



Rhino-maxillary aspergillosis in an immunocompetent patient. Case report.

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ABSTRACT

Introduction: Aspergillosis is the second most frequent opportunistic fungal infection of the paranasal sinuses. It primarily affects the maxillary sinus and occurs mainly in immunocompromised individuals. Infection is caused by inhalation of spores or by an oro-sinusal communication. Aspergillosis is classified into an invasive and non-invasive form or Aspergilloma, which usually affects immunocompetent patients. Violaceous lesions, ulcers, necrosis and tissue destruction can be manifested clinically. Patients may experience pain, paresthesias, increases in the volume of purulent or bloody nasal discharge and congestion. **Case report:** A 62-year-old female patient, immunocompetent, with a condition evolving for about six years. Condition began after a dental extraction, and consisted of absence of scarring and recurrent episodes of symptomatology suggestive of maxillary sinusitis with poor response to antibiotics. The patient was referred to the maxillofacial care unit, presenting an increase of volume in the right genial region, pain and paraesthesia of infraorbital region. The CT scan showed the presence of a radiopaque foreign body in the right maxillary sinus. A surgical procedure was carried out using the Caldwell-Luc technique and biopsy; the case was diagnosed with Aspergillosis. The patient was treated without antifungal therapy because she had a good immune status. **Conclusion:** Aspergilloma is the most common form of Aspergillosis in immunocompetent individuals. It is usually diagnosed late, as its clinical picture is similar to bacterial sinusitis. In most cases, patients respond well to surgical treatment, and systemic antifungal therapy is not necessary.

Keywords: *Aspergillosis, Aspergilloma, mycetoma, maxillary rhinosinusitis.*

INTRODUCTION

In recent years there has been an increase in the incidence of fungal rhinosinusitis due to diffusion of different pathogenic organisms and to the higher prevalence of diseases such as diabetes and chronic treatments with corticosteroids and immunosuppressants (Soler & Schlosser, 2012). It has been reported that approximately 10% of all patients treated surgically for chronic sinusitis correspond to fungal sinusitis (Lop-gros & Gras-Cabrero, 2016). Within these, it has been seen that Aspergillosis is the most frequent opportunistic fungal infection in rhinosinusitis (Monroe & Mclean, 2013). Aspergillosis is caused by *Aspergillus*, a species of fungus, formed by hyaline hyphae, belonging to Ascomycetes, found in soil, water, air and decomposing organic vegetation (Telles et al., 2017). It usually affects immunocompromised patients, although it can also affect healthy subjects. There are more than 800 species, of which *Aspergillus fumigatus*, *Aspergillus Niger* and *Aspergillus Flavus* are the species that most frequently affect humans. In addition to rhinosinusitis, *Aspergillus* can cause lung, heart, spleen, liver or meningeal infections (Fanucci et al., 2013).

Aspergillosis is mainly transmitted by inhalation of spores, but in the maxillary sinus it can also come through an oro-sinusal iatrogenic communication secondary to a dental procedure, such as a root canal treatment or a dental extraction; the maxillary sinus is usually the most commonly affected area (Peral-Cagigal et al., 2014). Anatomical variations in the osteomeatal complex, such as septal deviation, bullous nasal concha, Haller cells and the shape of unciform process, are associated with the development of rhinosinusitis (Shin & Baek, 2016). Based on clinical manifestations and extension, fungal rhinosinusitis is classified as invasive and non-invasive. The

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invasive form occurs more frequently in immunocompromised patients and may be classified as granulomatous, chronic invasive and acute fulminant (Montone, 2016). The invasive form is a very serious condition causing death in 90% of cases due to intracranial complications (Segal, 2009). The noninvasive form is subdivided into fungal allergic sinusitis and mycetoma or aspergilloma, which corresponds to a dense and non-invasive accumulation of fungi in the paranasal cavities (Ferguson, 2000).

Clinically, oral lesions show three distinctive clinicopathological stages. The early stages are characterized by isolated areas of marginal violaceous growth, corresponding to degenerate epithelium and fungal hyphae that infiltrate connective tissue. In the advanced stage, these lesions become gray necrotic lesions extending into the attached gingiva with ulceration and pseudomembrane. Vascular invasion is observed in the bases of ulcers. In the late stage, there is progressive destruction of surrounding bone and muscle tissues, with histopathological evidence of infiltration of fungal hyphae (Telles et al., 2017).

Aspergillus rhinosinusitis may occur with headache, fever, nasal congestion, facial swelling and purulent or bloody nasal discharge. It should be suspected in a patient with recurrent or refractory sinusitis, who does not respond to antibiotic therapy (Telles et al., 2017).

The aim of this report is to present a case of Aspergillosis with symptoms of recurrent sinusitis in an immunocompetent patient.

CASE REPORT

Sixty-two year old female patient, from the district of Tomé, Bío Bío Region, Chile. The patient was referred to maxillofacial surgery for right orofacial pain and a history of complication of right molar extraction performed six years ago, characterized by extensive, irradiated pain, and absence of scarring. Her condition was managed with curettage, intra-alveolar eugenate and treated with Amoxicillin, Metronidazol and repetitive Amoxicillin administration in combination with Clavulanic Acid. At the fourth week after extraction the pain continued and there was an increase of volume in the genial region, hence the patient was referred to the maxillofacial surgery unit. The patient reported pain and paresthesia of the infraorbital region.

Physical examination showed an increase of volume in the right genial region and an ulcerated lesion with areas of necrotic tissue in the right upper molar region (Figure 1). In addition to the physical examination, a CAT was requested for suspicion of maxillary sinusitis. The CAT revealed occupation of the maxillary sinus, nasal fossa, right ethmoidal labyrinth and presence of a radiopaque foreign body in the maxillary sinus (Figure 2).



Figure 1. Clinical appearance, extraoral frontal view.

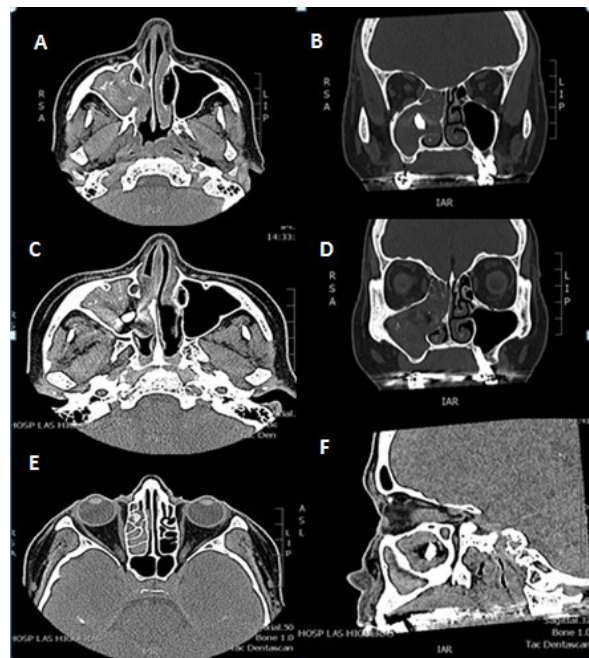


Figure 2. First CAT. Full involvement of the right maxillary sinus and presence of a radiopaque foreign body is observed. Axial cut (A, C, E), coronal cut (B, D) and sagittal cut (F).

As a differential diagnosis for this case, squamous carcinoma, osteomyelitis, maxillary sinusitis, and mucormycosis were considered. These can be found as white lesions in the oral cavity, in the form of ulcers, compatible with the lesion presented by this patient. In addition, they may be observed

radiographically occupying the maxillary sinuses, as in the case of this patient. However, all were discarded after the post-surgical biopsy, which yielded the diagnosis of Aspergillosis.

The patient underwent an intra-oral surgery and antrorhinotomy using the Caldwell Luc technique, in which repositioning of the bony window with osteosynthesis is performed (Figure 3). The excisional biopsy of the lesion was carried out, along with the removal of the foreign body housed in the maxillary sinus, which turned out to be eugenate. The biopsy was sent to histopathological study, where the sample was fixed in paraffin. The homology with the control CAT of *Aspergillus fumigatus* was determined by real-time PCR. The lesion was diagnosed as Aspergillosis (Figure 4) using the Grocott staining technique.

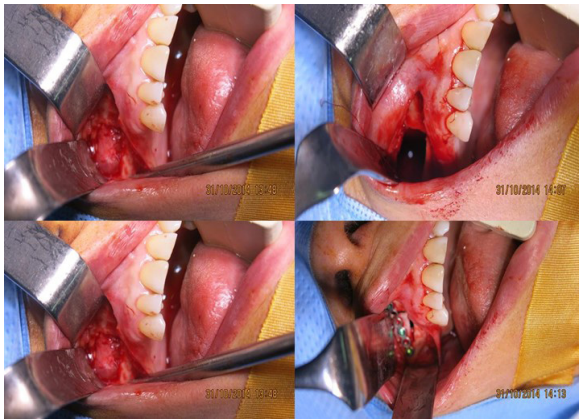


Figure 3. Surgical procedure, using the Caldwell-Luc surgical technique and repositioning of the bony window.

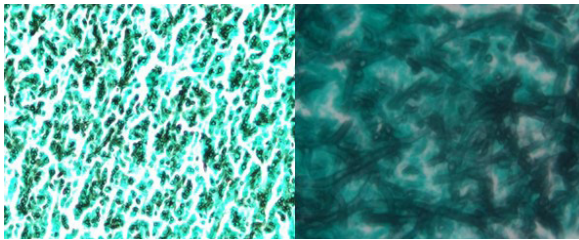


Figure 4. Histology obtained by Grocott staining.

As postoperative treatment, Ketoprofen 100mg every 8 hours, Clindamycin 600mg every 12 hours, paracetamol 1gr every 8 hours, Ranitidine 50mg every 8 hours were administered intravenously. The patient was discharged the following day and prescribed oral doses of Amoxicillin 875mg with Clavulanic Acid 125mg every 8 hours for 7 days, Diclofenac Sodium 50mg every 8 hours for 3 days, Piroxicam 20mg every 24 hours for 3 days, Omeprazole 20mg every 24 hours 10 days. This treatment was chosen because the patient was immunocompetent and the medical staff considered that she could evolve satisfactorily, avoiding the use of Amphotericin

B, which has a large number of adverse effects, especially on the renal system (Telles et al., 2017).

Subsequently, the patient was evaluated by clinical and CT examination at 6 months, showing no symptoms or recurrence of the lesion (Figure 5).

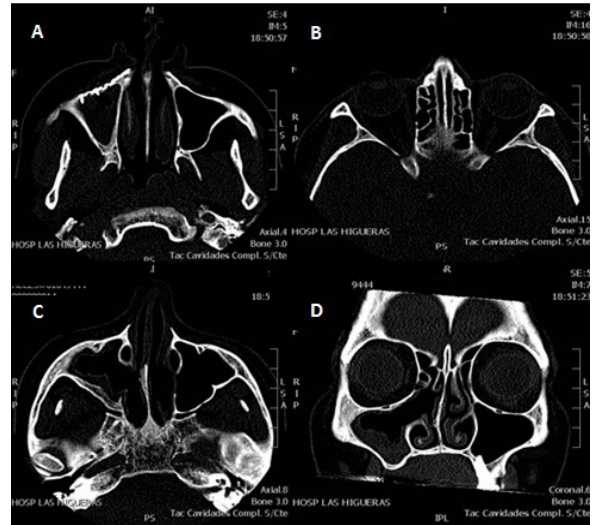


Figure 5. Evaluation by CAT scan at 6 months. Axial cuts (A, B, C) and coronal cut (D).

In June 2017, the patient was reevaluated by a clinician and a Cone Beam examination. The patient reported no discomfort, the infraorbital sensitivity had been recovered and there was no evidence of an increase in volume. No evidence of recurrence was observed when examining the Cone Beam images (Figure 6).

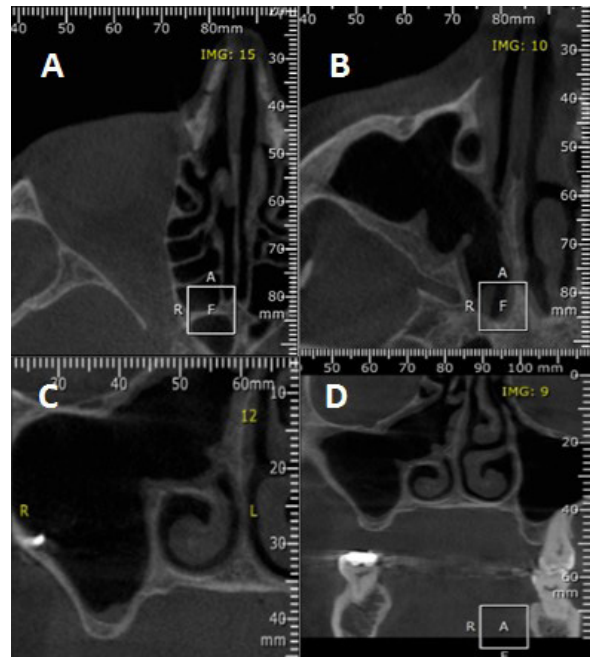


Figure 6. Evaluation by Cone Beam, June 2017. Axial cut (A and B) and coronal cut (C and D).

DISCUSSION

Within the noninvasive forms, mycosis or rhinosinusual aspergilloma occurs more frequently unilaterally, and it may rarely affect more cavities (Montone, 2016). In contrast, fungal allergic sinusitis frequently affects more than one paranasal sinus. Aspergilloma usually occurs in immunocompetent adults, with no significant alterations in immunoglobulin levels or subclasses of IgG,10 with an average age of 64 years (Segal, 2009), and a higher incidence in women (Fanucci et al., 2013), characteristics that coincide with those of the case presented in this report. Clinical manifestation is usually of slow evolution and oligo-symptomatic, characterized by headache, cough and facial algia. Since the symptoms are similar to those of chronic bacterial rhinosinusitis (Fanucci et al., 2013), patients are usually treated repeatedly with antibiotic therapies to which they do not respond (Raz et al., 2015). This coincides with the case of this patient as she had consulted for 6 years for symptoms of sinusitis, being treated with antibiotics repeatedly, without showing a favorable response, until she presented an increase of volume and paresthesia of the right genital area in recent months. Because of the above, the diagnosis of mycetoma is often late, in fact, only 29% of patients are diagnosed within one year of the onset of symptoms (Fanucci et al., 2013).

Computed tomography without contrast is the exam of choice for the initial diagnosis of Aspergillosis. In cases of invasive infections, magnetic resonance imaging may be used to assess the extent of the lesion in adjacent soft tissues (Raz et al., 2015). This was not necessary in the present report, since the infection was confined to the maxillary sinus, probably due to the good immune status of the patient.

Mycetoma affects more frequently the maxillary sinus, secondly the ethmoidal sinus, and more rarely the sphenoid sinus. Maxillary sinus involvement is observed radiographically as a radiodense area with linear or rounded central areas of calcified matrix. This is due to deposits of calcium and magnesium salts in areas of fungal growth, which look hyperdense in CT scans. These are characteristic of rhinosinusitis caused by fungi. Due to the expansive nature of the allergic mucosa and its capacity to produce local inflammation, erosive changes and expansion with bone remodeling of the maxillary sinus can be observed (Raz et al., 2015). This alteration is compatible with the evidence found in the patient's radiographs. She presented an involvement of both the maxillary and ethmoidal sinuses, with a radiodense image containing small radiopaque areas, which corresponded to calcified deposits.

It has been suggested in previous studies that any dental material containing zinc that has been propelled into the maxillary sinus has the potential to become infected and form an aspergilloma. Root canal cements and amalgam contain zinc

in amounts large enough to cause this reaction (Burnham et al., 2009). This may explain the possible cause of mycetoma in this patient, which had a radiopaque foreign body in the right maxillary sinus, which turned out to be eugenate. This cement is widely used in dentistry for temporary restorations, as endodontic material and for treatments of post-extraction alveolitis. It contains a high amount of zinc in its composition, and this was probably causing a reaction that favored conditions conducive to the growth of fungi.

The surgical treatment of aspergilloma can be performed with both classic surgery and the Caldwell-Luc technique, obtaining excellent results (Fanucci et al., 2013). It is important to open the ostium and allow proper ventilation of the sinus to completely eliminate mycetoma. Recurrence rates of 5% have been reported (Pagella et al., 2007). In most immunocompetent patients, surgical treatment is sufficient, and systemic antifungal therapy is rarely necessary (Fanucci et al., 2013). This is why in this case, it was decided not to administer antifungal drugs such as Amphotericin B (Telles et al., 2017), since it may become a very harmful drug for the renal system, and given the patient's immunological characteristics, its use was not justified. Because of its immunocompetent condition, surgery should be sufficient to completely remove the fungal infection.

CONCLUSION

Aspergilloma is a localized, non-invasive fungal infection that can affect the maxillary sinuses with a clinical presentation similar to bacterial rhinosinusitis, being commonly and incorrectly treated with antibiotics, leading in most cases to a late diagnosis. Treatment for immunocompetent patients consists of a surgical approach, with curettage and ostium release, consequently the use of systemic antifungals is not necessary.

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