCH often initially present with jaw symptoms.3 The exact differential diagnosis of LCH in the jaw is essential to oral and maxillofacial surgeons for early treatment.

Radiographs of LCH in the jaw are challenging to interpret because the disease may mimic a wide variety of conditions, such as periapical cysts, odontogenic or non-odontogenic tumors, osteomyelitis, vascular malformations, and malignancies.4 Although multiplanar imaging modalities, such as computed tomography (CT) scans and magnetic resonance (MR) imaging, have been used actively in the diagnosis of head and neck lesions, they have rarely been used to investigate the characteristics of LCH in the jaw. Most of the previous studies, which established radiographic features of LCH in the jaw, were based on plain radiography.4,5 Analyzing LCH, arising in the jaw, through multiplanar images might be able to present another features not observed on plain radiographs.

This study aimed to present clinico-radiologic features of LCH in the jaw, with special emphasis on CT and MR imaging characteristics, and to alert surgeons to the possibility of misdiagnosis.

2. Materials and methods

2.1. Patients

This retrospective study was approved by the Institutional Review Board of Seoul National University Dental Hospital (IRB071/07-14). All cases of LCH recorded in electronic pathology records of the Seoul National University Dental Hospital between January 2001 and December 2017 were reviewed. Seventeen consecutive patients with histopathologically confirmed LCH in the jaw were included in the study. Information from the patients’ records included age, sex, chief complaint, location of the lesion, history of LCH at another site, and treatment method. The lesions were categorized as alveolar type, if they were confined to the alveolar bone, or intraosseous type, if they were found outside the alveolar bone.

2.2. Image analysis

Because most patients were referred from other hospitals or clinics, panoramic radiographs and CT and MR images were obtained from a variety of scanners.

We retrospectively reviewed panoramic radiographs, CT, and MR images obtained from the 17 patients. Fourteen patients underwent CT (n=13) and/or MR imaging (n=4), and 3 patients underwent both CT and MR examinations.
3. Results

The subjects consisted of more females than males (M:F = 6:11). The average age was 14 years (range, 11 months to 59 years). Clinical and panoramic radiographic findings of all patients are summarized in Table 1. Patients complained of facial swelling (76.5%), pain (35.3%), tooth mobility (11.8%), and trismus (6%). Fifteen patients reported no history of LCH, though 2 patients had a history of LCH in the iliac bone and the lung, respectively. All the lesions occurred in the mandible. Twelve patients showed intraosseous type LCH, and only 5 patients had alveolar type LCH. The locations of the lesions were as follows: 7 mandibular bodies, 5 mandibular rami, 4 mandibular angles, and 1 mandibular condyle.

On panoramic radiographs, the margin was ill-defined in 9 cases (60%) and well-defined in 6 cases (40%). Periosteal new bone formation was detected in 6 lesions (40%), and sclerosis of adjacent bone was found in 13 of the lesions (87%).

CT and MR imaging features are summarized in Table 2. The mean size of the lesions was 23.8 mm (range, 19–31 mm). Four of the 8 cases with lesions located adjacent to the tooth root or tooth germ showed displacement of the tooth root or tooth germ. All 14 cases with CT and/or MR images exhibited cortical bone destruction, 12 (86%) of which showed expansion (Figs. 1–4). Twelve lesions (86%) presented with periosteal new bone formation (Fig. 2). The most common shapes of osteolytic margins were lobulated (79%), followed by infiltrative (14%) and round (7%). Sclerosis of the surrounding bone was demonstrated in all but 1 case. Of the 13 lesions with contrast-enhanced images, 11 lesions (85%) had various amounts of fluid attenuation or signal intensity throughout the lesion based on CT or MR imaging.

Findings were based on the consensus of 2 experienced oral and maxillofacial radiologists who conducted the imaging analyses and who had been practicing for >15 years.

4. Discussion

LCH is a rare and heterogeneous group of diseases of unknown etiology.[6] LCH comprises the neoplastic proliferation of Langerhans cells, which are dendritic mononuclear cells usually found in the epidermis, mucosa, lymph nodes, and bone marrow.[7] Although studies showed male predominance,[8,9] the present study showed a slight female predominance (M:F = 6:11); this may be due to the small number of cases. LCH can be found in any age group, however, children younger than 15 years of age are predominantly affected,[11] which is consistent with our findings.

LCH can present as a solitary lesion or as multiple lesions within a single organ, and it can also occur in multiple organs in a single patient. LCH most commonly affects the bone, although it...
may also affect the skin and lymph nodes.\textsuperscript{10} In LCH of the bone, common sites were vertebral bodies, long bones, and mandibles in children patients and the cranium and ribs in adults.\textsuperscript{1} Only about 10\% of cases were arising from the jaw.\textsuperscript{11} In the present study with LCH of the jaw, all lesions were located in the mandible, particularly in the mandibular body and ramus. Previous studies also showed that the most common location in the mandible was the posterior region.\textsuperscript{14,12} However, the case arising in the mandibular ramus has been rarely reported.\textsuperscript{8} This might be because we included both alveolar and intraosseous type of gnathic LCH, while most previous studies on gnathic LCH were about the alveolar type. One-third of the present cases were located in the mandibular ramus, which was much more than previous reports.

| Case no. | Modality | Size (mm) | Displacement | Expansion | Cortical bone destruction | Periosteal reaction | Shape of osteolytic lesion | Surrounding sclerosis | Inflammatory change of surrounding soft tissue | Fluid attenuation/signal | Internal |
|----------|----------|-----------|--------------|-----------|---------------------------|-------------------|--------------------------|-------------------|-------------------------------|----------------------|----------|
| 3        | NECT     | 25        | -            | -         | +                         | -                 | Lobulated                | +                 | +                            | n/a                  | Unknown |
| 4        | CECT     | 30        | -            | -         | +                         | +                 | Lobulated                | +                 | -                            | +                    | Mixed    |
| 5        | CECT     | 31        | B            | +         | +                         | +                 | Lobulated                | n/a               | +                            | +                    | Fluid    |
| 7        | MR (CE)  | 23        | +            | B         | +                         | +                 | Lobulated                | n/a               | +                            | +                    | Fluid    |
| 8        | CECT     | 21        | n/a          | BL        | +                         | +                 | Infiltrative             | +                 | +                            | -                    | Solid    |
| 9        | MR (CE)  | 23        | n/a          | B         | +                         | +                 | Lobulated                | +                 | +                            | +                    | Mixed    |
| 10       | CECT     | 23        | n/a          | BL        | +                         | +                 | Lobulated                | +                 | +                            | +                    | Mixed    |
| 11       | CECT     | 19        | n/a          | B         | +                         | +                 | Ovoid                    | +                 | +                            | +                    | Mixed    |
| 12       | CECT     | 26        | +            | B         | +                         | +                 | Lobulated                | +                 | +                            | +                    | Fluid    |
| 13       | CECT     | 22        | n/a          | BL        | +                         | +                 | Lobulated                | +                 | +                            | +                    | Mixed    |
| 14       | CECT     | 24        | +            | BL        | +                         | +                 | Lobulated                | +                 | +                            | +                    | Mixed    |
| 15       | CECT     | 24        | n/a          | BL        | +                         | +                 | Lobulated                | +                 | +                            | +                    | Mixed    |
| 16       | CECT     | 23        | -            | B         | +                         | +                 | Lobulated                | +                 | +                            | +                    | Mixed    |
| 17       | CECT     | 20        | -            | B         | +                         | +                 | Lobulated                | +                 | +                            | +                    | Fluid    |

\textsuperscript{8} = buccal, \textsuperscript{BL} = buccolingual, \textsuperscript{CBCT} = cone-beam computed tomography, \textsuperscript{CECT} = contrast-enhanced computed tomography, \textsuperscript{MR (CE)} = magnetic resonance (contrast-enhanced), \textsuperscript{NECT} = non-enhanced computed tomography.

**Figure 1.** Case 8: Langerhans cell histiocytosis in the left condyle in an 11-year-old boy. Panoramic radiograph (A), axial contrast-enhanced computed tomography (B), fat suppressed T2-weighted (C), and fat suppressed contrast-enhanced T1-weighted MR images (D) show an ill-defined, infiltrating lesion in the condyle. Note the fluid signal intensity within the lesion with hyperintense T2 signal intensity and non-enhancement. MR = magnetic resonance.
Gnathic LCH lesions can be classified as either alveolar, in which the lesion is confined to the alveolar process, or intraosseous, in which the lesion is outside the alveolar bone. This classification is meaningful because a differential diagnosis depends on the location of LCH lesions in the jaw. In the present study, 5 patients had alveolar LCH, and 12 patients had intraosseous LCH. In the previous reports, patients usually present with a toothache, tooth mobility, and symptoms associated with periodontal disease, such as swelling, bleeding, and gum ulceration in alveolar LCH. These symptoms were similar to those with alveolar LCH in the present study. The radiographic appearance of alveolar LCH in the present study was also the scooped-out alveolar bone destruction, commonly centered in the middle of roots. On the other hand, most patients with intraosseous LCH present with facial swelling and pain at the involved site. The radiographic features of intraosseous LCH are central osteolytic destruction with an expansion of the jaw, periosteal reaction, or fracture of the cortical bone. Because of these features, intraosseous LCH could be mistaken for many other conditions, such as an odontogenic cyst, a tumor, osteomyelitis, and even a malignant tumor. Consistent with the previous studies, chief complaints of the patients who had intraosseous LCH were swelling and pain and most of the lesions showed ill-defined osteolysis with adjacent sclerotic changes on panoramic radiographs.

Although the appearance of gnathic LCH on plain radiographs is well-established, just a few reports describe CT and MR images of LCH of the jaw. Furthermore, these descriptions have been limited to alveolar LCH, showing only alveolar bone destruction and floating teeth. In the present study, we analyzed CT and/or MR images of gnathic LCH, most of which were the intraosseous type. Bone destruction, lamellar periosteal new bone formation, perilesional sclerosis, fluid attenuation or signal, and inflammatory changes in adjacent tissues were characteristic imaging features of gnathic LCH on CT and/or MR images. CT and/or MR imaging features of LCH arising in other bones have been reported relatively often, and these were consistent with the present study.

We found that several imaging features of LCH in the jaw were similar to those of osteomyelitis with geographic osteolysis. In the oral and maxillofacial area, pain and facial swelling, which were presented as the most frequent complaint in gnathic LCH of the present study, are the most common symptoms related to dental infection. So, the osteolytic lesion with fluid attenuation or edematous change could be easily misdiagnosed as osteomyelitis. Actually, most of the initial diagnosis of the present cases made by clinicians was osteomyelitis. In some of our patients studied, differentiating LCH of the jaw from osteomyelitis with abscess was difficult even though using multiplanar images. An 11-year-old boy, case number 8, visited our hospital with a complaint of preauricular pain, swelling, and mouth opening limitation. A diagnosis of septic arthritis of the left temporomandibular joint was considered. Based on CT and MR images, a diagnosis of osteomyelitis with abscess could not be ruled out because of the fluid attenuation/signal within the osteolytic lesion, a periosteal reaction, and inflammatory changes in adjacent soft tissues (Fig. 1). A 3-year-old girl, case number 12, was referred from another hospital seeking further evaluation and management of midfacial swelling and pain. She had been treated for osteomyelitis, supposedly originating from the right mandibular second
primary molar, but her symptoms persisted a month after root canal treatment and medication including antibiotics. The lesion along the buccal cortical expansion was shown on dental cone-beam CT imaging, and fluid signal intensity with adjacent inflammatory changes was detected with MR images (Fig. 4). Although osteomyelitis with abscess formation was strongly suspected, LCH was also considered because of the mass effect that displaced the tooth germs. The presence of an expansile soft tissue mass with cortical bone destruction and displacement of tooth germs or roots helped differentiate LCH from osteomyelitis.

The histopathologic features of LCH are well characterized and easily recognizable by oral and maxillofacial pathologists. Aside from Langerhans cells, a variable number of eosinophils, neutrophils, plasma cells, lymphocytes, and multinucleated giant cells are observed in LCH lesions. To distinguish LCH from other inflammatory lesions, lesional Langerhans cells need to be identified using immunohistochemical staining of CD1a or CD-207.[19] It is well known that necrosis and hemorrhage may be present within the lesion, and this might explain the fluid attenuation or signal within the lesion on CT and MR images. In our study, a necrotic portion within the lesions was detected in a few cases based on histopathologic examination. Only a small number of patients underwent surgical removal of a lesion, so radiologic-histopathologic correlation could not be made for most cases in the present study. Inflammatory changes seen in surrounding soft tissues on CT and MR images might be related to the recruitment of inflammatory cells mediated by chemical mediators in LCH.[8]

There were some limitations in our study. The main limitations were the small number of patients and retrospective study design. The statistical analysis could not be performed because of the small sample size. The CT and MRI examinations were performed using a variety of scanners, as the cases were referred from various centers. Moreover, histopathologic correlation of total mass was not possible because most of our patients undertook a chemotherapy. A further study using a large number of LCH lesions is needed to investigate the fluid attenuation or signal intensity within the lesion and the inflammatory changes in surrounding soft tissues, through radiologic-histopathologic correlation.

LCH is presented on CT and/or MR images as an expansile lesion with periosteal new bone formation, sclerosis of adjacent bone, fluid attenuation/signal within the lesion, and inflammatory changes in surrounding soft tissues. Considering the major symptoms of LCH are swelling and pain, the differential diagnosis of LCH from osteomyelitis might be even more
difficult. The differential diagnosis for osteolytic lesions of the jaw with surrounding inflammatory changes should include LCH, especially in young patients.

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References

[1] DiCaprio MR, Roberts TT. Diagnosis and management of langerhans cell histiocytosis. J Am Acad Orthop Surg 2014;22:643–52.

[2] Badalian-Very G, Vergilio JA, Fleming M, et al. Pathogenesis of langerhans cell histiocytosis. Annu Rev Pathol 2013;8:1–20.

[3] Erdem AP, Kasmoglu Y, Seper E, et al. Oral manifestations may be the first sign of langerhans cell histiocytosis. Oral Health Prev Dent 2013;11:575–9.

[4] Li Z, Li ZB, Zhang W, et al. Eosinophilic granuloma of the jaws: an analysis of clinical and radiographic presentation. Oral Oncol 2006;42:574–80.

[5] Dagenais M, Pharoah MJ, Sikorski PA. The radiographic characteristics of histiocytosis X. A study of 29 cases that involve the jaws. Oral Surg Oral Med Oral Pathol 1992;74:230–6.

[6] Badalian-Very G, Vergilio JA, Degar BA, et al. Recent advances in the understanding of langerhans cell histiocytosis. Br J Haematol 2012;156:163–72.

[7] Swerdlow SH, Campo E, Harris NL, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon: IARC; 2008.

[8] Cho YA, Yoon HJ, Hong SD, et al. Hypothetical pathogenesis of eosinophilic infiltration in langerhans cell histiocytosis of the jaw. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:734–42.

[9] Wang J, Wu X, Xi ZJ. Langerhans cell histiocytosis of bone in children: a clinicopathologic study of 108 cases. World J Pediatr 2010;6:255–9.

[10] Bechan GI, Egeler RM, Arceci RJ. Biology of langerhans cells and langerhans cell histiocytosis. Int Rev Cytol 2006;254:1–43.

[11] Trosman SJ, Krakovitz PR. Pediatric maxillary and mandibular tumors. Otolaryngol Clin North Am 2015;48:101–19.
[12] dos Anjos Pontual ML, da Silveira MM, de Assis Silva Lima F, et al. Eosinophilic granuloma in the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:e47–51.
[13] Ryan PL, Piper KM, Hughes FJ. Langerhans cell histiocytosis: a diagnostic dilemma. Dent Update 2012;39:716–8.
[14] Key SJ, O’Brien CJ, Silvester KC, et al. Eosinophilic granuloma: resolution of maxillofacial bony lesions following minimal intervention. Report of three cases and a review of the literature. J Craniomaxillofac Surg 2004;32:170–5.
[15] D’Ambrosio N, Soohoo S, Warshall C, et al. Craniofacial and intracranial manifestations of langerhans cell histiocytosis: report of findings in 100 patients. AJR Am J Roentgenol 2008;191:589–97.
[16] Samet J, Weinstein J, Fayad LM. MRI and clinical features of langerhans cell histiocytosis (LCH) in the pelvis and extremities: can LCH really look like anything. Skeletal Radiol 2016;45:607–13.
[17] Zhang X, Zhou J, Chai X, et al. The application of x-ray, computed tomography, and magnetic resonance imaging on 22 pediatric Langerhans cell histiocytosis patients with long bone involvement: A retrospective analysis. Medicine (Baltimore). 97(17):e0411. doi:10.1097/MD.00000000000010411.
[18] An CH, An SY, Chos BR, et al. Hard and soft tissue changes of osteomyelitis of the jaws on ct images. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;114:118–26.
[19] Takahashi K, Harada M, Kimoto M, et al. Diagnostic confirmation of langerhans cell histiocytosis of the jaws with cd1a immunostaining: a case report. J Oral Maxillofac Surg 2003;61:118–22.