Langerhans' Cell Histiocytosis: A Case Report of an Eosinophilic Granuloma of the Mandible Treated with Bone Graft Surgery and Endosseous Titanium Implants

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Eosinophilic granuloma is the localized and most benign form of Langerhans' cell histiocytosis. The disease shows a particular predilection for the head and neck region and usually involves the skull bones, where it manifests as well-defined lytic lesions on standard radiographs. The case of an extensive lesion involving the body of the mandible in a 52-year-old man is reported. Operative procedures consisted of enucleation of the lytic lesion and follow-up with clinical examinations and computerized tomographic studies of the mandible at 2, 12, and 18 months postoperatively. Reconstructive surgery without radiotherapy was performed with an autologous bone graft from the iliac crest and implant placement to provide support for a dental restoration. Int J Oral Maxillofac Implants 2006;21: 124–130

Key words: *bone grafting, dental implants, eosinophilic granuloma, Langerhans' cell histiocytosis*

Langerhans' cell histiocytosis (LCH), previously known as histiocytosis X,[1] consists of a group of syndromes of unknown etiology characterized by the abnormal proliferation and infiltration of benign histiocytes.[2–4] Lesions tend to occur in organs with a resident population of histiocytes and macrophages, such as the skin, bone marrow, lymph nodes, spleen, liver, and lungs.[5] LCH exhibits a wide range of clinical presentations, which reflect the extent of involvement. It has been divided into 3 clinical entities[6]: Letterer-Siwe disease, an acute, disseminated form; Hand-Schüller-Christian disease, a chronic disseminated form; and eosinophilic granuloma (EG), a localized form of the disease that is frequently seen as a solitary lytic bony lesion in the head or neck.

Histologically, LCH is characterized by an infiltration of Langerhans' histiocytes. The Langerhans' cell is a dendritic histiocyte found in the skin and mucosa as part of skin-associated lymphoid tissue (SALT), which is involved in cutaneous immune surveillance. Langerhans' cells are also normally found in the T zone of lymph nodes and in the thymus. Such cells process and present antigens to T lymphocytes. The proliferation of Langerhans' cells is thus linked to the immune system.[7,8] The causes of Langerhans' cell proliferation and infiltration are not known.

Eosinophilic granuloma is the most benign and localized of the 3 clinical manifestations of Langerhans' cell histiocytosis. It accounts for about 70% of all cases of LCH[7] and less than 1% of all tumorlike lesions. Eosinophilic granuloma primarily involves the skull, ribs, and long bones.[9] Skull manifestations commonly involve the calvaria, temporal bone, and

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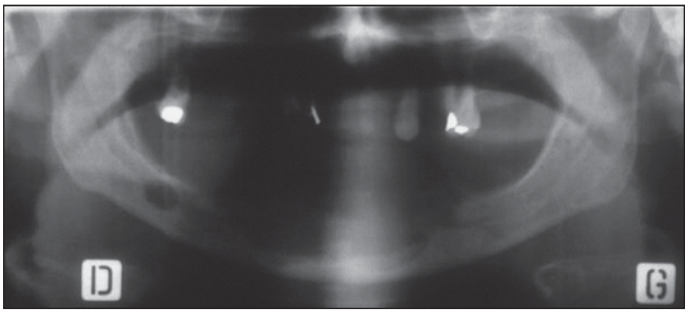


Fig 1 Preoperative panoramic radiograph.

jaws.[10] The jaws are involved in approximately 10% of cases; the mandibular body and angle are generally more common sites than the maxilla, especially in patients over 20 years of age.[11,12] The lesion may be solitary or multiple. Multiple sites in both the mandible and the maxilla are usually involved[13]; about 20% of patients have polyostotic disease. In a series reported by DiNardo and Wetmore,[14] 86% of the mandibular lesions were unifocal.

The clinical presentation is usually a soft-tissue mass with a well-circumscribed lytic lesion in the underlying bone, without a sclerotic rim. When the lesion involves the alveolar ridge around a tooth, resorption of the bone by histiocytic infiltration appears as a periapical, nonsclerotic lucency that imparts a "floating tooth" appearance on standard radiographs.[15] Soft tissue involvement may occur, affecting mainly the lymph nodes, lungs, and mucous membranes.[16]

Eosinophilic granuloma tends to affect younger adults; individuals over the age of 50 years are rarely affected. Pain is the most common complaint of patients with eosinophilic granuloma,[9,17] and diabetes insipidus is the most frequent endocrinopathy associated with this disorder, occurring in 25% to 50% of patients.[7,8]

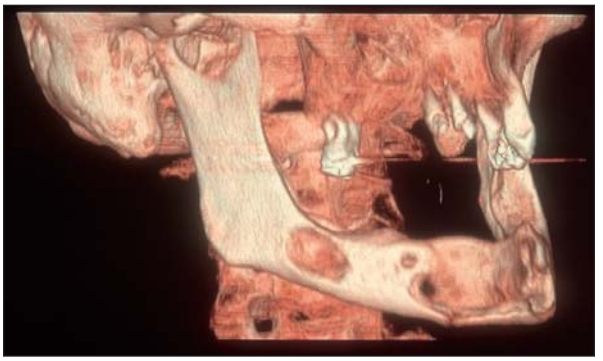
The Histiocyte Society, which was founded in 1987, has provided some basic diagnostic criteria.[18] Birbeck's granules detected via electron microscopy or CD1 antigen on the cell detected immunohistochemically results in a "definitive diagnosis" of LCH. A "diagnosis" of LCH is made if the typical histologic appearance is evident on light microscopy and the tissue exhibits 2 or more of the following: ATPase staining, S-100 protein, alpha-D-mannosidase, or peanut lectin binding. On the other hand, if the histology alone is consistent with LCH and no other features are noted, a "presumptive diagnosis" is to be made.[19,20] Differential diagnosis includes periapical abscesses, odontogenic cysts, osteomyelitis, metastatic disease, and primary bone neoplasms; misdiagnosis is common.[12,21,22] Computerized tomography (CT) and magnetic resonance imaging (MRI) can define the extent of osseous or soft tissue involvement.

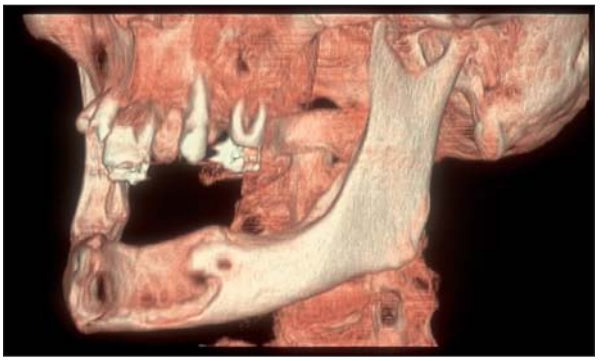
Solitary eosinophilic granuloma and the multifocal, systemic form of the disease may exhibit varying histologic patterns. Bone lesions, whether solitary or multiple (multiple in about 20% of cases),[17] generally have syncytial sheets of Langerhans' cells with indistinct cell membranes and, frequently, eosinophils, giant cells, and necrosis. The disorder is characterized by the CD-1 surface antigen and S-100 intracellular protein and a finding of pentalaminar cytoplasmic Birbeck's granules on electron microscopy.[7] The prognosis of LCH depends on the age at onset, the extent of the disease, its histologic features, and the presence or absence of dysfunction of certain organ systems.[23]

CASE REPORT

A 52-year-old male patient was referred with an extensive osteolytic lesion of the mandible. The patient was asymptomatic, and the lesion was diagnosed incidentally through a panoramic radiograph obtained for dental treatment purposes. The patient was completely edentulous in the mandible, and only 5 teeth or roots were still present in the maxilla. The panoramic radiograph showed a large area of radiolucency in the central portion of the mandible and a smaller radiolucent area on the right side of the body of the mandible (Fig 1). Routine clinical laboratory investigations revealed a normal profile and no evidence of diabetes insipidus.

On the basis of radiographic findings and clinical evidence, surgical treatment was planned and limited to excision of the lesion followed by curettage of





Figs 2a and 2b One year postresective surgery. Three-dimensional rendering of spiral CT data sets of *(a)* the right side and *(b)* the left side of the mandible.

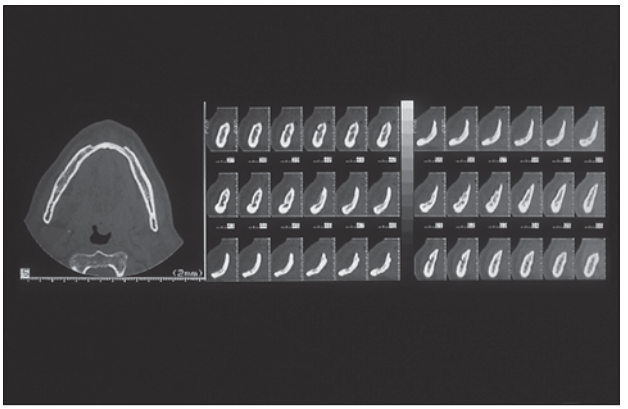


Fig 3 Dental scan obtained 18 months after resective surgery.

2 mm of peripheral healthy bone utilizing an intraoperative view of 2.5× magnification. The alveolar nerves on both sides and the inferior lingual cortex of the mandible, which did not show any sign of infiltration, were preserved. An irregular residual cavity, mainly a 3-wall defect, was left in the central mandible. The lingual mandibular wall of the residual defect was represented by poor, thin bone. On the right side the erosion extended up to the ramus. All the excised material was subjected to histologic examination. The microscopic diagnosis posed was eosinophilic granuloma and the neoplastic immunophenotypic profile was: intracellular protein S100 +; histiocytes surface antigen CD68 +/–; cytokine–; leukocyte common antigen (LCA)–.

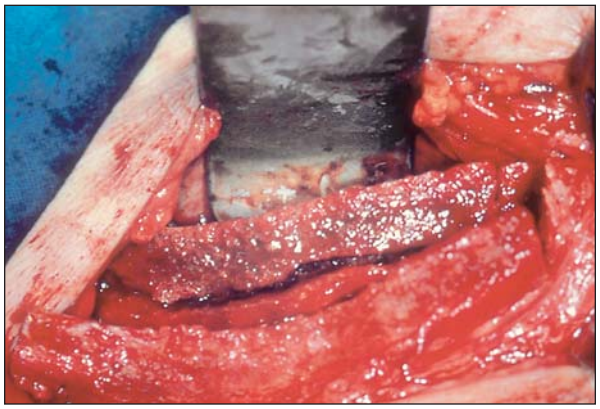
Postoperatively, further clinical investigations were conducted, including hematologic surveys, to rule out systemic involvement of the disease. Based on histologic and medical findings, no further surgical procedures or radiotherapy were deemed necessary. As the patient lived far from the treatment center, the follow-up schedule was planned to fit his needs. Complete clinical follow-up examinations, which included multirow CT (Light Speed Plus; GE/Medical Systems, Milwaukee, WI) of the jaws,[24,25] were conducted at 2, 12 (Fig 2), and 18 months postoperatively.

No further osteolytic defects were detected. Healing of the area that underwent the surgery was normal, and systemic involvement was excluded.

At 18 months postsurgery the patient appeared stable and pressed vehemently for satisfactory dental rehabilitation. CT of the mandible showed thin residual bone in the central region (Fig 3), graded as class V/VI according to the Cawood and Howell classification system.[26] The bone quality was considered class D2 or D3 according to Misch's classification.[27] It was decided to treat the severe atrophy of the central mandible surgically to allow for the placement of titanium endosseous implants for dental rehabilitation.

Reconstruction of the anterior mandible was performed with an autologous bone graft, consisting of the inner table and adherent cancellous bone of the anterior iliac crest, harvested via a trap-door technique (Fig 4).[28,29] When the mandibular access flap was raised (Fig 5a), the buccal side was beveled to obtain a periosteal flap, which was used at the time of suturing to further protect the bone graft at the mucosal incision line. The bone graft was split into a "V" shape and adapted to the defect as buccal onlay grafts; each graft was rigidly fixed with 2 titanium lag-screws[30,31] (Fig 5b). Residual graft bone was particulated, included in platelet-rich plasma gel,[32] and applied where needed for maximal graft-to-bone contact. Multiple parallel horizontal periosteal releasing incisions (following Rehrmann and Schettler[33]) were executed up to the area of the inferior mandibular border. A molding/compressive external dressing was applied to the chin area.[34] Twenty-four hours postoperatively, echography of the ilium was performed; neither hematomata at the site of harvesting nor ecchymotic lesions of the iliac muscle were detected.

Fig 4 Autogenous bone graft retrieved from the iliac crest using a trap-door technique.



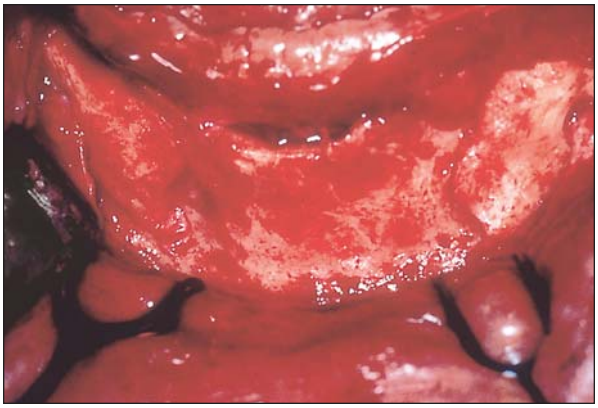


Fig 5a Recipient site 18 months after resective surgery.

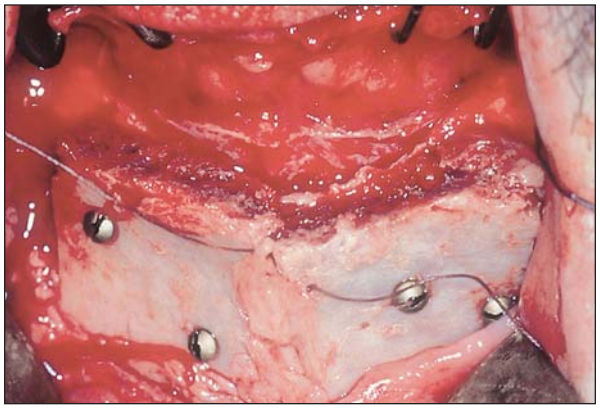


Fig 5b Bone graft positioned and secured by titanium lag-screws.

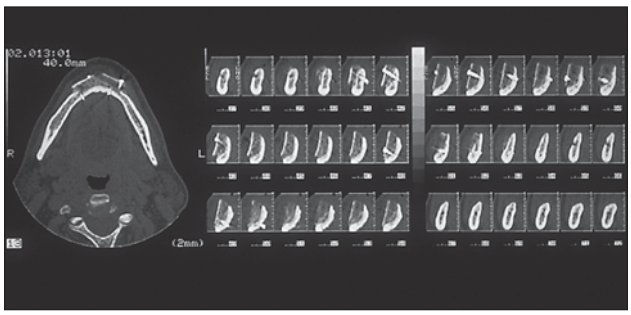


Fig 6 Dental scan obtained following reconstructive surgery.

To better follow the disease's evolution, 4 bone biopsies were recovered from the area of the central mandible previously affected by the disease. No histologic evidence of recurrence was detected. Four months after reconstructive surgery a new CT study of the mandible was obtained and showed satisfactory graft integration (Fig 6). Five titanium endosseous implants (*out*-Link, PRO-Link dental implant systems; Sweden & Martina, Due Carrare, Padua, Italy) were surgically placed in the central mandible to support a dental restoration[35–37] (Figs 7a to 7c).

Monthly clinical follow-up over a period of 8 months confirmed the osseointegration of the implants. At the end of this follow-up period prosthetic rehabilitation of the mandibular arch was performed. The prosthesis utilized all 5 of the implants via an implant-fixed prosthesis in accordance with Zarb and coworkers.[38]

The prosthesis was extended to include the second premolars on both the left and right sides. Clinical follow-up every 3 months during the first year, then at 18 and 24 months after prosthesis placement, revealed the implants and surrounding soft tissue to be in satisfactory clinical condition. Twenty-four months after implantation, there were no signs of peri-implantitis, and bone loss around the implants was minimal, in accordance with the implant success criteria set forth by Albrektsson and colleagues.[39] The patient expressed complete satisfaction with the outcome from both the functional and esthetic points of view (Fig 8).

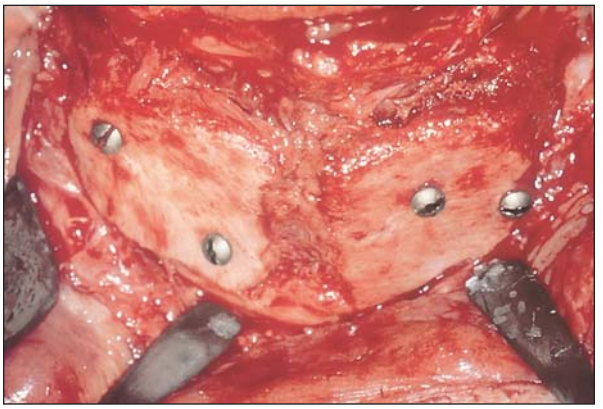


Fig 7a Implant placement surgery 3 months after reconstructive surgery.

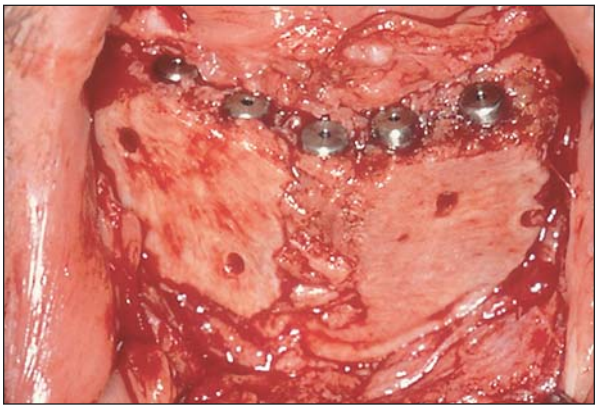


Fig 7b Implants positioned following graft screw removal.

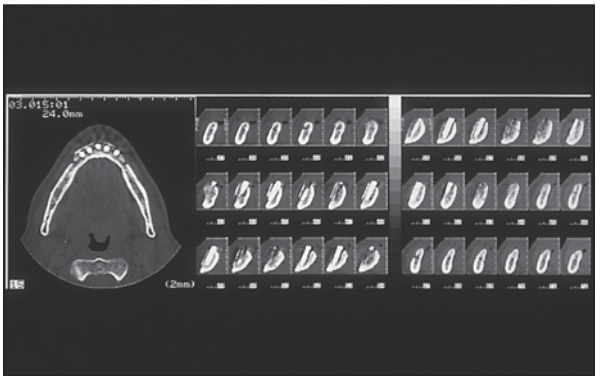


Fig 7c Dental scan obtained following implant placement.

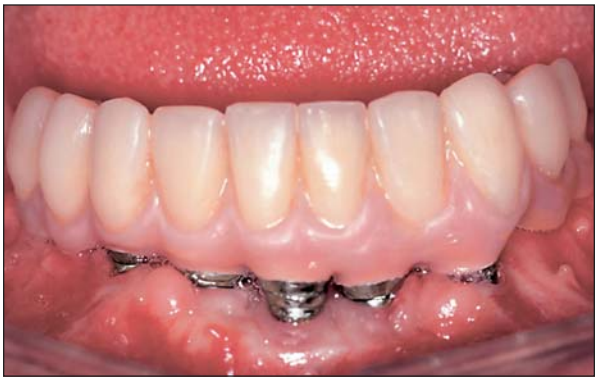


Fig 8 Fixed prosthesis.

DISCUSSION

A good deal of controversy has surrounded the role of therapy for patients with eosinophilic granuloma as a nonsystemic disease entity and whether treatment alters the outcome in those with severe disease. A number of therapies have been proposed for isolated bone lesions, including enucleation with curettage, intralesion steroid injections,[40] low-dosage radiotherapy,[6] and reconstruction with autologous bone. Schreuder and colleagues have reported on the use of cryosurgery in addition to curettage and bone grafting to treat 6 patients, with good results in 5 cases.[41] For systemic disease, on the other hand, various chemotherapies have been proposed. Surgical procedures are called for only when severe local problems occur,[23,42–44] while radiation is reserved for patients with lesions that are either inaccessible or threatening to vital structures.[7,45] A single report has shown some cases of spontaneous remission, even with polyostotic manifestations.[4]

The patient presented herein was followed for 18 months before implant surgery, during which time no recurrence, local or systemic, of the disease was detected. The therapeutic approach followed in the first surgical intervention was in conformity with the current literature. To the authors' knowledge, there have been no controlled studies to determine the optimal treatment for the monostotic form of LCH, nor are there guidelines for bone reconstruction and subsequent dental implant placement.[7] The decision to undertake reconstructive surgery was made on the basis of the following considerations:

- Lack of evidence of systemic involvement of the disease
- Lack of evidence of local or system recurrence of the disease over a reasonably long follow-up period (20 months)
- Risk of pathologic fracture of the mandible because of residual bone thinness strongly supported the need for reconstructive surgery

The decision to place implants was based on:

- The lack of evidence of local recurrence of the disease found at the time of bone reconstruction during follow-up CT examination
- The fact that CT of the mandible showed good graft integration and no local recurrence of the disease 3 months postsurgery
- The patient's insistent requests that satisfactory dental restoration be undertaken

CONCLUSIONS

Surgical removal of the lesion, with subsequent clinical and radiographic follow-up, reconstructive surgery through autologous iliac crest bone graft, and placement of dental implants and a prosthesis provided a promising therapeutic protocol for satisfactory dental rehabilitation in the present patient affected with eosinophilic granuloma.

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