

Treatment and Rehabilitation of Repetitively Recurrent Langerhans Cell Histiocytosis: A Case Report

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Langerhans cell histiocytosis (LCH) is characterized by proliferation of histiocyte-like cells (Langerhans cell histiocytes) with characteristic Birbeck granules, accompanied by other inflammatory cells. Treatments of LCH include surgery, chemotherapy, and radiotherapy. One of the representative forms of chemotherapy is intralesional injection of steroids. Surgical treatment in the form of simple excision, curettage, or even ostectomy can be performed depending on the extent of involvement. Radiotherapy is suggested in case of local recurrence, or a widespread lesion. This article shows the case of repetitively recurrent LCH of a 56-year-old man who had been through surgical excision and had to have marginal mandibulectomy and radiotherapy when the disease recurred. After the first recurrence occurred, lesions involved the extensive part of the mandible causing pathologic fracture, so partial mandibular bone resection was performed from the right molar area to the left molar area followed by the excision of the surrounding infected soft tissues. The resected mandibular bone was reconstructed with a segment of fibula osteomyocutaneous free flap and overdenture prosthesis supported by osseointegrated implants.

Key Words: Fibula osteomyocutaneous free flap; Histiocytosis, Langerhans cell; Reconstruction; Recurrence

Introduction

Langerhans cell histiocytosis (LCH) is a rare clinicopathologic disorder characterized by proliferation of histiocyte-like cells (Langerhans cell histiocytes) with characteristic Birbeck

granules, accompanied by other inflammatory cells. It has a varied clinical course, either local or disseminated, and considerable debate has been stimulated about its categorization and whether it is a reactive disorder or a truly malignant process¹. Recently, it has been classified by the

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World Health Organization based on the hallmark of LCH: the proliferation and accumulation of a specific histiocyte². LCH includes three subtypes; eosinophilic granuloma (EG), Hand-Schüller-Christian disease, and Letterer-Siwe disease. EG is the major type; it is a localized form and presents as unifocal or multifocal bone lesions.

LCH can involve any bones, especially skull, pelvis, spine, and mandible. The clinical symptoms of LCH vary depending on the site and extent of involvement³⁻⁵. Bone is the most frequently involved single organ, with a solitary skull lesion being the most common presentation of LCH. The most frequent symptom within mandible is pain which sometimes accompanies adjacent soft-tissue swelling.

Treatments of LCH include surgery, chemotherapy, and radiotherapy. Surgical approach is the first treatment choice particularly for solitary bone lesions. Surgical treatment includes the form of simple excision, curettage, or even ostectomy, depending on the extent of involvement. Another approach is intra-lesional injection of steroids. Radiotherapy is suggested in case of local recurrence or if surgical treatment is not possible^{6,7}.

Case Report

A 56-year-old male presented with history of pain and swelling of the periodontium in the left

mandible. An initial panoramic radiograph was taken in a local dental clinic and the patient was tentatively diagnosed with osteomyelitis, and then he was referred to general hospital. The patient received surgical curettage from an oromaxillofacial surgeon who considered the problem to be an infection in his jaw. Nine months later, post-operation radiography was taken in the local dental clinic for further dental prosthetic treatment. But osteolytic lesion was still detected.

Subsequently, the patient visited the Department of Oral and Maxillofacial Surgery, Kyung Hee University Dental Hospital (Seoul, Korea). To establish a diagnosis, an incisional biopsy was performed. Histologically, clusters of cells with coffee bean-like nuclei that were grooved were shown; the specific feature of Langerhans cells. These clusters of cells were consequently confirmed as Langerhans cells by their strong immunohistochemical activity for S-100 protein and



Fig. 1. Extensive bony destruction was detected on left mandible.

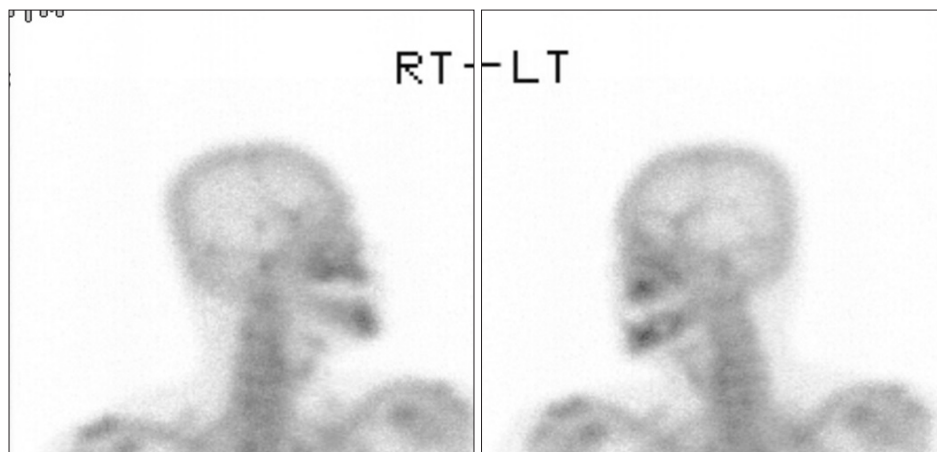


Fig. 2. Nuclear bone scintigraphy with technetium-99m was conducted to evaluate whether other bones were involved; only focal active bony lesion on left mandible was identified.

cluster of differentiation (CD) 1a. The diagnosis of LCH was finally identified by histopathology.

An initial panoramic radiography showed poorly defined and infiltrative osteolytic lesion on left mandibular body, both lower anterior and posterior regions with punched-out radiolucency with floating teeth on the lower right molar area. Extensive bony destruction was also detected on the left maxilla area (Fig. 1).

Nuclear bone scintigraphy with technetium-99m was conducted to evaluate whether other bones were involved; only focal active bony lesion on left mandible was identified (Fig. 2).

Generally, LCH responds well to surgical therapy, especially when in the solitary form. In addition, even in case of extensive lesions, surgery alone can mostly give good results. Therefore, we chose surgical excision as the first choice of a treatment modality for this case. The region was surgically excised and involved teeth were extracted (Fig. 3).

Four months after the surgery, a suspicious lesion

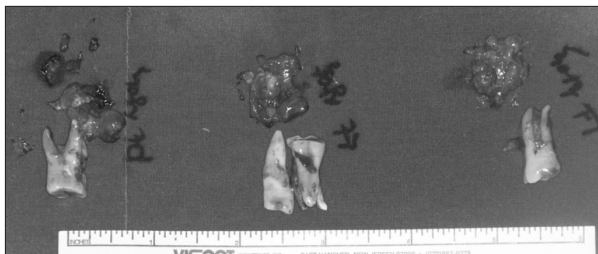


Fig. 3. The region was surgically excised and involved teeth were extracted.

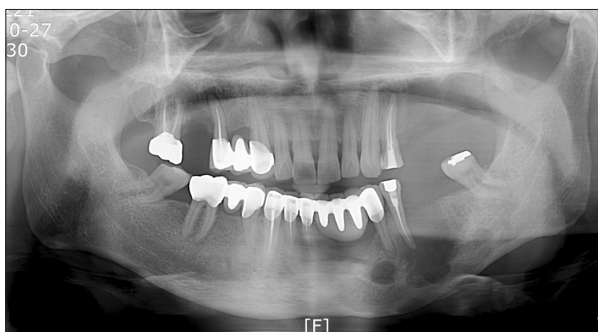


Fig. 4. After four months following first surgery, a suspicious recurrent lesion was observed on panoramic radiography.

was observed on panoramic radiography (Fig. 4).

An additional surgery was undertaken due to the appearance of expanded lesion in the left mandible. From left body to symphysis, the mandible was excised and reconstructed with bridging plate and fixation screws (Fig. 5).

After four years following the second operation, the patient presented with pain and swelling in both mandible areas. Although LCH seemed to be recurrent in the left mandible area, it was considered that acute periodontitis occurred on the lower right molar area because the panoramic radiograph showed localized vertical alveolar bone resorption (Fig. 6).

However, an incisional biopsy was done on soft tissue of the lower left and right second molar areas and the diagnosis of LCH was identified histopathologically. A ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomo-



Fig. 5. Panoramic view of post second surgery. From left body to symphysis, the mandible was excised and reconstructed with bridging plate and fixation screw.



Fig. 6. After four years following the second operation. Langerhans cell histiocytosis or periodontitis seemed to be recurrent.

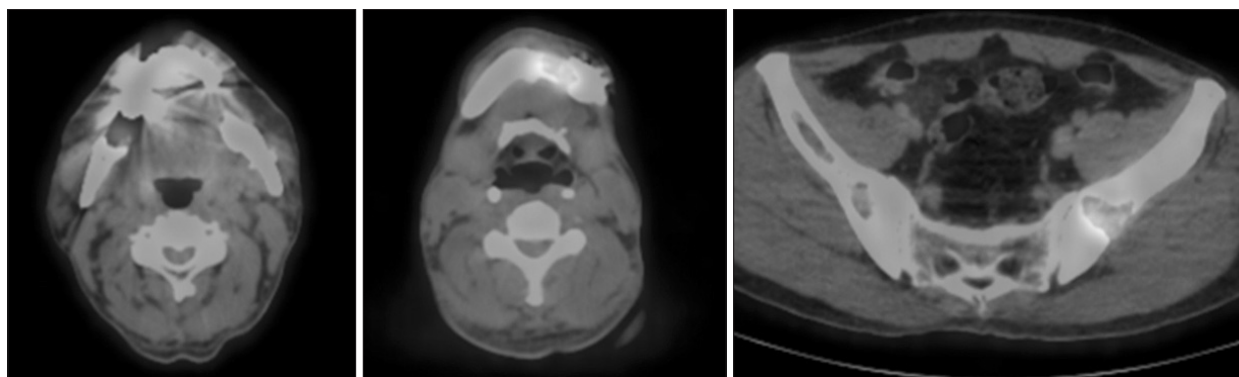


Fig. 7. A ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography scan view. Hypermetabolic lesions are observed in both mandible and left pelvic bone.

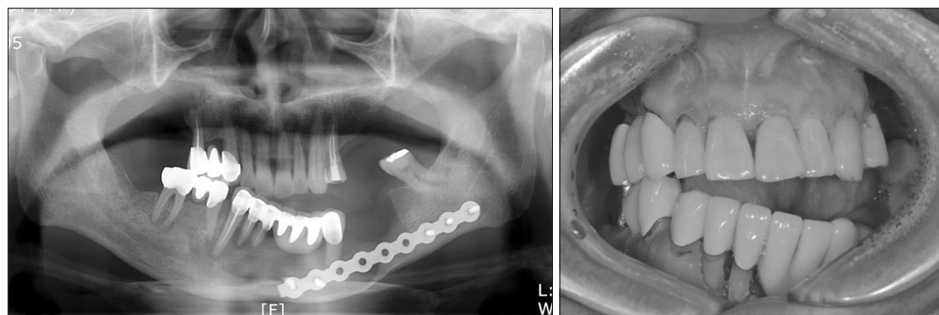


Fig. 8. Three years after second recurrence. Displacement of anterior dentition was observed. In intraoral clinical photo, the periodontal tissue was severely destructed and tooth roots were exposed to oral cavity.

graphy (PET-CT) scan was taken to evaluate the activity of the lesion and detect other invaded bones or tissue. PET-CT view shows hypermetabolic lesions in both mandible and left pelvic bone area (Fig. 7).

Radiation therapy was taken as a treatment modality because the lesion seemed to have been disseminated from left to right site of mandible; the lesion was no more in solitary form. Radiotherapy was done on the mandible and the left pelvic bone area (mandible: 2,500 cGY/10 Fx, left pelvic bone: 2,200 cGY/10 Fx).

Three years after the second recurrence and radiation therapy, the patient showed up with displacement of lower left dentition. There was extensive destruction with gross gingival recession and alveolar bone loss, involving a group of anterior teeth and exposure of the tooth roots. In panoramic radiography, pathologic fracture and displacement were detected on the left and mandibular body and symphysis area. In addition to the both mandible

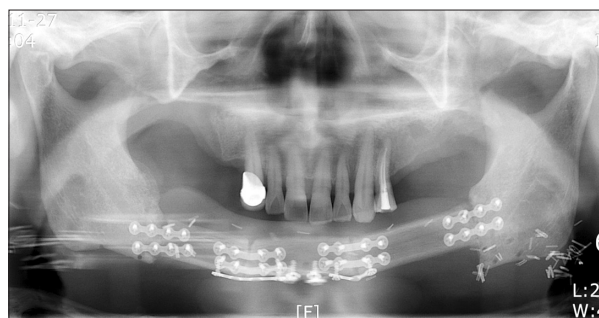


Fig. 9. After the third recurrence, mandibular body was resected. To recover the bony defect, fibula osteomyocutaneous free flap was harvested and the mandible was reconstructed.

areas, poorly defined and infiltrative osteolytic lesion was shown on the right maxilla area (Fig. 8).

Unfortunately, in this case, it had been proved that past radiotherapy was insufficient to prevent recurrence of LCH. In the mandible, the lesion spread too wide from left second molar area to right first molar area. Regarding the range of lesion and high inclination of recurrence, more radical excision was decided on. At the third surgery,

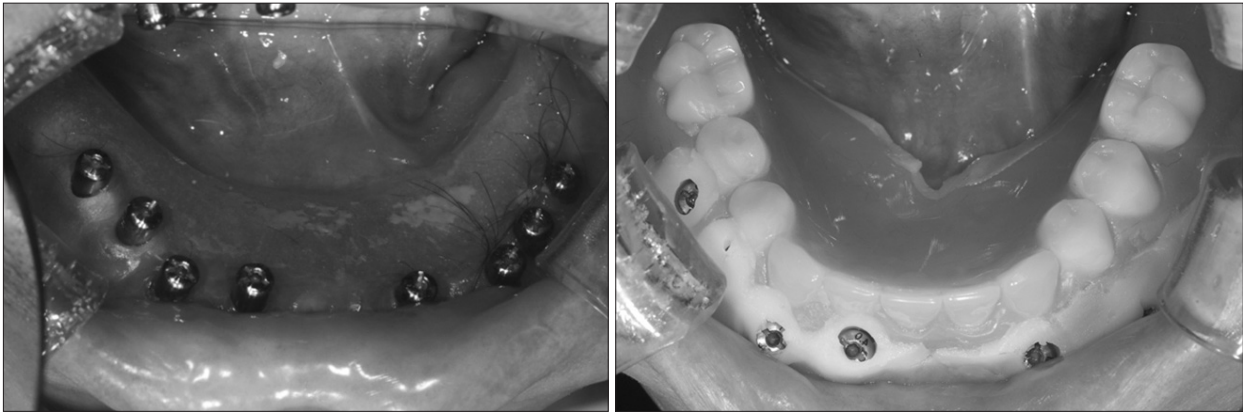


Fig. 10. Oral function was rehabilitated with dental implants and overdenture. Until now, there has been no more recurrence.

partial mandibulectomy and partial maxilla bone resection on the right were done. The resected mandibular bone was reconstructed with fibula osteomyocutaneous free flap (Fig. 9).

About one year after the third operation, the patient experienced no more recurrence. In radiographic examination, the harvested fibula bone was long and wide enough for rehabilitation of masticatory function with overdenture supported by osseointegrated implants. We installed eight implants on fibula. Then, the patient received further prosthetic treatment. He has now been free of recurrence for more than a year. The denture has been stable and functional without complications, and the patient is still under our follow-up (Fig. 10).

Discussion

LCH is a disease that primarily affects bones but in some cases could affect other organs and presents as a multisystemic disease⁸. The prognosis of patients with LCH depends on their age at the initial diagnosis as well as the site and range of involved structures. Therefore, LCH has a varied clinical course and expectation of prognosis is difficult. Diagnosis must be confirmed by biopsy examination. Thirty percent of the cases present with lesions that affect the jaws⁹. Recurrence usually occurs within the first 9 to 12 months after

the halt of treatment. The percentage of patients with recurrence was from 9.0% to 17.4% for single-site disease; 37% for single-system, multifocal disease; 46% for multisystem (nonrisk organ) disease; and 54% for patients with risk-organ involvement¹⁰.

The treatment modalities of LCH include surgical excision, chemotherapy and radiotherapy. Since the disease more commonly occurs in children than adults, a definitive treatment regimen is not yet established. In recent times, aged-patients with solitary bone lesions are managed with surgical curettage of the lesion with or without chemotherapy (intralesional corticosteroids injection)^{11,12}. Systemic or local corticosteroids therapy will cause bone lesions to regress. Although children respond well to chemotherapy, the disease in adult patients tends to be more chronic and shows periods of relapse and remission. In addition to those chemotherapy, low-dose radiation therapy may be indicated and should be tried before any radical surgery that leads to extensive loss of function and disfigurement for LCH¹³⁻¹⁵. After radiation therapy, patients frequently experienced pain relief; however, a complete remission was rarely achieved¹⁶.

If LCH on mandible frequently recurs and is broadly disseminated, radical and wide resection of mandibular body is unavoidable. In recurrent

and widely disseminated disease, chemotherapy and radiotherapy could be considered as adjunctive treatment for remission of lesion and relief of pain.

Reconstruction of the mandible is essential after partial or subtotal resection. In 1989, the first significant experience with the fibula free flap for mandibular reconstruction was published, and since that time, as this flap has sufficient length and volume to replace the whole body of the mandible, free vascularized osseous or osteocutaneous fibula flap has become one of the most optimized options for reconstruction^{17,18)}.

For patients with dentition, osseointegrated implants are essential to the final reconstructive outcome. Dental implants have been proved to be a very reliable means for dental rehabilitation, not only in healthy edentulous patients but also in patients with bone flap after tumor surgery. The recipient bone must have adequate height (>10 mm) and width (>6 mm) to accept osseointegrated implants, making the fibula bone flap an excellent source of vascularized bone for prosthodontic reconstruction¹⁹⁾.

Although LCH has successfully been treated and the mandible was reconstructed by surgical procedure, there is still the possibility of recurrences or new lesions, which makes a long-term follow-up necessary.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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