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# Histiocytosis X: A Case Report of Langherans Cell Histiocytosis with the 3D Surgery

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## Abstract

**Background:** Langerhans Cell Histiocytosis (LCH) is a relatively rare disorder with a strong inflammatory component. It has diverse clinical manifestations, which range from a single lesion or multiple bony lesions to severe multi-system involvement. Approximately 10% to 20% of cases of LCH occur in the jaw, with the posterior mandible being the most frequently involved site. The majority of patients are children younger than three years, and the incidence in adults is approximately 1-2/million. There is no universally accepted treatment protocol; treatment options include observation only, surgical curettage, radiation therapy, steroid injections, and chemotherapy.

**Objective:** Use the Computer-Aided Design and Computer-Aided Manufacturing (CAD/CAM) technology for the treatment of Langerhans cell histiocytosis in the adult mandible.

**Case Presentation:** We report on the case of a 56-year-old woman who presented an osteolytic lesion in the mandible body that was discovered incidentally during routine radiographic screening. Single-stage treatment was achieved by 3D surgery for bone resection, nerve preservation, and mandibular reconstruction by an autologous bone graft from the iliac crest.

Histological examination of the specimen confirmed the diagnosis of LCH. In addition, the patient did not show any recurrence in clinical and medical records at 12 months and 24 months after surgery.

**Conclusion:** 3D surgery is a potential treatment choice for this type of oral pathology as it allows for a tailored, safe, reliable therapy.

## Introduction

Langerhans cells (LCs) are inflammatory dendritic cells that are derived from the bone marrow, migrate through the bloodstream to the epidermis of the skin and the epithelium of oral mucosa, and play an important role in the development of local immune response [1]. Clinically, its presentation can range from affecting only a single system, such as the skin or bone, to a life-threatening multi-system disease that involves other organs, including the lungs, spleen, bone marrow, and liver [2,3]. The incidence of LCH in adults ranges from 1 to 2 cases per million [2,4,5].

There is much debate about whether LCH represents a reactive or neoplasm process.

The term 'histiocytosis' refers to the proliferation of histiocytes and other inflammatory cells, whereas the letter 'X' was added to denote the unknown etiology of the disease [6,7].

Histologically, LCH, in general, is characterized by immature LCs proliferation accompanied by an infiltrate of lympho-monocytes together with eosinophilic and neutrophilic cells, which results in the destruction of the affected tissues [2]. As the atypical cellular proliferation of LCH occurs in various organs and tissues, clinical manifestations may be particularly different and complex [3]. The LCH study group divides LCH into single-system LCH and multi-system LCH; the single system is further subdivided into a single site and multiple sites, while the multi-system into low risk and high risk according to the involvement of some organs (liver, lungs, spleen, hematopoietic system), with high-risk patients presenting a higher mortality rate [3].

Skull manifestations commonly involve the calvaria, the temporal bone, and the jaws [8]. The jaws are involved in approximately 10% of cases; the mandibular body and angle are generally reported as more common sites than the maxilla, especially in patients over 20 years of age [9,10]. The lesion may be solitary or multiple. Multiple sites in both the mandible and the maxilla are usually involved; about 20% of patients have a polyostotic disease. In a series reported by Di Nardo and Wetmore, 86% of the mandibular lesions were unifocal [11].

There is not a gold standard treatment for LCH in the oral maxillofacial region; nevertheless, surgical therapy is included in the guidelines as the first choice treatment for the LCH single-system single site for oral localization [12]. The surgical therapy is varied and depends on the site and number of localizations; it can range from curettage up to resection followed by reconstruction [13]. Unfortunately, curettage can cause relapse, and the resection can be too aggressive and/or too wide, making the reconstruction challenging [14].

CAD/CAM surgery was progressively applied to maxillo-facial surgery over the years. As a result, different studies demonstrate the accuracy and the advantages of CAD/CAM-assisted surgery in oral and facial reconstruction [15–17]. The CAD/CAM technique allows the creation of Virtual Surgical Planning (VSP) and simulation by realizing and producing cutting guides and stereo-lithographic models. All of these tools enable the surgeon to achieve the best optimization for the treatment because they allow analyzing the patient-specific anatomy preoperatively in order better to understand the resection and better project the reconstruction; pre-bending of standard osteosynthesis plates, and production of customized implants, when achievable, reduce operative time and improve precision. As a result of a more precise resection and reconstruction in a shorter operative time, patient outcomes and quality of life are improved.

There are many studies showing the benefit of CAD/CAM use for treating oral cancer or facial deformities, but, at this time, there are no studies about the use of CAD/CAM for LCH treatment reported. The authors report a single system-single site LCH involving the mandible in a 56-year-old woman, with a special emphasis on surgical treatment by CAD/CAM surgery for the mandible resection and reconstruction.

## Case Presentation

A 56-year-old female patient was referred with an extensive osteolytic lesion of the mandible. The patient was asymptomatic, and the lesion was found incidentally through a panoramic radiograph obtained for dental treatment purposes. The panoramic radiograph showed a large area of radio transparency in the left molar region of the mandible (Figure 1). A biopsy under local anesthetic was performed, and histological examination reported a pattern compatible with the diagnosis of LCH. Nuclear bone scanning with Technetium 99 m was then performed to investigate whether other bones or organs were involved, and no other localization was found.

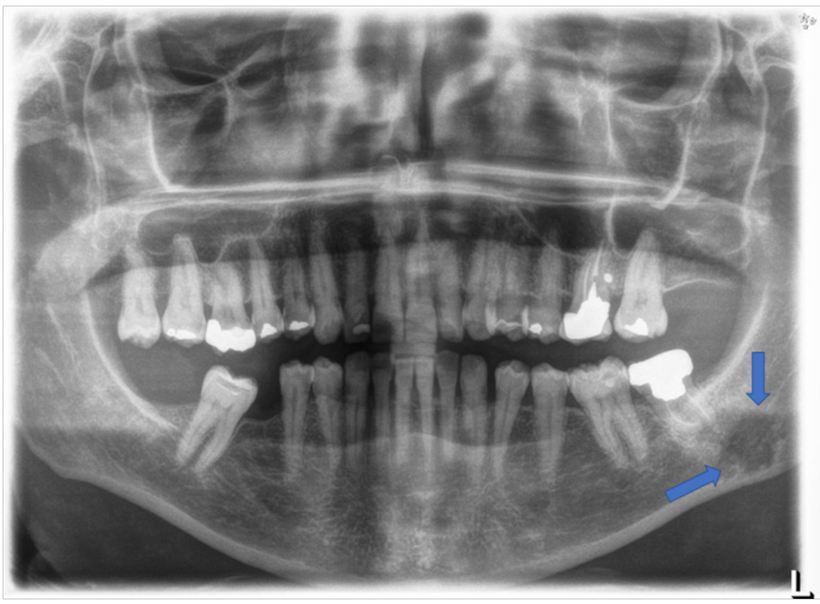

**Figure 1:** Panoramic radiograph showing area of radiotransparency (blue arrows) in the left molar region of the mandible.

Based on the radiographic findings and clinical evidence, surgical treatment was planned by virtual surgical planning (VSP) and 3D printed surgical templates. To process VSP, pre-operative Computed Tomographic (CT) scans of head and neck and hip bone regions were performed with 0.6 mm slice thickness, and the digital imaging and communications in medicine (DICOM) data were imported (Figure 2). The VSP was simulated in HA3Dtm Ortopedia software, and 3D printed templates were designed and fabricated by medics tools for medicine.

**Virtual surgical planning:** Frankfort Horizontal Plane (FHP), mid-facial plane (perpendicular to the FHP through the nasion), and coronal plane (perpendicular to the FHP through the Sella point) were used as reference planes to allow the study of the boundary and anatomic structure of the mandible lesion on the 3D model. After orientation, the planes for the osteotomy were settled, and the lesion resection was performed virtually (Figure 3). Then, the bone defect was defined. Next, the left iliac bone STL (Stereo Lithography interface format) file was successfully imported to plan the mandible reconstruction. Finally, the osteotomy planes for the iliac crest bone graft were set and cut (Figure 4). After the cutting step, the bone graft was virtually oriented to fit the defect (Figure 5).

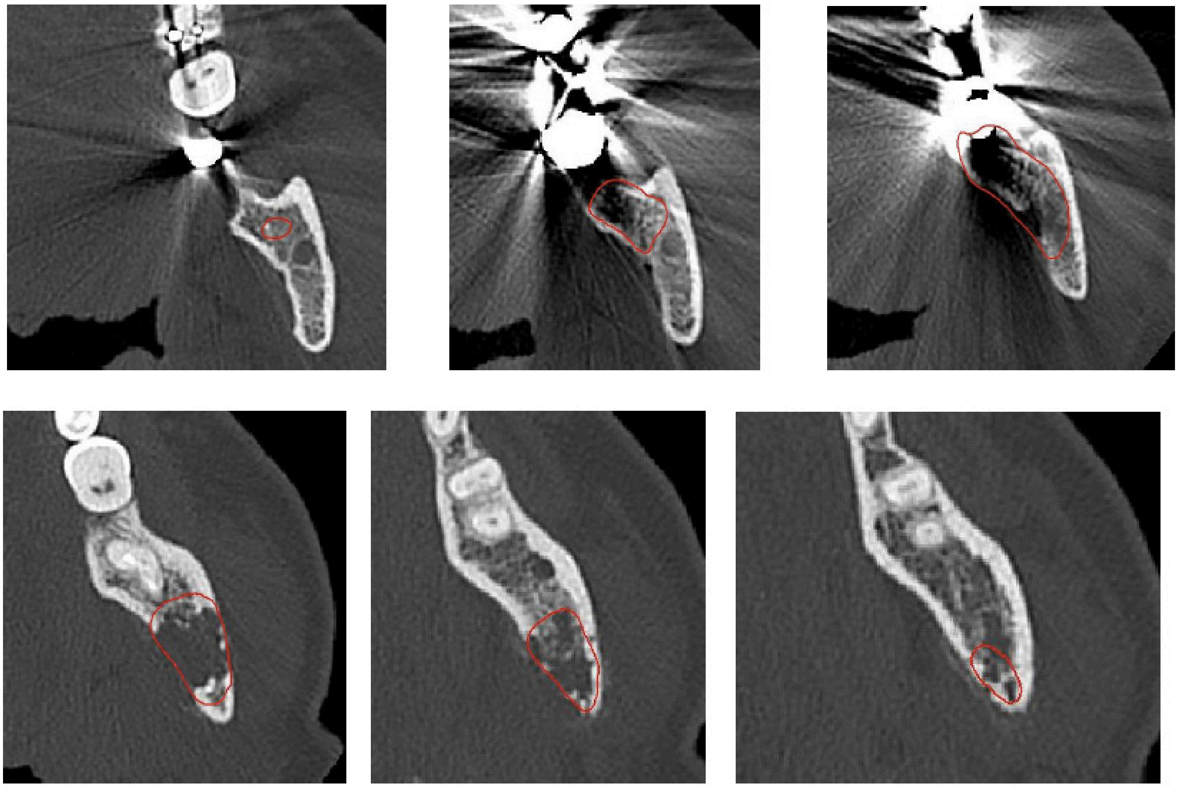

Figure 2: The red line in Axial CT scan showing the osteolytic area into the left mandible ramus.

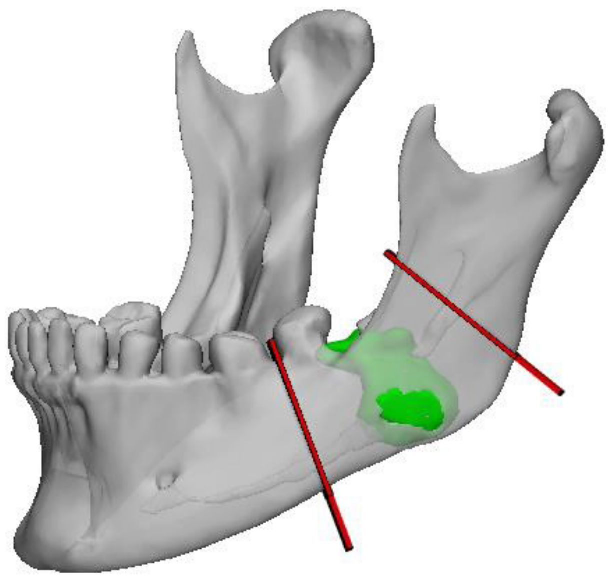

Figure 3: 3D model showing the mandible lesion (green area) and the osteotomy setting (red line) on the safe margins.

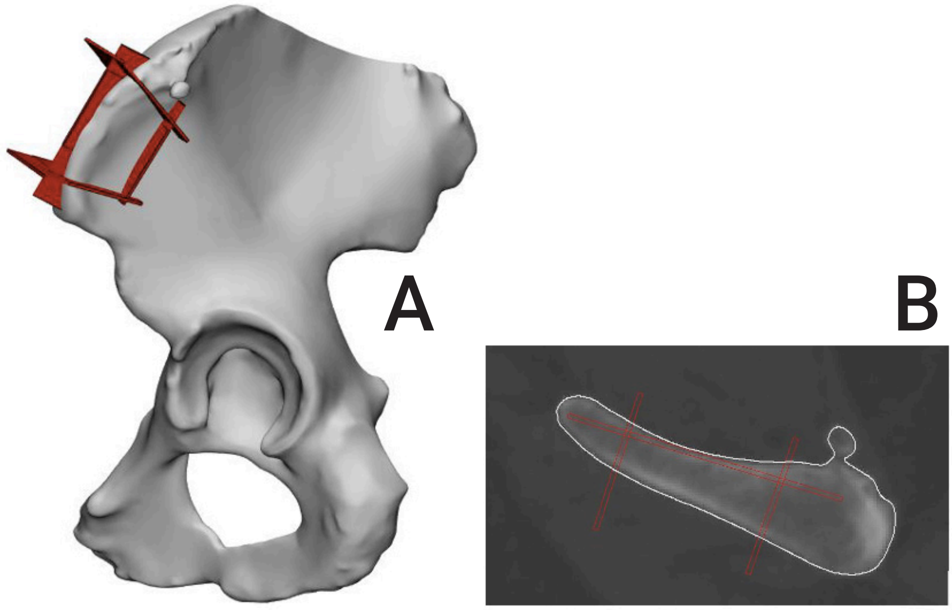


**Figure 4:** 3D model of left Iliac Bone **(a)** and axial CT scan **(b)**. The red lines pointed the osteotomy edges.

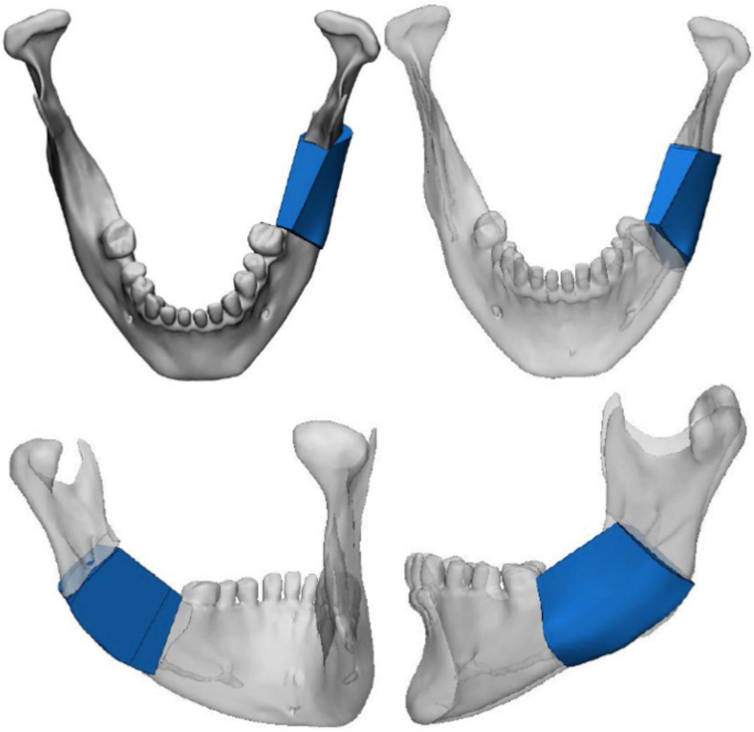

**Figure 5:** 3D model of mandible reconstruction with left iliac crest graft without osteosynthesis plates.

**Guide design:** To transfer the planning information to the operating room, the surgeon determined the cutting guides, who considered the clinical aspects of intraoperative feasibility. In addition, the cutting guide was packaged in a single piece in order to keep the two resulting mandibular stumps in a stable position. Finally, a 3D replica (stereolithographic model) of the reconstructed mandible with iliac graft positioned on site was fabricated in order to prebend one osteosynthesis mandibular plate that was sterilized preoperatively.

**Surgical procedure:** Under general anesthesia, the left mandible was accessed via a submandibular approach. Once the sub-mandibular access flap was raised, the periosteal flap was preserved, both on the lingual and the vestibular sides, in order to create a protective fold for the bone graft (Figure 6a, Figure 6b). Next, the diseased bone was removed by resecting the mandible segment according to the preplanned cutting and drilling guide (Figure 6a), and inferior alveolar nerve preservation was obtained by splitting the resection into two pieces (Figure 6b). Next, the corticocancellous graft for the reconstruction was harvested freehanded via the anterior approach to the iliac crest as the cutting guide could not be used because of its steric bulk. Next, the bone graft was shaped by drill on the lingual side to create a groove for the mandibular nerve (Figure 7a). Finally, it was planted to reconstruct the surgical gap with two mini plates onto the superior border with the cutting guide aid (Figure 7b), and the pre-bended reconstruction (mandibular) plate was placed on the inferior border (Figure 7c).

The patient's postoperative course was complicated at one month by a left perimandibular abscess; a CT control scan showed an iatrogenic lesion of the first molar roots (Figure 8); the Authors performed tooth extraction and plate removal under local anesthesia followed by antibiotic therapy (Figure 9). After three weeks, the clinical abscess was resolved.

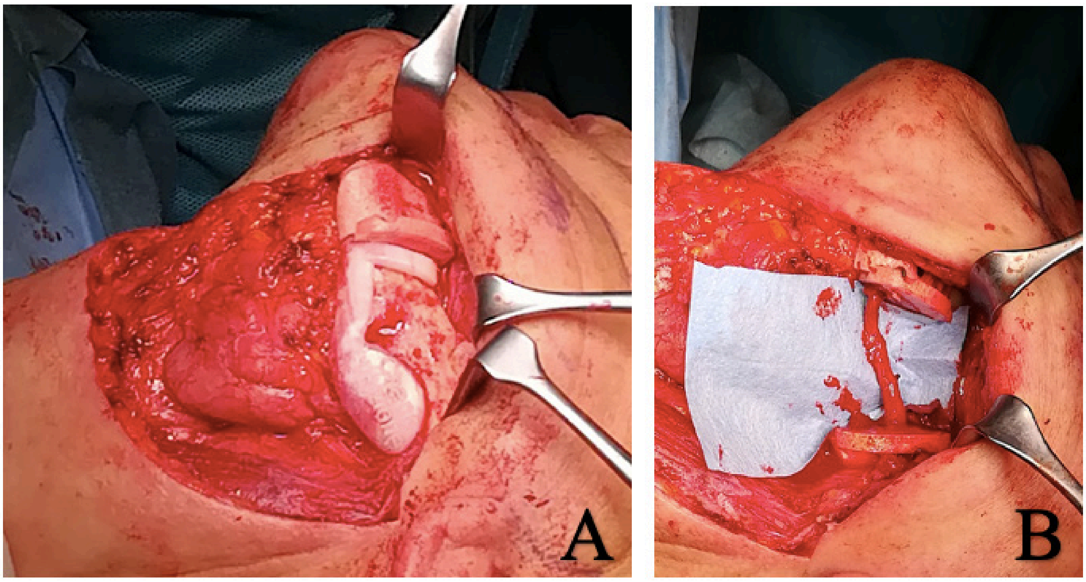


**Figure 6: a)** The submandibular approach with the cutting guide placed; **b)** preservation alveolar nerve after resection.

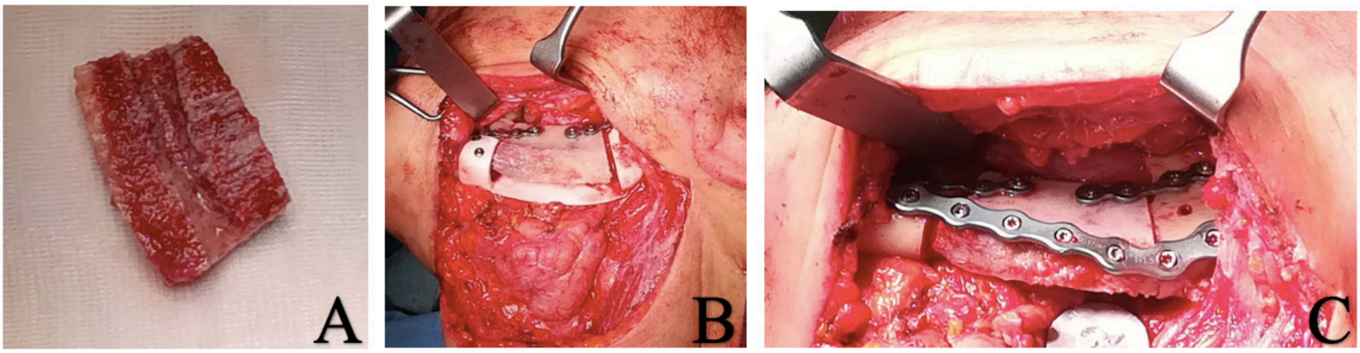


**Figure 7:** The corticocancellous graft with the alveolar groove **(a)**; the graft placed to fill the surgical gap between the mandible stumps and the former fixation with the mini plates **(b)**; the latter fixation with reconstruction plate.

**Figure 8:** CT scan after surgery showed roots lesion by the screws.

**Figure 9:** RX-OPT after tooth extraction and plate removal.

Temporary dysesthesia along the V3 branch of the trigeminal nerve was recorded but resolved spontaneously after three months.

Histology revealed that the lesion was Langerhans Cell Histiocytosis (LCH) (Figure 10). Therefore, the patient was finally diagnosed with LCH single-system single-site (S-S).

The patient did not show any recurrence in clinical and medical records at 12 months and 24 months after surgery (Figure 11). In addition, no deficit regarding the inferior alveolar nerve and no aesthetic disorders were recorded.

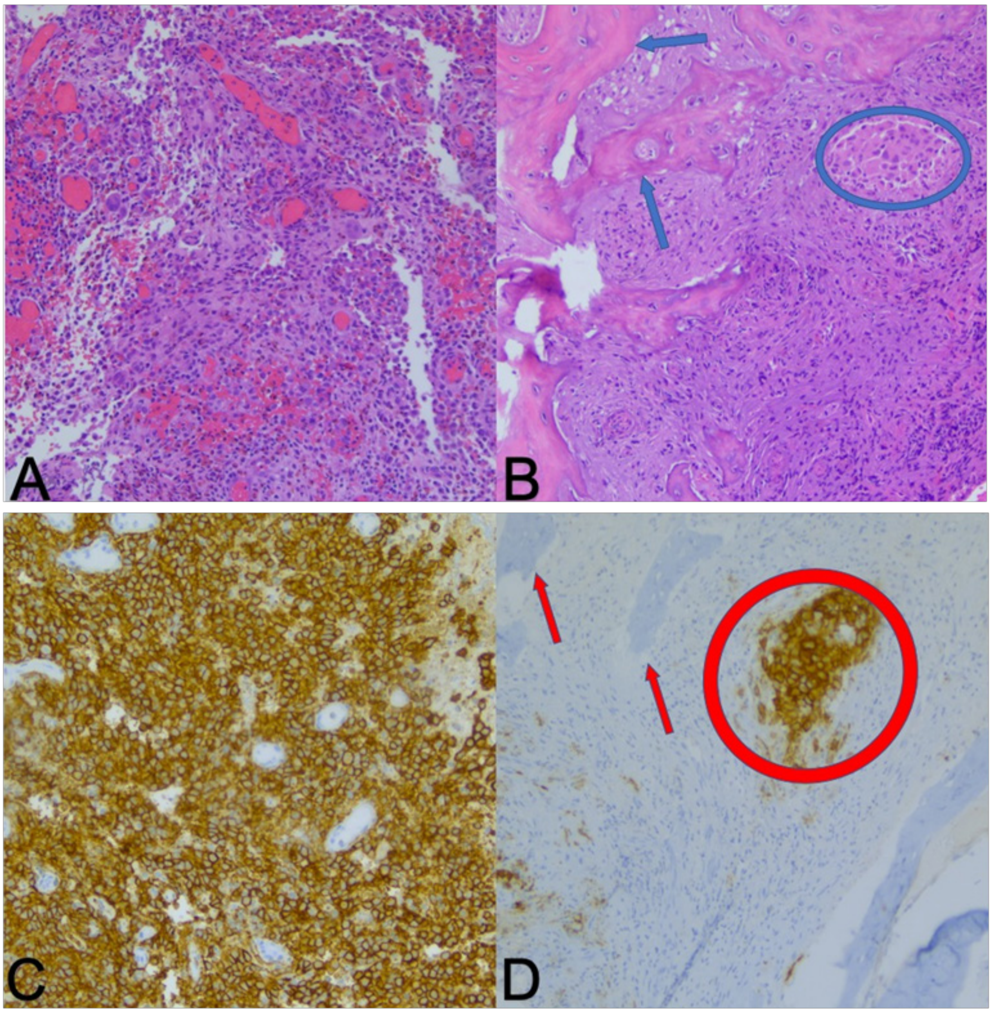


**Figure 10:** Microphotograph at 10 X : **a)** Hematoxilin and Eosin (HE) showing cell proliferation of histiocytes with grooved nuclei and copius eosinophilic cytoplasm; **b)** HE showing a set of histiocytes (blue circle) and bone trabecular with desmoplastic tissue around (blue arrows); **c)** Immunohistochemistry with CD 1a positivity; **d)** A set of cell CD1a + (red circle) and bone trabecular (red arrows).

**Figure 11:** CT scan two years after surgery showed graft osteointegration and no pathology recurrences.

## Discussion

Nowadays, there is a great debate about the gold standard therapy for patients with Langerhans Cell Histiocytosis (LCH) [2]. LCH treatment involves surgical interventions (from curettage to resection) [18,13], radiotherapy [3], and chemotherapy [3]; all of those can be used either alone or in a combined fashion.

The efficiency of radiotherapy of the jaws is discussed controversially: some studies have shown that radiotherapy might produce local control of bone lesions [3], while Watzke et al. have recorded completely unsuccessful results [19].

Surgical procedures are only called for if severe local problems occur, while radiation is reserved for patients with lesions that are either inaccessible or threatening vital structures.

Regarding surgical therapy, curettage is known to yield successful outcomes, but a number of recurrences have been reported [14]; on the other hand, bone resection requires demanding reconstructive procedures along with possible undesirable outcomes, such as paresthesia, infections, and excessive bone loss after reconstruction. The decision to undertake reconstructive surgery should take into consideration:

- Lack of evidence of systemic involvement of the disease.
- Lack of evidence of local or systemic recurrence.
- The risk of pathologic fracture of the mandible because residual bone thinness may support the need for reconstructive surgery.

Computer-assisted planning, surgery, and 3D printing for treating maxillo-facial pathologies have been documented extensively over the last decade [15–17]. However, at the time of publication, the authors are unaware of any paper reporting 3D-assisted surgical treatment for LCH of the mandible.

Our experience in the presented case shows that surgeons can clearly benefit from the technology described, but we hit some pitfalls. First of all, the unavailability of STL models of the plates did not make it possible to predict the steric size of the cutting guide with the placement of the plates, so we had to remove the guide to perform the osteosynthesis. Moreover, it was not possible to pre-bend the plates on virtual planning but on 3D replica only; consequently, it was not possible to match the holes of the plates with those of the cutting guide. So, after the bone resection, the cutting guide did not allow to perform osteosynthesis but checked the fitting of the bone graft only.

Another pitfall was the steric bulk of the cutting guide produced for the graft harvesting; it has to be noted that in some cases, surgeons will have to perform larger approaches due to the bulk of the guides, while we did not extend our approach and preferred free hand harvesting to avoid higher morbidity.

We could have prevented the pitfall using the STL of the plates for virtual planning to plan a cutting guide that provides housing for the plates and, consequently, a correct alinement of the holes. However, for the same reason, we could not predict the holes plates' position, which led to damaging the first left inferior molar roots. Therefore, tooth extraction and plate removal under local anesthesia were necessary one month after the surgery. In this second surgical time, we checked the graft's stability and the bone callus formation. The latter pitfall was due to lack of experience because preoperative planning takes time and requires a certain degree of mastery in computer sciences if done by the surgical team.

In conclusion, our case showed that surgical therapy (resection and reconstruction) offers a good choice to treat LCH single site-single system of the jaws. Computer-Aided Design and Computer-Aided Manufacturing implementation showed how technologies improve surgeon skills and patient outcomes but are not a tool for the unskilled surgeon in virtual surgical planning as issues during the surgical procedure are to be expected.

## Conflicts of Interest

We would like to confirm that the submitted manuscript has been read and approved by all the authors and that there are no conflicts of interest to be disclosed.

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