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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.

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Table 1

Clinical and panoramic radiographic findings in 17 patients with Langerhans cell histiocytosis of the jaw.

Case no.	Sex	Age (yrs)	Chief complaint	Location in the mandible	Type	Treatment	Panoramic radiograph Margin	Periosteal reaction	Displacement of tooth germ or root resorption	Surrounding sclerosis
1	M	4	Tooth mobility	Molars, bilateral	Alveolar	Curettage and chemotherapy	Well	–	+	+
2	F	34	Swelling	Premolar region	Alveolar	Chemotherapy	Ill	–	+	–
3	M	58	Pain	Premolar region	Alveolar	Curettage	Well	–	–	+
4	M	59	Swelling	Molar region	Alveolar	Radiation therapy	Well	–	–	+
5	F	4	Tooth loss during chemotherapy of pulmonary LCH	Molars, bilateral	Alveolar	Chemotherapy	Well	–	+	+
6	F	7	Swelling and pain	Angle	Intraosseous	Curettage and Indomethacin	Well	+	–	+
7	F	8	Swelling	Angle	Intraosseous	Chemotherapy	Ill	+	–	+
8	M	11	Preauricular pain and swelling	Condyle	Intraosseous	Curettage and Indomethacin	Ill	+	–	–
9	M	4	TMJ swelling	Ramus	Intraosseous	Chemotherapy	Ill	–	–	+
10	F	2	Swelling	Ramus	Intraosseous	Chemotherapy	Ill	–	–	+
11	M	15	Spontaneous pain	Molar region	Intraosseous	Curettage	Well	+	–	+
12	F	3	Mid face swelling	Molar region	Intraosseous	Chemotherapy	Ill	+	–	+
13	F	3	Swelling, pain, and trismus	Ramus	Intraosseous	Chemotherapy	Ill	–	–	+
14	F	1	Facial swelling	Ramus	Intraosseous	Chemotherapy	n/a	n/a	n/a	n/a
15	F	15	Facial swelling and pain	Ramus	Intraosseous	Chemotherapy	Ill	–	–	+
16	F	6	Facial swelling	Angle	Intraosseous	Chemotherapy	Ill	+	–	+
17	F	4	Facial swelling	Angle	Intraosseous	Chemotherapy	n/a	n/a	n/a	n/a

Ill = ill-defined, Well = well-defined.

Using panoramic radiographs (n = 15), several characteristics, such as location, margin, periosteal new bone formation, displacement or root resorption, and sclerosis of adjacent bone, were analyzed.

Using CT and MR images, size of the lesion, effects on surrounding structures, margin shape and features, internal characteristics, and inflammatory changes in adjacent soft tissues were investigated. The size of the lesion was measured at its greatest diameter. The effects on adjacent structures were as follows: displacement of root or tooth germ, cortical bone destruction and expansion, and periosteal new bone formation. The shape of the margin was classified as ovoid, lobulated, or infiltrative. Inflammatory changes in the surrounding soft tissues were recorded as positive when swelling and increased enhancement with/without streak appearance of the adjacent fat plane was seen on CT or MR images. The internal characteristics of the lesions were classified into solid, fluid, or mixed, where "fluid" was defined as lesions containing fluid-like 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.

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 in the lesion (Figs. 1, 3 and 4). Of particular interest, inflammatory changes in the surrounding soft tissues were associated with 12 lesions (85%) (Figs. 1–4).

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,[1] 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

Table 2

CT and MR imaging features in 14 patients of Langerhans cell histiocytosis.

Case no.	Modality	Size (mm)	Displacement of root or tooth germ	Expansion	Cortical bone destruction	Periosteal reaction	Shape of margin 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	+	–	–	Solid
7	MR (CE)	23	+	B	+	+	Lobulated	n/a	+	+	Fluid
8	CECT MR (CE)	21	n/a	BL	+	+	Infiltrative	+	+	+	Fluid
9	CBCT MR (CE)	23	n/a	B	+	+	Infiltrative	+	+	–	Solid
10	CECT	23	n/a	BL	+	+	Lobulated	+	+	+	Mixed
11	CECT	19	n/a	B	+	+	Ovoid	+	+	+	Mixed
12	CBCT MR (CE)	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

B = buccal, BL = buccolingual, CBCT = cone-beam computed tomography, CECT = contrast-enhanced computed tomography, MR (CE) = magnetic resonance (contrast-enhanced), NECT = non-enhanced computed tomography.

may also affect the skin and lymph nodes.[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.[1] Only about 10% of cases were arising from the jaw.[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.[4,12] However, the case arising in the mandibular ramus has been rarely reported.[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.

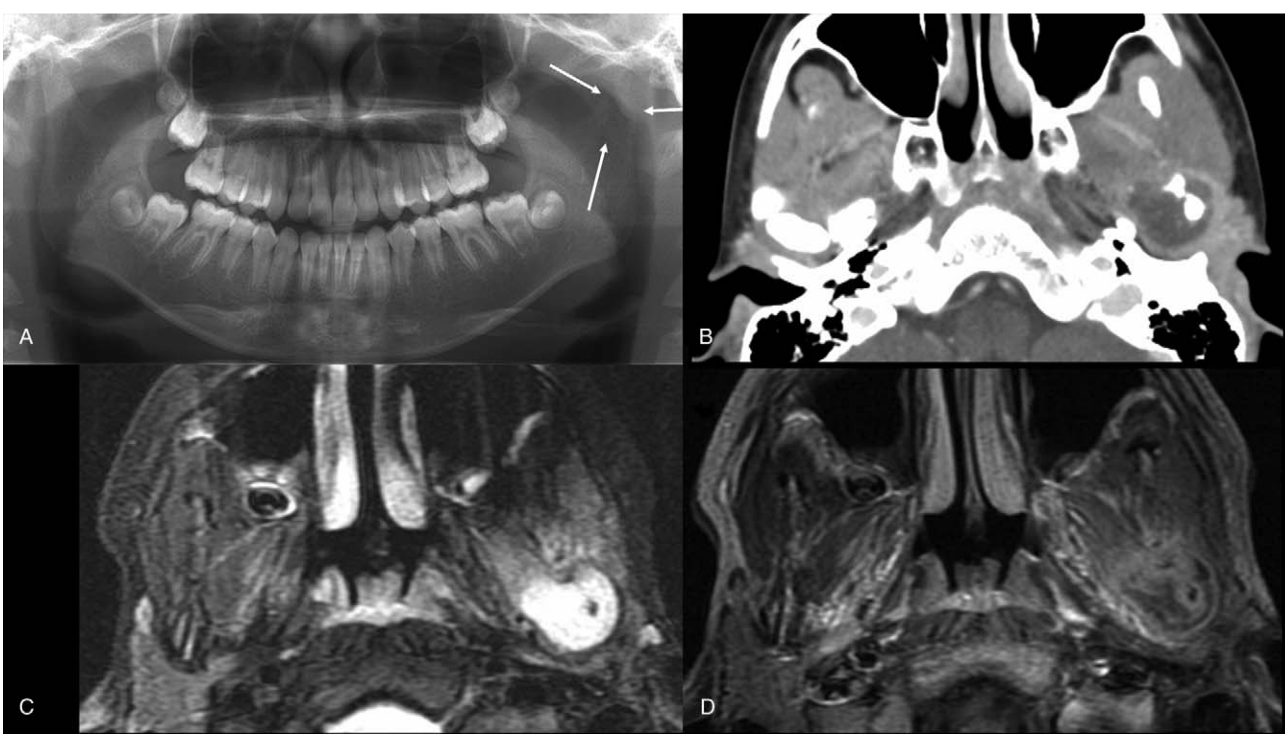

Figure 1. Case 8: Langerhans cell histiocytosis in the left condyle in an 11-year-old boy. Panoramic radiograph (A), axial contrast-enhanced computed tomography (B), fat suppressed T2-weighted (C), and fat suppressed contrast-enhanced T1-weighted MR images (D) show an ill-defined, infiltrating lesion in the condyle. Note the fluid signal intensity within the lesion with hyperintense T2 signal intensity and non-enhancement. MR = magnetic resonance.

Figure 2. Case 9: Langerhans cell histiocytosis in the left condylar neck. Coronal cone-beam computed tomography (A), fat suppressed axial T2-weighted MR images (B), and fat suppressed coronal contrast-enhanced T1-weighted MR images (C) show an ill-defined, expansile solid mass. Periosteal new bone formation is observed in the buccal and lingual aspects, and the margin of the osteolytic lesion is infiltrative (A). Note the diffuse inflammatory changes in surrounding masticatory muscles, showing hyperintense T2 signal intensity and enhancement (B, C). 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.[4] 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.[3,13] 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.[4] On the other hand, most patients with intraosseous LCH present with facial swelling and pain at the involved site.[4] The radiographic features of intraosseous LCH are central osteolytic destruction with an expansion of the jaw, periosteal reaction, or fracture of the cortical bone.[4,5] 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.[14,15] Furthermore, these descriptions have been limited to alveolar LCH, showing only alveolar bone destruction and floating teeth.[15] 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,[16,17] 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.[18] 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

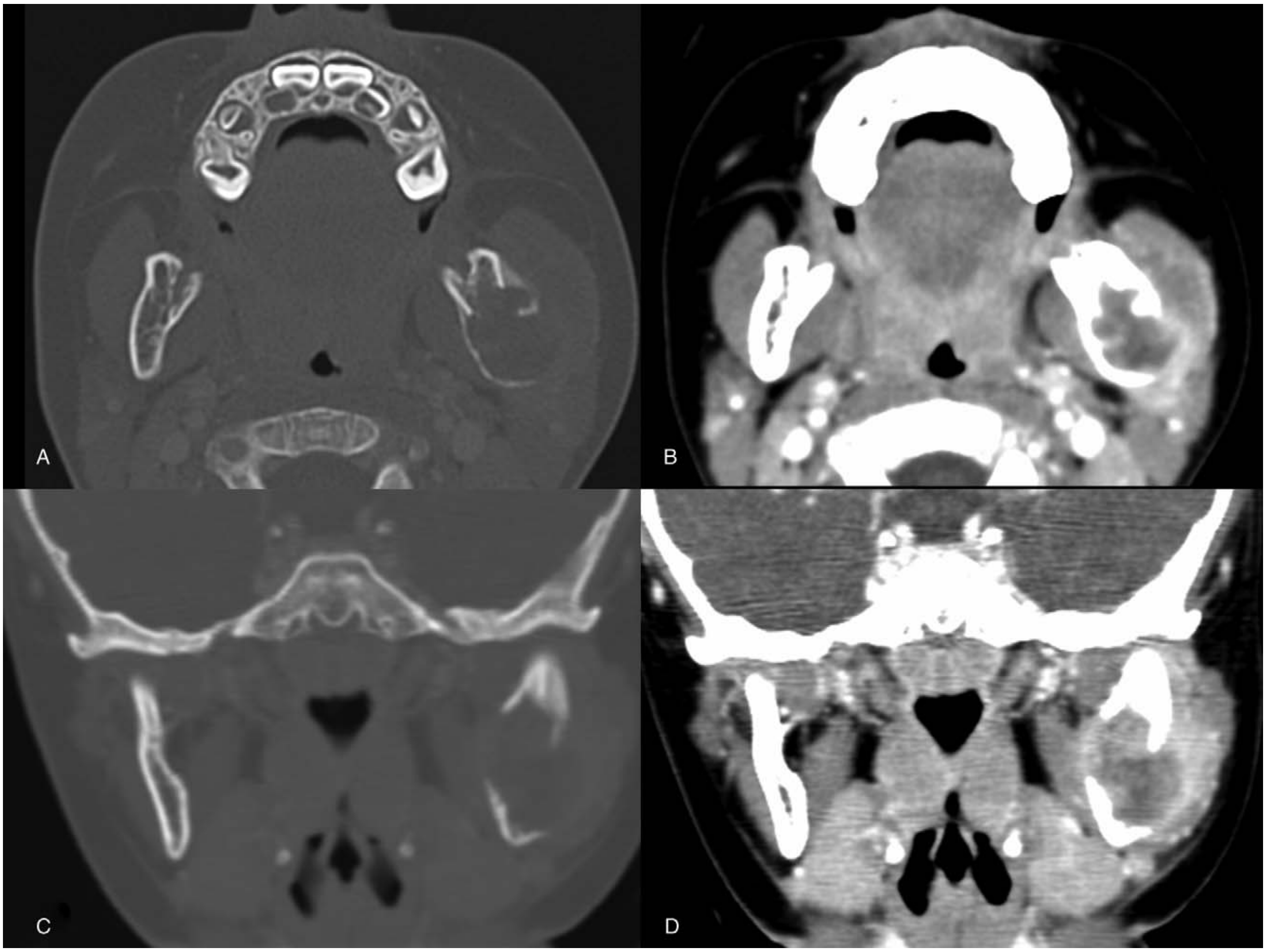

Figure 3. Case 10: Langerhans cell histiocytosis involving the left ramus of a 2-year-old girl. Axial bone window and soft tissue window contrast-enhanced CT images (A,B) and coronal bone window and soft tissue window contrast-enhanced CT images (C,D) demonstrate an expansile soft tissue mass with mixed attenuation. CT=computed tomography.

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

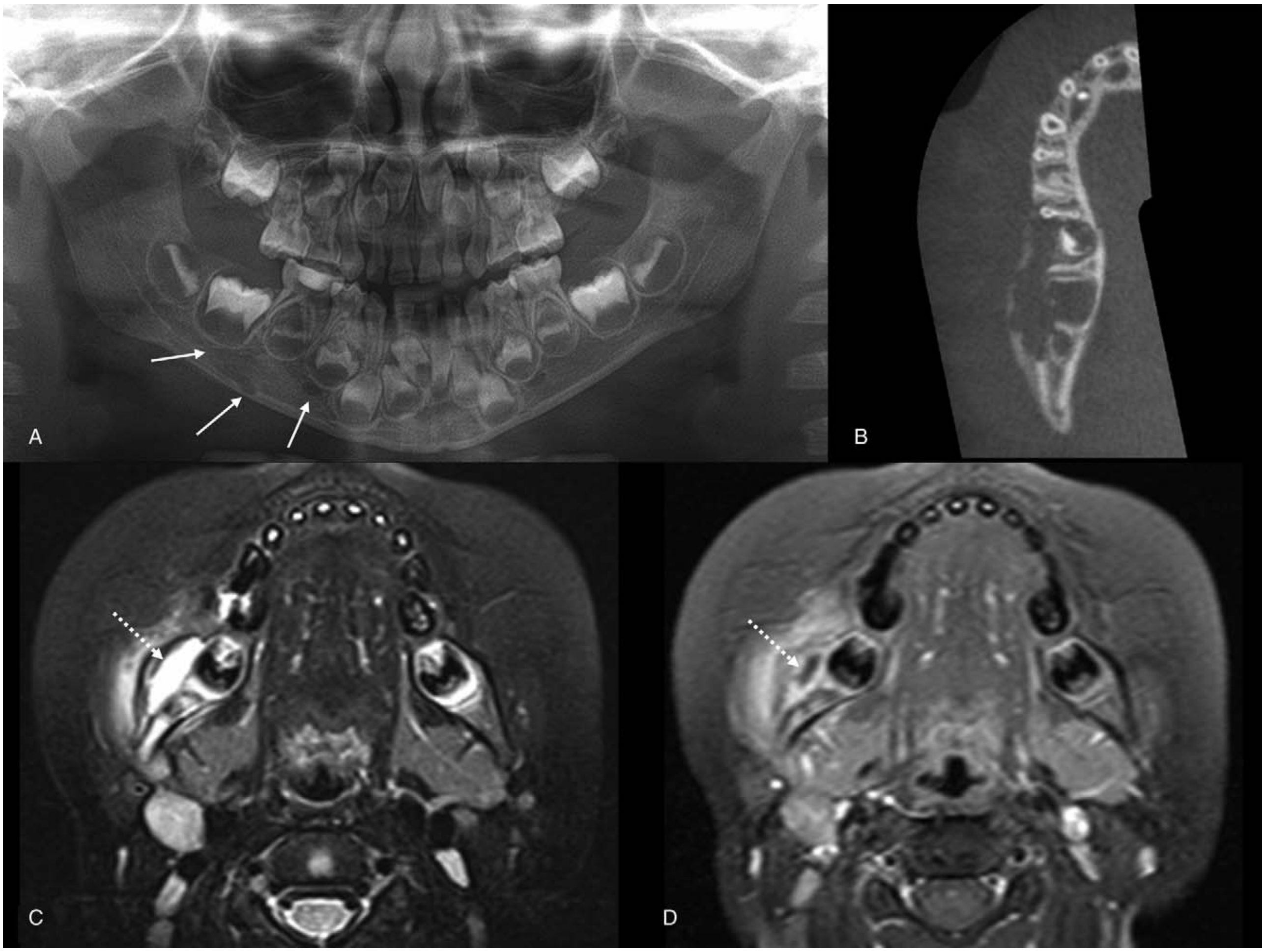

Figure 4. Case 12: Langerhans cell histiocytosis involving the right posterior mandible of a 3-year-old girl. A panoramic radiograph (A) demonstrates a radiolucent lesion (arrows) with a thinning of the inferior border of the right mandibular body. Axial cone-beam computed tomography (B), fat suppressed axial T2-weighted MR (C), and fat suppressed axial contrast-enhanced T1-weighted MR images (D) show an ill-defined osteolytic lesion along the buccal aspect of the mandible. Note the fluid signal intensity (dotted arrow) within the lesion with hyperintense T2 signal intensity and non-enhancement. Diffuse inflammatory change in the adjacent soft tissue is also observed. MR = magnetic resonance.

difficult. The differential diagnosis for osteolytic lesions of the jaw with surrounding inflammatory changes should include LCH, especially in young patients.

Author contributions

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