Implications of Endodontic-related Sinus Aspergillosis in a Patient Treated by Infliximab: A Case Report

Maud Guivarc'h, DDS,[*†] *Ugo Ordioni, DDS,*[*‡] *Jean-Hugues Catherine, DDS,*[*†] *Fabrice Campana, DDS,*[‡] *Jean Camps, DDS, PhD,*[*] *and Frédéric Bukiet, DDS, PhD*[*§]

Abstract

Introduction: Sinus aspergillosis is a potential complication after root canal therapy of antral teeth. Indeed, zinc oxide–eugenol cement overfilling in the sinus may promote fungal infection. Moreover, if sinus aspergillosis triggers chronic sinusitis with aspergilloma, it may also lead to invasive phenomena, especially for immunocompromised patients. **Methods:** We reported a sinus aspergillosis case of a patient treated with infliximab (Remicade; Janssen Biologics BV, Leiden, Netherlands). The purpose of this article was to explore the mechanisms of this pathosis, especially the impact of the root canal sealer overextension, which is a contributing factor for fungal infection. The surgical management and the follow-up are also described. **Results:** Six months after surgery, the patient showed no clinical signs and presented with a healthy and airy right maxillary sinus on the computed tomography scan. **Conclusions:** In conclusion, prevention and screening of aspergillosis of maxillary sinus may be considered before starting an anti–tumor necrosis factor alpha therapy. *(J Endod 2015;41:125–129)*

Key Words

Aspergillosis, endodontics, maxillary sinusitis, root canal filling, therapeutic use, tumor necrosis factor

From the *UFR Odontologie de Marseille, Aix Marseille Université, Assistance Publique des Hôpitaux de Marseille, Marseille, France; †UMR 7268 ADES Aix-Marseille Université-EFS-CNRS, Faculté de Médecine de Marseille; ‡Centre Massilien de la Face, Marseille; and §Laboratoire Biologie Santé et Nanosciences, UFR Odontologie de Montpellier 1, Montpellier, France.

Address requests for reprints to Dr Frédéric Bukiet, UFR Odontologie de Marseille, Aix Marseille Université, Sous-section d'Odontologie Conservatrice-Endodontie, 27 Boulevard Jean-Moulin, 13005, France. E-mail address: frederic.bukiet@univ-amu.fr

0099-2399/$ - see front matter

http://dx.doi.org/10.1016/j.joen.2014.09.022

Sinus aspergillosis is a scarce but well-known complication after root canal therapy of antral teeth (1, 2). *Aspergillus fumigatus* needs heavy metals such as zinc oxide for proliferation and metabolism (3, 4). Therefore, zinc oxide–eugenol cement overextension in the sinus may promote fungal infection. Moreover, if sinus aspergillosis triggers chronic sinusitis with aspergilloma, it may also lead to invasive phenomena, especially for immunocompromised patients. Invasive forms of sinus aspergillomas can be chronic or fulminant. In both cases, computed tomographic (CT) scanning shows tumorlike images with bone destruction and extensive infiltration of neighboring structures (orbit and base of the skull) (5, 6) with a risk of dissemination, which can lead to intracranial and/or lung aspergillosis. In fulminant forms, which occur mostly in immunocompromised patients, extension is quicker, and there is a higher risk of dissemination (7).

Anti–tumor necrosis factor alpha (anti–TNF-α) agents are used for treating patients with inflammatory arthritis and inflammatory bowel disease (8). This kind of treatment leads to an increased risk of infection. Many opportunistic infections including legionellosis, listeriosis, pneumocystosis, histoplasmosis, and aspergillosis have been reported (9, 10).

Infliximab (Remicade; Janssen Biologics BV, Leiden, Netherlands) is a monoclonal antibody anti–TNF-α often prescribed for psoriasis, rheumatoid arthritis, Crohn disease, ulcerative colitis, spondylarthrite spondylitis, and psoriatic arthritis. We report a patient with sinus aspergillosis treated with infliximab. The purpose of this article was to explore the mechanisms of this pathosis, especially the impact of the root canal sealer overextension, which is a contributing factor for fungal infection. The surgical management and follow-up are also described.

Case Report

Clinical Observation

A 64-year-old patient was referred for an oral health evaluation before starting prosthetic treatment. Anamnesis showed many health problems such as psoriatic rheumatism history, stabilized non–insulin-dependent diabetes, dyslipidemia, chronic cough, and sinusitis associated with facial pains. Consequently, the patient provided her prescriptions, which included an anti–TNF-α (Remicade), biguanide (metformin), and statin (pravastin).

Overall, the clinical examination revealed poor oral health without associated symptoms. The panoramic view highlighted the anatomic continuity between the maxillary sinus and the apex of the upper molars and also an important sealer overextension in the right sinus close to tooth 16 (Fig. 1). Rhinoscopy was implemented but did not reveal any nasal sign. A CT scan was prescribed to thoroughly check the sinus obstruction and the overfilling extent and its aspect. The sealer overfilling in the right sinus appeared as a hyperdense structure and was surrounded by peripheral and nonhomogeneous opacification associated with a severe hypertrophic mucous membrane (Fig. 2). A slight bone densification of the sinus lining was also observed, and the patency of the maxillary ostium sinus was correct. No invasion of the surrounding structures was noticed.

Symptoms could either correspond to chronic sinusitis of bacterial origin or sinus aspergillosis. Taking into account the clinical and paraclininal data and the specificity of the radiologic image, noninvasive sinus aspergillosis was suspected.

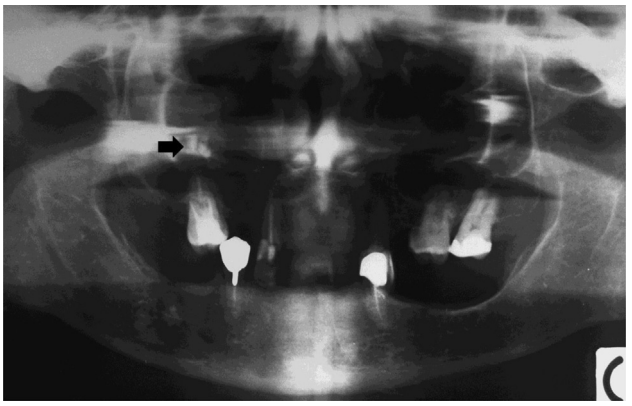

Figure 1. Orthopantomography.

The patient was referred to a pneumologist to check breathing function and detect potential chronic obstructive bronchopathologies. A thoracic CT scan was normal, and, except the chronic cough, no bronchopathologies or lung issues were noticed including lung aspergillosis. With the suspicion of aspergillosis and the potential risk of complications, it was decided to implement a surgical procedure.

Treatment

The surgical therapy was based on tooth extraction associated with Cadwell-Luc surgery. A periapical lesion with inter-radicular bone resorption of tooth 16 was visible on the CT scan. Although this issue could have probably been solved by endodontic retreatment, a collegial decision of extraction was made by the rheumatologist and the odontologic team because of 2 main elements: (1) the rheumatologist wanted a radical and quick attitude toward infection sources considering that anti–TNF-α treatment would not be resumed after the surgery until the patient was free of dental infectious sources and (2) the tooth showed no strategic importance for the future prosthetic rehabilitation considering the poor bone level and its isolated position.

The surgical procedure indicated for clearing the infected maxillary sinus was Cadwell-Luc surgery. The indications for which surgical technique should be used (ie, Cadwell-Luc surgery, endoscopic surgery for meatotomy, or a combination of these 2 techniques) have remained controversial for more than 20 years. According to Costa et al (11), endoscopic surgery is the treatment of choice for sinus aspergillosis, and Cadwell-Luc surgery must be considered as a complementary technique (11). However, Ferreiro et al (12) showed no recurrence with Cadwell-Luc therapy, and a recurrence rate of 6.8% after endoscopy. Because the accessibility of the sinus is more difficult during a meatotomy, the risk of residual remnants, an important factor of recurrence, would be more important. According to Dufour et al (13), Cadwell-Luc surgery is always insufficient when the maxillary ostium is blocked, and endoscopic treatment is more often indicated to restore drainage.

In the present case, Cadwell-Luc surgery alone was preferred for the following reasons: (1) there was good ostium patency, (2) it allowed good accessibility to the fungal balls localized in the lower part of the sinus, and (3) the extraction of tooth 16 and closing the oroantral fistula with a buccal flap were scheduled at the same time and the same flap would allow access to the anterior wall of the sinus for curettage.

The surgical treatment required infliximab interruption 4 weeks before the surgical procedure to reduce risks of severe infection (14). The surgery was performed under general anesthesia. After incision, the soft tissues over the maxillary sinus were elevated thanks to a trapezoidal flap to visualize the frontal wall of the right sinus. Then, a round bur was used to fenestrate the maxillary sinus and to make a sufficient opening for the cleaning step (Fig. 3). The sealer debris were carefully removed as well as brown soft tissue mass (Figs. 4 and 5) and the hypertrophic mucous membrane. Then, a gentle rinse was performed with Betadine (Meda Manufacturing, Merignac, France). A periosteal incision allowed closure of the surgical site without tension.

Finally, mycologic and anatomopathologic examinations were implemented to confirm the diagnosis. Histology showed a heterogeneous material with large and strong eosinophilic areas, which corresponded to fibrin enclosing a few red blood cells. Hematoxylin-eosin-safran and periodic acid–Schiff colorations indicated many aggregations of tightly packed hyphae with 45° dichotomous branching, characteristic of *Aspergillus*. Some fragments containing neutrophils, lymphocytes, and plasma cells were also observed, but cultures were

Figure 2. A CT scan showing sealer overfilling in the right sinus appeared as a hyperdense structure surrounded by a peripheral opacification.

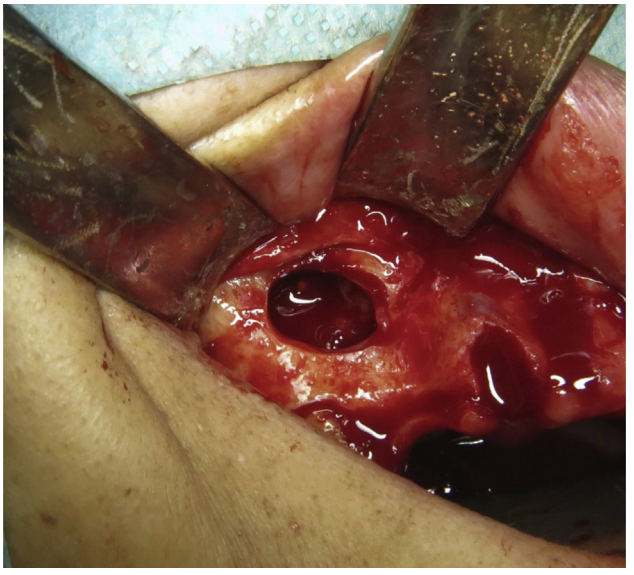

Figure 3. A clinical view of Cadwell-Luc surgery.