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IDEAS AND INNOVATIONS

Application of low-cost fused deposition modeling additive manufacturing rapid anatomic models in patients with rhino-cerebral mucormycosis treated with maxillectomy

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Abstract

Mucormycosis is a fungal infection mainly of immunocompromised patients. It has many clinical manifestations depending on the system that is affected. Rhinocerebral mucormycosis and pulmonary infection are the most common. In this pathology, the fungi invade the endothelium of the blood vessels with partial or total obliteration, with tissue ischemia and necrosis. The initial symptoms are unspecific making difficult to identify from other infections and need an expert suspicion level. The gold standard is the culture of the fungi; histopathology analysis shows empty hyphae with thin walls. Combined treatment is strongly recommended surgical extended debridement and Amphotericin B is the gold standard of treatment. The craniofacial skeleton (CS) has a very peculiar bone and soft tissue distribution that maintains height, width, and projection. In RCM, aggressive debridement is prognostic for patient survival. Extensive maxillectomies, often with orbital exenteration represent a reconstructive challenge for plastic surgeons. Recently different types of additive manufacture (AM) technology had been proposed in surgical planning. Fused deposition manufacture (FDM) technology could be the most cost-effective for patients. To the best of our knowledge, this is the first report of the use of FDM and reconstruction of patients with RCM. RCM is a very serious life-threatening condition. When treated in time with the adequate surgical approach and a correct antifungal medicine RCM can be a cured. The goals in treating this condition are very clear. A free flap reconstruction is an adequate approach to patients with RCM and FDM RAM can help the surgeon to plan the free flap in site. We present two cases reconstructed with MSAP and ALT-FL respectively with success assisted with FDM RAM.

Level of Evidence: Level V, therapeutic study.

Keywords 3D printing · Rhinocerebral mucormycosis · Rapid prototyping · Free flap

Introduction

Mucormycosis is a fungal infection predominant in immunocompromised patients. It has many clinical manifestations depending on the system affected (rhino-cerebral mucormycosis (RCM), skin, pulmonary, or systemic) [1, 2].

In Mexico, Garcia et al. [3, 4], reports 12 cases in 7 years only in 2 centers but is obviously underestimated [3, 4]. In the USA, the incidence is 1.7 cases per million habitants representing approximately 500 cases in 1 year. [5] The risk factors are diabetes acidosis, metabolic acidosis, glucocorticoids therapy in high doses, penetrating trauma, burn injury, persistent neutropenia, deferoxamine, and treatment chronic hematologic transfusions [1]. Other risk factors are malnutrition and HIV infection [1].

The microorganisms responsible are 18 groups of fungi that live in the environment. They produce spores that are the dissemination medium. The species of fungi more frequently involved are *Rhizopus* 47%, *Mucor* 18%, *Cunninghamella bertholletiae* 7%, *Apophysomyces elegans* 5%, *Absidia* 5%, *Saksenaea* 5%, *and Rhizomucor pusillus* 4% [1, 6].

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In this pathology, the fungi invade the endothelium in blood vessels with partial or total obliteration. These events cause tissue ischemia and necrosis [1, 2]. The infected tissue shows wide necrosis with infiltrating of polymorphonuclear cells. Clinical syndromes are variable: Rhinocerebral infection, pulmonary infection, cutaneous infection, gastrointestinal infection, and systemic infection [1]. The initial symptoms are unspecific making it difficult to identify from other infections [1, 2].

RCM should be suspected in patients with diabetes or polytraumatized who present metabolic imbalance (acidosis). Who had some injury in the face or oral cavity (cheeks, lips, eyelids, palate, etc.). In this case, there will be a mandatory culture/biopsy of the lesion and immediate debridement. The gold standard is the culture of the fungi. In the histopathology, analysis shows empty hyphae with thin walls. Depending on the clinic presentation resonance magnetic image (IRM) or computer assisted tomography (CAT) scan could be useful to determine the extent of the infection and plan the surgical approach for debridement [1, 2].

Combined treatment is strongly recommended; surgical extensive debridement and Amphotericin B are the gold standard of treatment. Even with correct treatment mortality is high as 95% in pulmonary presentations. RCM mortality is between 10 and 70% even with correct treatment [1, 2].

Method

RCM surgical debridement and reconstruction

The craniofacial skeleton (CS) has a very peculiar bone and soft tissue distribution. These structures maintain height, width, and projection of the face. The analogy of facial buttress system of the CS has improved results in oncology and trauma [7] (Fig. 1). The maxilla could also be anatomically represented by a cube (Fig. 2). Where the orbital floor is the roof and the anterior hard palate and alveolar ridge is the floor, the nasal passage is the medial wall and the zygoma the lateral wall [8]. The cube analogy helps to understand the different types of maxillectomy resections while the buttresses help to understand its reconstruction.

In RCM, aggressive debridement is prognostic for patient survival. Extensive maxillectomies, often with orbital exenteration represent a reconstructive challenge for plastic surgeons. The goals of the RCM are: (1) Stop the infection by extensive debridement (leaving borders free from hyphae), (2) close the wound (with appropriate autollogous tissue), (3) obliterate the maxillectomy defect, (4) support the globe if preserved or fill the orbital cavity (if the globe is exenterated), (5) maintain a barrier between the nasal sinuses and the anterior cranial fossa, (6) restore l/face shape and projection, and (7) reconstruct the palate to promote an adequate swallowing mechanism [8].

Types of maxillectomy [8]: (Fig. 3)

Type I limited: involves two of the six walls of the maxilla.
Type II subtotal: involves five walls.
Type IIa: < 50% of the transverse palate.
Type IIb: > 50% of the transverse palate or the anterior arch defect with the orbital floor intact.
Type III total maxillectomy: involves all of the six walls.
Type IIIa: preserve orbital contents.
Type IIIb extended maxillectomy: resection of entire maxilla including the orbital contents.
Type IV orbitomaxillectomy: Involve resection of the orbital entire contents leaving dura and brain exposed. It can involve the palate or not.

Additive manufacturing and reconstructive surgery

Recently different types of additive manufacture (AM) technology had been proposed in surgical planning. Fused deposition manufacture (FDM) technology could be the most cost-effective [9]. To our knowledge, this is the first report of the use of FDM and reconstruction of

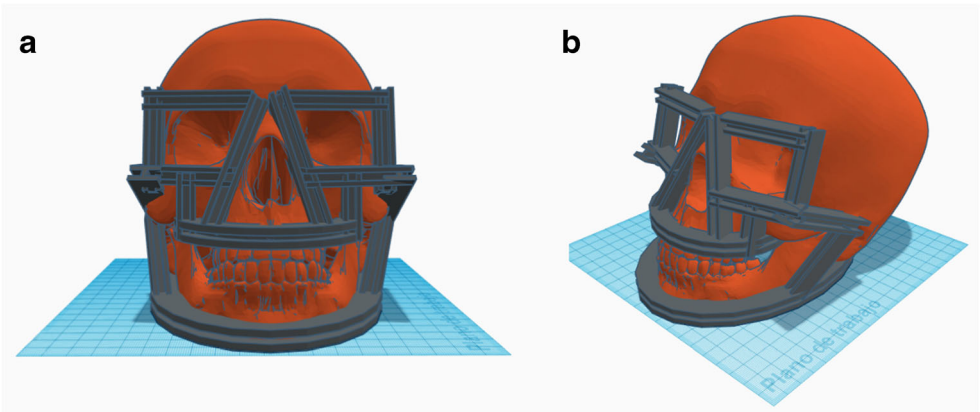

Fig. 1 The facial buttresses in a 3D STL model

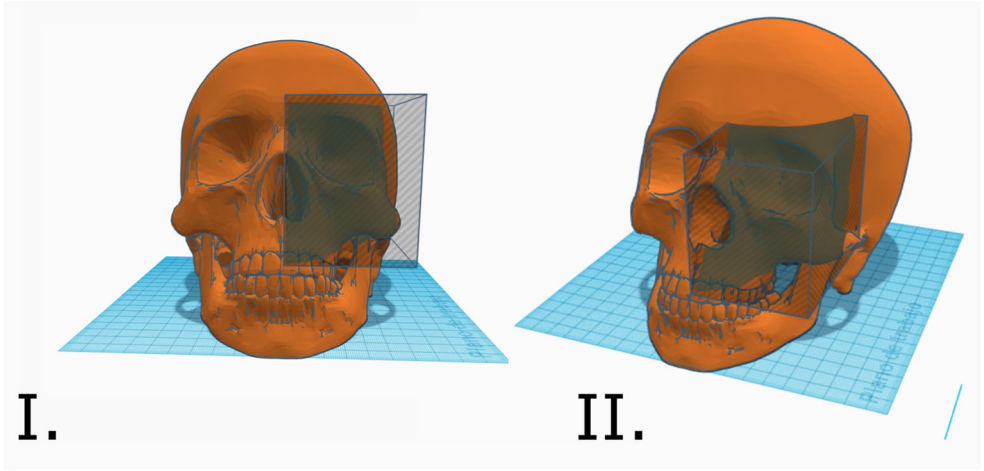

Fig. 2 The cube analogy in a 3D STL model

patients with RCM. When AM is used in surgical plan, some benefits described are improved surgical plan, preoperative simulation, production of surgical implants, prebending plates reducing surgical time and others [9–16].

The diagnosis and treatment of patients with RCM is a complete medical challenge. Very few literature present surgical treatment planning assisted with low-cost FDM technology. The aim of this paper is to present two cases of RCM with free flap reconstruction assisted we low-cost FDM technology.

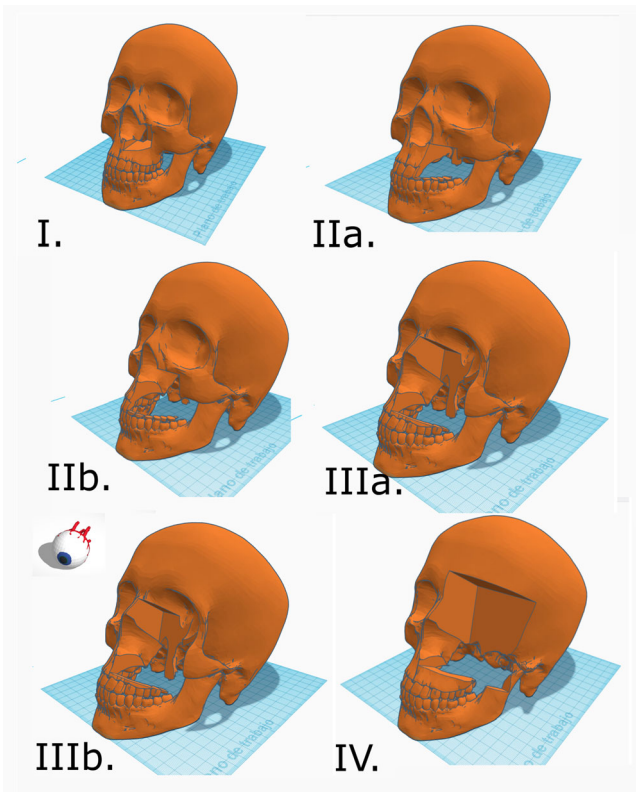

Fig. 3 The different maxillectomies

Clinical representatives cases

Case 1, a 17-year-old female, with newly diagnosed diabetes mellitus type 2. Admitted for an oro-nasal fistula, with signs of chronic sinusitis and periocular edema. An endoscopic biopsy was performed thanks to a high suspicion of RCM Amphotericin B was initiated. The mucosal biopsy of the right sinus was taken, finding *Rhizopus* sp. a angio-CAT scan was performed and showed eye and ocular muscle involvement. So a Type IIIb right extended maxillectomy was performed. Transoperative hematoxylin and eosin microscopic analysis from the resected tissue margins. Was reported negative by > 1 cm in all directions, although hyphae invasion was reported in the temporal receptor vein wall. So delayed reconstruction was decided meanwhile covering the wound with Aquacel AG (ConvaTec, Deeside, UK). The patient presented a naso-orbital and an oro-antral fistula post-operatively. We continued with antifungal therapy for five more weeks until reconstructive surgery was made. Using the FDM technology and protocol previously described by Rendon et al. [9] a rapid anatomic model (RAM) was built for surgical planning [9]. The protocol started with a facial CAT scan. Then using the digital imaging communications in medicine (DICOM) file was converted to standard triangle language (STl) format. The STL format was converted to G-code format. And finally the RAM was printed. The RAM was used to simulate the surgery. Measurements where registered to plan soft tissue architecture. Later, a 12 × 7 cm medial sural artery perforator (MSAP) flap was harvested and anastomosed to the facial artery. The flap covered the naso-orbital and oro-antral fistula successfully. The patient continued asymptomatic, with no evidence of fistula or mucormycosis in 2-6 months follow-up. (Fig. 1).

Case 2, a 46-year-old male with a 3-year history of diabetes and smoking tobacco for 20 years. The patient

came to emergency department presenting headache of 3 weeks of evolution. Later conjunctival edema and proptosis appeared. Initially was treated by an ophthalmologist. Who diagnosed him with Reis-Buckers dystrophy and performed gland biopsy. Later metabolic acidosis with severe glycemic decontrol and fever emerged. The patient presented palpebral/eyelid edema of the left eye accompanied with a wound in the upper eyelid. Also proptosis of the left eye, altered mental functions and motor aphasia. The rest of the physical examination without any alterations. Due to the clinical state, the diagnosis of RCM was established. Immediately a left type IIIB and right type IIB subtotal maxillectomy were performed. Later, using the protocol previously described, a RAM was built for surgical planning [9]. The RAM was used to simulate the surgery. Measurements where registered to plan soft tissue architecture. And later the reconstruction was performed with an ALT with vastus lateralis (ALT-VL) chimeric flap. The flap was anastomosed to the temporal artery. He persisted with metabolic acidosis and some central nervous system symptoms. After 2 weeks, the family requested the transfer to another hospital due to personal economic and hospital location reasons (Fig. 2).

Discussion

Evidence shows that mucormycosis has a predilection for endothelial invasion and vascular dissemination. A cell-surface protein GRP78 acts as a receptor for the fungi in human's allowing the damage to the endothelium [17]. This endothelial damage causes tissue ischemia representing a potential risk for the microvascular immediate reconstruction.

Murphy et al. [18] presented a case of RCM reconstructed with an ALT free flap with 2 weeks of delay with no flap loss. Seitz et al. [19] presented a case of skin mucormycosis treated with a latissimus dorsi/rib intercostal perforator myo-osseocutaneous free flap with thrombosis 24 h posterior to surgery. They saved the flap by rapid re-intervention with no flap loss. Reinbold et al. [20] presented a case reconstructed by a 2 week delayed Diep Epigastric Perforator (DIEP) flap with no flap loss. Our group has an experience of five cases of rhinocerebral mucormycosis with immediate debridement and immediate reconstruction, all of them survived without complications. One patient died of pulmonary complications on intensive care unit. Many other cases had been described with free flap reconstruction success. Despite the fungi endothelial predilection, microvascular reconstruction is an excellent resource for reconstruction [18–22].

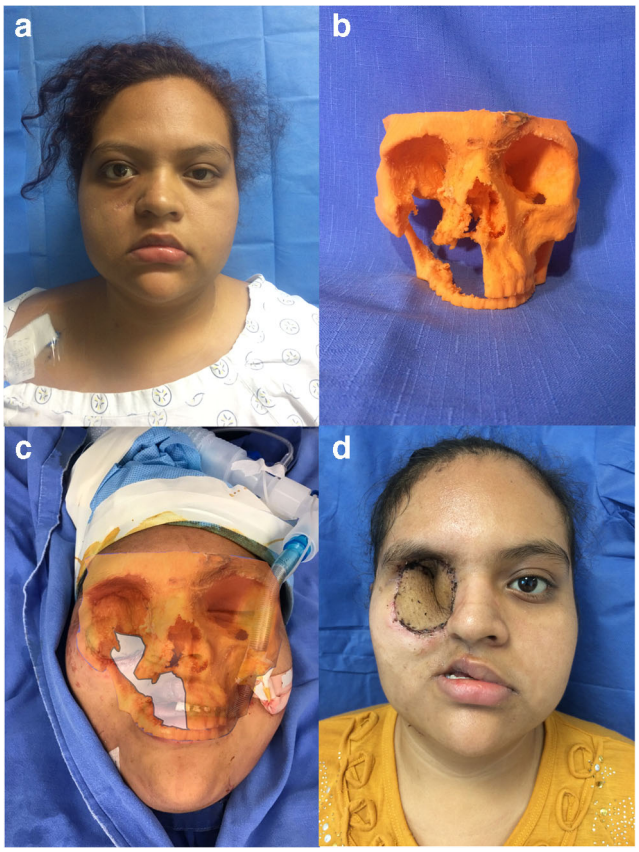

Fig. 4 **A** Preoperative image with right affection. **B** Rapid prototype. **C** Surgical plan patient perception. **D** Postoperative result

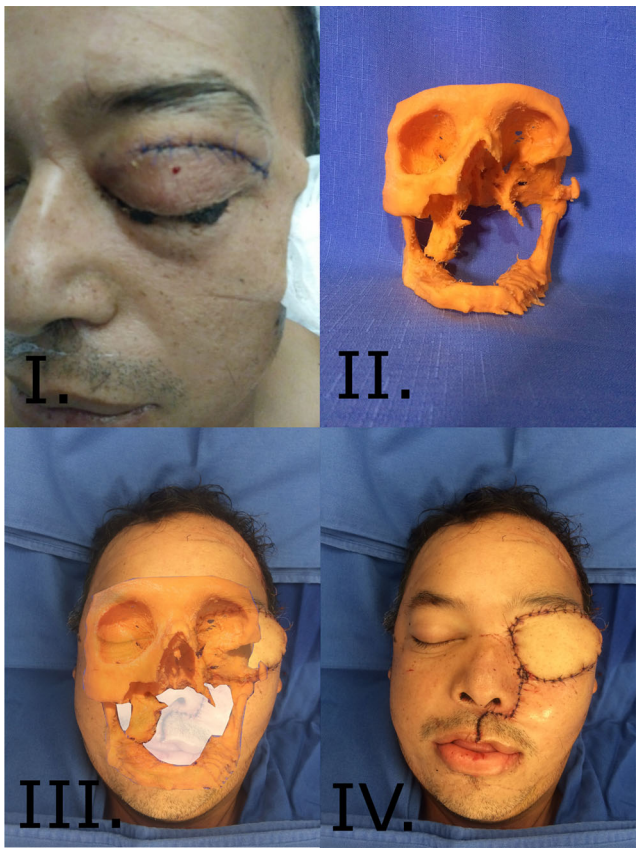

Fig. 5 **I** Preoperative image with left affection. **II** Rapid prototype. **III** Surgical plan patient perception. **IV** Postoperative result

In our 2 cases in this paper, microvascular reconstruction was performed following the craniofacial reconstruction recommendations [7, 8, 23, 24]. No osseous component was used because the globe was exenterated in both cases so no support was required. It is important to report that we had no flap loss nor thrombosis. FDM technology aided to plan the flap in site configuration and, to accomplish the reconstructive goals previously described. It is possible that RAM help surgeons to improve the surgical results with surgical time reduction. Other AM techniques had been described like stereolithography but with more elevated cost and similar dimensional error [9]. To our knowledge, this is the first two cases reported with FDM open source software RAM used for RCM free flap reconstruction reported in the literature. (Figs. 4 and 5).

The main disadvantage of FDM RAMs is that the creation of a single model could take several days, limiting their disposition for immediate reconstructions. Futhermore, the main limitation of this study is the short follow-up time.

Conclusions

RCM is a very serious life-threatening condition. When treated in time with the adequate surgical approach and a correct antifungal medicine RCM can be a cured. The goals in treating this condition are very clear: (1) Stop the infection by extensive debridement (leaving borders free from hyphae), (2) close the wound (with appropriate autollogous tissue), (3) obliterate the maxillectomy defect, (4) support the globe if preserved or fill the orbital cavity if the globe is exenterated, (5) maintain a barrier between the nasal sinuses and the anterior cranial fossa, (6) restore /face shape and projection, and (7) reconstruct the palate [8]. A free flap reconstruction is an adequate approach to patients with RCM and FDM RAM can help the surgeon to plan the free flap in site.

Compliance with ethical standards

Funding We received no funding from the government nor private organizations.

Conflict of interests Marco Aurelio Rendón-Medina and Erik Hanson-Viana declare that they have no conflict of interest.

Ethical approval The protocol was approved by the ethical committee of the Hospital Regional de Alta Especialidad de Ixtapaluca.

Informed consent Patients provided verbal and written consent beofre their inclusion in this study.

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