

Cavernous sinus thrombosis secondary to non-invasive sphenoid aspergillosis*

A. Devèze¹, F. Facon¹, G. Latil², G. Moulin³, H. Payan-Cassin⁴, P. Dessi¹

1 Department of Oto-rhino-laryngology, Unit of Endoscopic Functionnal Sinus Surgery. La Timone University Hospital, Marseille, France

2 Department of Oto-rhino-laryngology, Aix-en-Provence General Hospital, Aix-en-Provence, France

3 Department of Radiology, La Timone University Hospital, Marseille, France

4 Department of Radiology, Aix-en-Provence General Hospital, Aix-en-Provence, France

SUMMARY

The sphenoid localization of aspergillosis is a rare sinusal disease, often latent or asymptomatic. The neurological complications are the result of invasive forms occurring in most cases for the immunocompromised or diabetic patients. Nevertheless, non-invasive sphenoid aspergillosis may cause also several complications and affect the vital prognosis of non-immunocompromised patients. This report is about two cases of cavernous sinus thrombosis secondary to a non-invasive sphenoid aspergillosis. The authors refer to the clinical and radiological findings and therapeutic approach of this rare complication.

Key words: Aspergillus fumigatus, sphenoid sinusitis, cavernous sinus thrombosis, non-invasive aspergillosis, complications of sinusitis.

INTRODUCTION

The presence of *Aspergillus* within the paranasal sinuses is manifested in different anatomico-clinical settings [1]: (1) **the non-invasive aspergillosis (NIA)** is defined by the absence of invasion of the mucosa upon the pathological exam. Hartwick and Batsakis [2] distinguished three different sub forms: simple colonization, pseudo-tumoral aspergillosis (mycetoma) and allergic aspergillosis [3]; (2) **the invasive aspergillosis (IA)** is defined histopathologically by the invasion of the mucosa, sub-mucosa, blood vessels, or bone by the fungal process that can spread to the adjacent anatomical structures [4]. Those IA are constantly associated with severe neurological complications. We present in this paper two cases of complicated non-invasive aspergillosis of the sphenoid sinus that both occurred with immunocompetent patients.

CASE 1

Mrs R., a 68 years old patient, was referred to our institution presenting right ophtalmoplegia with exophthalmia and visual impairment, diffuse headache and bilateral purulent rhinorrhea. The inaugural symptoms occurred for two weeks, initially as frontal and vertex pain with fever. The first CT-scan showed a bilateral opacity of the ethmoid and sphenoid sinuses associated with a right cavernous sinus thrombosis that was immediately confirmed by a cerebral angiography (Figure 1). The initial diagnosis was a cavernous sinus thrombosis secondary to purulent ethmoidal and sphenoidal sinusitis. A medical treat-

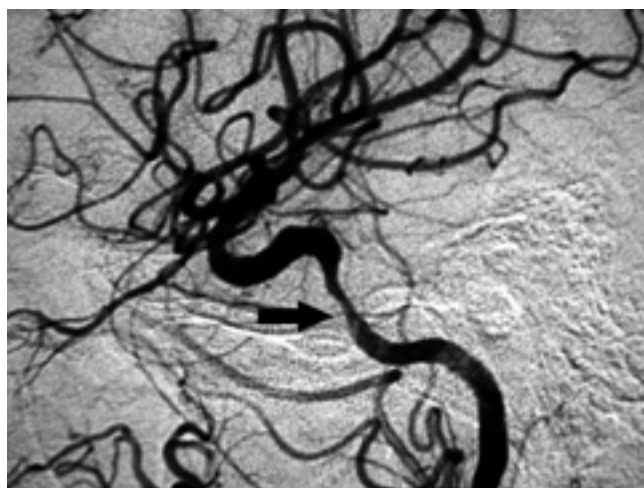


Figure 1. First case. Angiography of the right internal carotid artery. There is a stenosis of the intra cavernous segment of the carotid artery (A) that suggests an extrinsic compression within the cavernous sinus.

ment was started which associated intravenous bi-antibiotherapy (cefotaxim 3 grams + ofloxacin 400 mg per day), prednisolone (1mg/kg/day), intravenous heparin at curative dose, and epinephrine inhalation. Recovery of the exophthalmia occurred after 48 hours. Five days after starting treatment, a second CT scan showed a bilateral sphenoid opacity with calcium tonality (Figure 2). At this time, the diagnosis of primary fungal sphenoiditis was presented. The surgical procedure con-

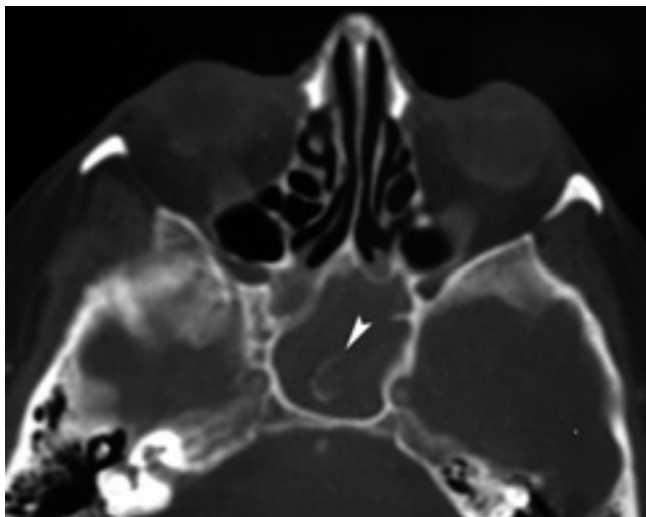


Figure 2. First case. Axial CT-scan realized after intravenous antibiotic therapy. There is a bilateral sphenoiditis and numerous calcium opacities within it (white arrow), demonstration of the fungal origin.

sisted of a bilateral video-assisted sphenoidotomy. The sphenoid sinuses were filled with the characteristic buttery brown-grey material. The identification revealed an *Aspergillus fumigatus*. The histopathological data confirmed the diagnosis of non-invasive aspergillosis. The immediate post-operative period has been uneventful. After one month, a CT scan showed that the whole paranasal sinuses were completely clear. Currently, with 2 years of follow-up, the patient has not presented any recurrence of disease.

CASE 2

It concerns a 56 years old woman who had been initially admitted in emergency to explore a large right chemosis without visual impairment. She also complained progressive and increasing headaches, remarkably localized on the vertex area. The inaugural CT-scan showed a left-sided sphenoiditis that was confirmed by the MRI assessment which also showed a bilateral cavernous sinus thrombosis with a right ophthalmic vein thrombosis (Figure 3). An intravenous treatment was started consisting of the administration of bi-antibiotherapy (cefotaxim 3 grams + ofloxacin 400 mg. per day) added to continuous heparin anticoagulation. Five days later, after resolution of the ophthalmic signs, a second CT-scan demonstrates a persistent left sphenoid opacity with calcium tonality and thickening of bony partition of the sinus that suggested a chronic and fungal origin that probably led to the suprainfection (Figure 4). The surgical treatment consisted of a video-assisted bilateral sphenoidotomy. At opening the sphenoid, the mucosa was thickened with a granulomatous aspect. The sinus was also filled with the characteristic brown material that suggests the fungal process. The sinus mucosa was removed with the aspergilloma. The pathologic examination demonstrates the species (*Aspergillus*) but the culture failed to identify the kind. There was no invasion of the mucosa. The postoperative



Figure 3. Second case. (A) T1-weighted axial MRI with gadolinium. Left sided sphenoid sinusitis (Δ) with a right (contra-lateral) exophthalmia and chemosis. Note the thrombi, as a hypointense signal (Ü), expression of the cavernous sinus thrombophlebitis. (B) There is a thrombophlebitis of the right ophthalmic vein (Ü). The ophthalmic vein is dilated with an inflammatory hypersignal.

period has been uneventful. The antibiotics were administered intravenously for 8 days, relayed by 8 days of oral amoxicillin plus clavulanate (3 grams per day). No antifungal drugs were used. After 8 months of follow-up time and six consecutive months of anti-vitamin K, the patient is currently free of recurrence with a normal angio CT-scan.

DISCUSSION

The aspergillosis of the paranasal sinuses is a disease frequently found in the literature and associates invasive and non-invasive forms. The sphenoid localization is rare and the proximity of the neuro-vascular structures explains the major complication that can occur. Non-surprisingly, the immunocompromised patients suffer by invasive and complicated aspergillosis more often than the immunocompetent ones [5, 6]. The complications are consecutive to the mycelial growth and to production of cytotoxic metabolites allowing bone and tissue



Figure 4. Second case. Thickening of the bony wall of the sphenoid sinus, demonstrating the chronic etiology (white arrow). There is some slight calcium-like opacity within the sinusitis. In this case, note that the sphenoid aspergilloma occurred on the left side, with a right cavernous sinus and ophthalmic vein thrombosis, due to the diffusion of the inflammatory process.

destruction [7, 8]. It is a classical fact of the invasive forms, possibly fulminating [5, 9, 10, 11] and frequently responsible for neurological and vascular complications [12, 13]. This is not the case of the non-invasive aspergillosis and explains the reason why we were surprised to see that an aspergilloma was the cause of the cerebral thrombosis. In fact, a non-invasive aspergillosis might cause several complications either by the inflammatory process that it generates within the sphenoid cavity [8, 14] or merely by an acute bacterial suprainfection. In both cases, the inflammation localized to the skull base near the cavernous sinus can induce hypercoagulability, and explains the diffusion of the cerebral venous thrombosis [15, 16]. The second case is particularly demonstrative: there was a contra-lateral venous thrombosis (left sphenoiditis and right thrombosis). Such a situation can only be explained by the diffusion of the inflammation far beyond the sphenoid cavity,

what a latent aspergilloma rarely induces, contrary to an acute purulent sphenoiditis. By the way, the aspergilloma should be considered as the adjuvant factor for the bacterial sphenoiditis, which induced a secondary cavernous sinus thrombosis. Associated to the antibiotics whose aim is to treat the suprainfection, the surgical procedure objects a triple aim: to eradicate the inflammatory process and the cause of suprainfection (aspergilloma), to give the histological proof of the diagnosis and to warn for recidivism. It requires the realization of a large sphenoidotomy, the attentive cleaning of the whole cavity and the removal of all the pathological mucosa [7, 8, 17]. Surgery is rarely urgent. We recommend treating the suprainfection first, which is usually the cause of the symptomatology. The surgical procedure should be done after improvement of the clinical status or in case of aggravation despite antibiotherapy. In this latter situation, the sphenoidotomy is done for drainage and bacterial identification, rather than for the mycetoma. In both cases, the surgical approach should be a minimal-invasive way as possible. The advantage of the video-assisted technique results in a better control of the sinus cavity at the end of the procedure with a simplest postoperative time. An anticoagulation consisted in intravenous heparin is required to obtain a curative level of anticoagulation. Endovascular treatment is usually reserved for selected cases after failure of anticoagulation [18]. After surgical treatment of the sinusitis, the heparin is relayed by oral anticoagulation consisted of antivitamin K for at least 6 months [19]. This prolonged anticoagulation is usually stopped after the normality of a controlled angio-CT or MRI-scan [18]. Antifungal chemotherapy (usually intravenous amphotericin-B and oral itraconazole) is not necessary in case of non-invasive form of aspergillosis [10, 11, 14].

CONCLUSION

These two cases show that, even latent, a sphenoid aspergillosis might induce severe neurological complication, such as cavernous sinus thrombosis, only by the hypercoagulability induced by the surrounding inflammation and bacterial suprainfection. In case of acute purulent sphenoiditis, a persistent sphenoid opacity after antibiotherapy, even more if there are calcium-like opacities, must evoke the diagnosis of primitive mycetoma. The treatment of choice, except the systematic antibiotherapy, is both a surgical clean-up of the whole cavity using as far as possible a minimal invasive endoscopic approach and anticoagulation for at least 6 months. In absence of aggravation, the surgical procedure can be performed after initial improvement. The antifungal therapy is not necessary in case of non-invasive forms, only proved by the final histopathological exam.

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Arnaud Devèze, MD.
 Fédération d'Otorhinolaryngologie
 Hôpital de la Timone
 264, rue Saint Pierre
 13005 Marseille
 France

Fax: +33-491-3-6057
 E-mail: arnaud.deveze@orl.net