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Erdheim–Chester disease in a child presenting with multiple jaw lesions

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BACKGROUND: Erdheim–Chester disease is a rare histiocytic disease entity related to juvenile xanthogranuloma. It is a systemic condition, usually occurs in adult, characterized by infiltration of foamy histiocytes within the bone and soft tissues.

METHODS AND RESULTS: We report a case of 13-year-old female patient who first presented with multiple osteolytic lesions of the jaws followed by bilateral symmetrical bone lesions affecting the lower extremities, as well as brain and abdominal involvement. Histological findings of the jaw lesions showed lipid-storing CD68 (+), CD1a (−) histiocytes with Touton type giant cells.

CONCLUSION: To the best of our knowledge, this is the first case of Erdheim–Chester disease with jaw bone lesions occurring as initial presenting symptom.

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Keywords: bilateral symmetrical bony lesions; Erdheim–Chester disease; jaws; lipid-storing histiocytes; Touton-type giant cells

The patient, a 13-year-old girl, was referred to the Okayama University Dental Hospital from a private clinic for management of a large radiolucent lesion at the premolar molar area of the left mandible. The presenting complaint was pain and swelling at the affected side. Upon initial examination, the patient was otherwise healthy and her family and medical histories were non-contributory. Panoramic radiograph and CT scan showed a single, large, well-defined radiolucent lesion extending from the distal of tooth 35 to mesial of tooth 37 (Fig. 1). There was also lingual plate perforation at the apical area of 36. A biopsy was performed and subsequently reported to be suspected of non-ossifying fibroma. Total curettage of the lesion was performed and post-operatively healing was uneventfully. During the follow-up period of 6 months, the patient presented with complaint of discomfort at the left maxillary region and epileptic attacks. Complete examination of the patient by X-ray, CT scan, 3D CT (Fig. 2) and MRI revealed multiple bone lesions bilaterally in the maxillae, tibias and fibulas and a brain lesion as well. Curettage of the maxillary lesions was performed. She also underwent her brain surgery at Okayama University Medical Hospital and the lesion removed was diagnosed as juvenile xanthogranuloma. However, the long bone lesions were only under surveillance and no interventive surgery was done. In the most recent follow-up, the patient was diagnosed to have an abdominal lesion as well (Fig. 3).

Histopathological examination of the mandibular lesion revealed that the lesion was composed of spindle-shaped cells arranged in short fascicles forming whorl pattern, extensive areas of necrosis and xanthogranulomatous areas with hemorrhages and haemosidrin deposits (Fig. 4a). Cytologically, these spindle cells have large vesicular nuclei, eosinophilic cytoplasm and indistinct cytoplasmic borders. Small, clear cytoplasmic vacuoles were also observed. There was neither calcifi-

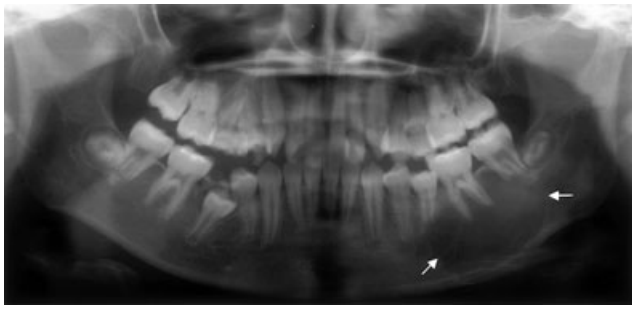

Figure 1 Panoramic radiograph of the mandibular lesion at the first admission: a large well-defined, radiolucent lesion at the apex of the left first molar was detected (shown by arrows).

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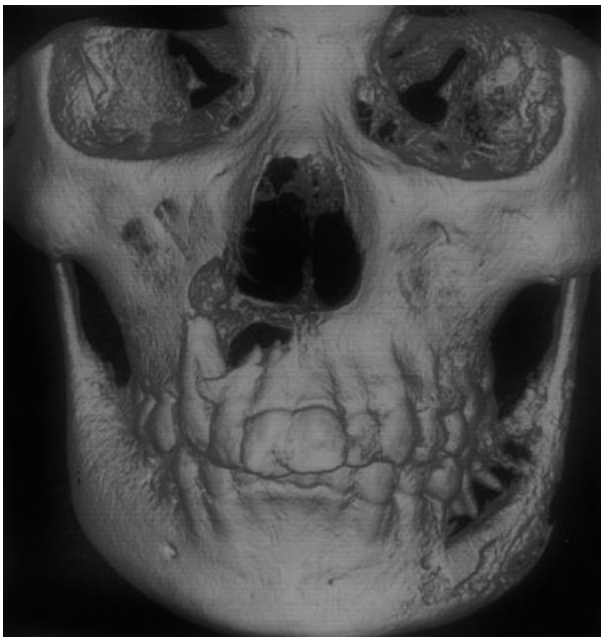

Figure 2 Three-dimension reconstruction CT image of the skull showing maxillary lesions and the operated mandibular lesion.

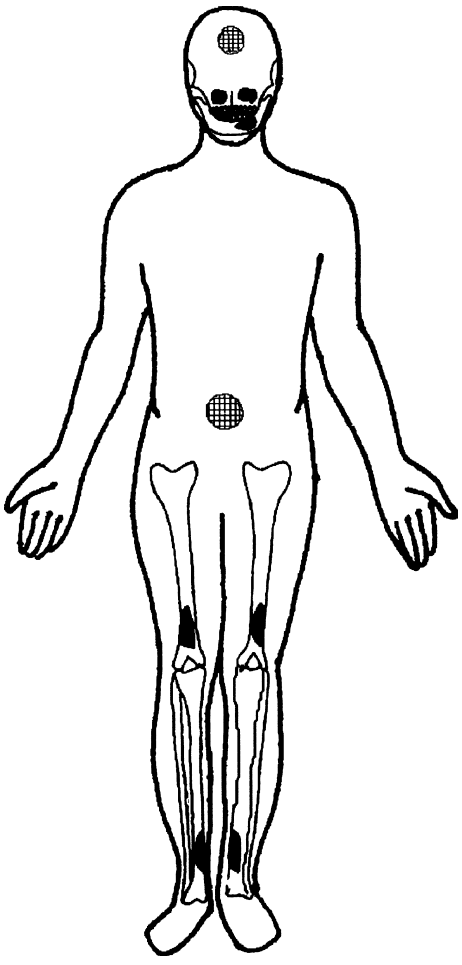

Figure 3 Schematic diagram showing the lesions detected in the patient. (●) Bony lesions in mandible, maxillae, femurs and tibias; (○) soft tissue lesions in brain and abdomen.

cation nor hard tissue formation in the lesional areas examined. No feature of malignancy was detected.

The histologic examination of the maxillary lesions showed fundamentally similar features with the mandibular lesion, but necrotic areas were absent. The whorl pattern was more prominent, and two cell types were identified: spindle-shaped cells with darker elongated nuclei and the other with large, oval and lobulated vesicular nuclei. Small mononuclear cell foci, Touton type giant cells and xanthomatous cells were also seen especially at the periphery of the lesion (Fig. 4b,c).

Immunohistochemical study showed that the lesional cells were strongly and diffusely positive for CD68 (Fig. 4d) vimentin and actin but non-reactive to CK, desmin and NF. S-100 protein and CD1a immunoreaction were also absent.

Electron microscopic study revealed biphasic cells: fibroblastic cells with interspersed collagen fibers between them and histiocytic cells with irregular indented nuclei, and many lipid vacuoles and lysosomes within their cytoplasms. However, Birbeck's granules were not detected.

Comments

In view of the miscroscopic findings of this case, a broad range of benign disorders namely multiple non-ossifying fibroma and more aggressive histiocytic disorders affecting multiple organ systems were considered as differential diagnoses. The patient was young and multiorgan involvement favored the histiocytic disorder especially Langerhans cell histiocytosis (LCH). However, immunohistochemical analysis and electron microscopic examination excluded LCH as the lesional cells were negative to CD1a and Birbeck's granules respectively. Histologic similarity of the lesions to juvenile xanthogranulomas and multisystem involvement of bone and soft tissues suggest a very rare disorder, common in adults, named Erdheim–Chester disease. First, it was reported by William Chester in 1930 (1). The disease can affect different organs including bone, lungs, retroperitonium and central nervous system. Radiographic finding of bilateral symmetrical osteosclerosis of the long bones especially in the lower extremities is striking (2). Histopathologically the lesions show similar xanthomatous histopathology to juvenile xanthogranuloma composed of lipid storing CD68(+), S100(−), CD1a(−), Birbeck's granules (−), non-Langerhan's cell histiocytes (3, 4). Most of these reported features are consistent with the findings in our case. There were only 2 reports of Erdheim–Chester disease occurring in the children (5, 6) and this is the first case to report Erdheim–Chester disease in a child with jawbone lesions occurring as initial presenting symptoms.

Recent data suggest that Erdheim–Chester disease most likely is a monoclonal lesion consistent with a neoplastic disorder (7). Erdheim–Chester disease is a multisystem syndrome that usually affects bone (bone pain), skin (xanthomas, xanthelasma), retroorbital tissues (exophthalmos), pituitary gland (diabetes insipitus), retroperineum (kidneys) and lung. The prognosis for

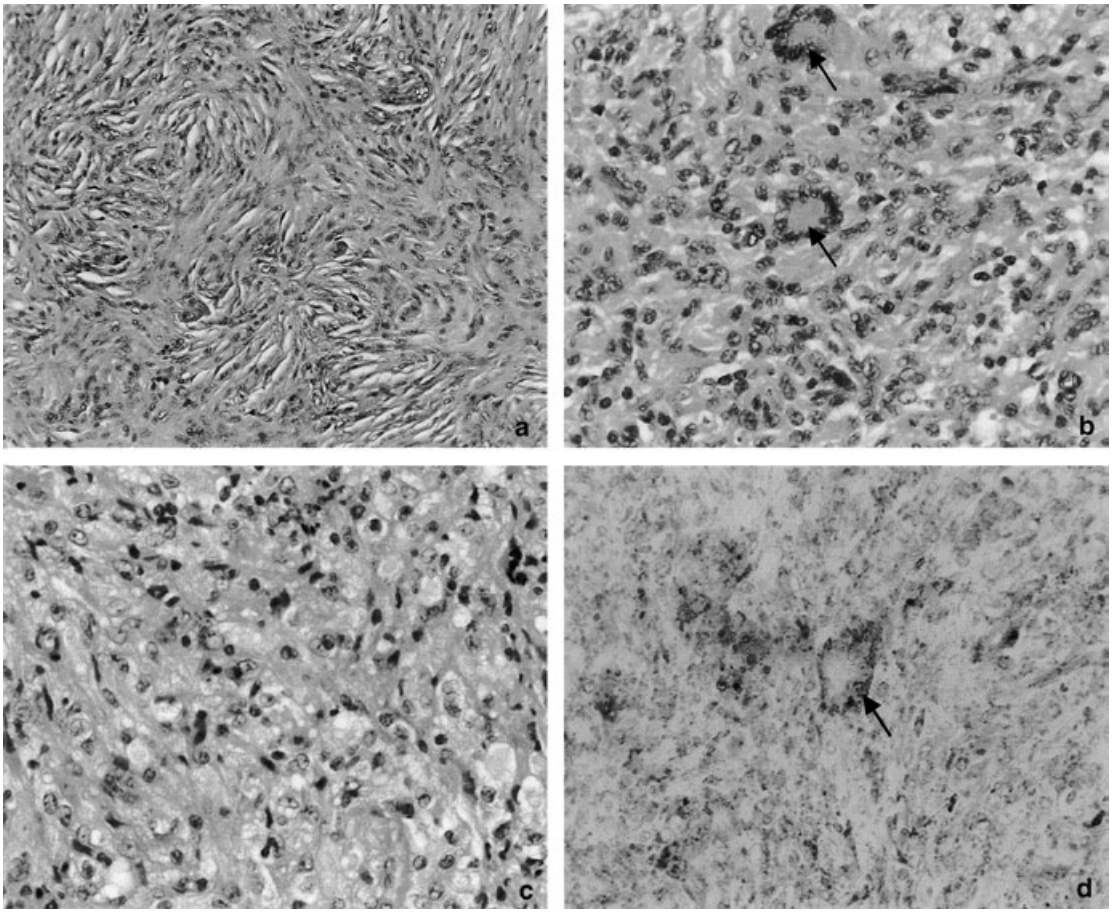

Figure 4 Microscopic features of the jaw lesions. (a) Spindle-shaped lesional cells forming the prominent whorl pattern. (b) Areas with small mononuclear cells and Touton type giant cells (arrow). (c) Foamy histiocytes with lipidized, clear cytoplasms at the periphery of the lesion. (d) The lesional mononuclear cells as well as the Touton type giant cells (arrow) were diffusely and strongly positive for CD68.

Erdheim–Chester disease is related to the extent of visceral involvement. Most patients die within two to three years after diagnosis due to congestive heart failure, lung fibrosis or renal insufficiency. Treatment options include corticosteriods, radiotherapy, chemotherapy and immunotherapy or combination therapy (2, 8). None have been highly effective and the disease is typically relentless in its course.

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