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Case report

Management of Isolated sphenoidal aspergillosis: Case report and review of literature

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ABSTRACT

Introduction and importance: Sphenoidal aspergillosis is an uncommon serious condition that could lead to a fatal outcome. There is dilemma in its management. Published data concerning this pathology are limited so we find interesting in adding our experience to the literature mass. In fact, this work focused on the description of the clinical features of this entity as well as its management by presenting a case report and reviewing literature.

Case presentation: We report a case of 53 years old male who presented to the outpatient department of our university teaching Hospital with isolated chronic headache complaint that evolving through two years. His physical examination revealed no abnormalities. CT scan of facial bone and MRI showed an aspect in favor of sphenoidal aspergillosis. He underwent an endoscopic sphenoidotomy. Microscopic examination was consistent with the diagnosis of sphenoidal aspergillosis. There were no needs to associate an antifungal treatment since we estimate the surgery excision was complete. The patient remained free of disease after surgery for a follow-up of 4 years.

Clinical discussion: Aspergillosis is ubiquitous in nature, currently causing severe disease in both immunocompetent and immunocompromised patients. Its frequency has increased over the past few years due to the widespread use of antibiotics, corticosteroids, and improved diagnostic methods. Surgery is the primary form of treatment, however if signs of invasion are present, it should be supplemented with an anti-fungal treatment.

Conclusion: Sphenoidal aspergillosis is a rare condition whose diagnosis is not always obvious. The clinician should always bear this diagnosis in mind in patients with chronic sinusitis avoiding invasive and fulminant forms which could be life-threatening.

1. Introduction

Sphenoidal aspergillosis is a rare disease whose incidence is estimated at 1.2 % per year [1]. This incidence has undergone an increase in the last decade, due to an epidemiological shift towards fungal infections, and this, in front of the use of antibiotics, corticosteroids, and the development of diagnostic means [2]. Besides, this entity could be probably underestimated due to the lack of systematic mycological sampling and anatomopathological study [3].

Mycotic infection is serious, fatal and its prognosis depends closely on the treatment delay. Diagnosis is usually delayed in the absence of specific clinical signs. Clinician must keep this rare entity in mind, in order to avoid the progression into invasive forms, prognosis of this latest is poorer even with a fatal outcome, and since surgery won't be curable, thus urgent antifungal treatment will be required. Herein we report a case of sphenoidal aspergillosis collected in the ENT Department of Farhat Hached Hospital Sousse. We aimed through this work to precise the incidence rate, mode of presentation, treatment, and outcome measures associated with this uncommon disease. This case has been reported in line with the SCARE 2020 criteria [4].

2. Observation

We report a case of a 53 years old male, agriculture, who had a medical history of diabetes on oral antidiabetics and Rheumatoid arthritis on corticosteroid therapy. He did not smoke or drink alcohol. He consulted our university teaching hospital for an isolated chronic headache, evolving for 2 years intermittently, resistant to the usual analgesics, without other associated signs neither ENT nor ophthalmological or neurological signs. Physical examination found a preserved

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general condition.

ENT examination including nasal endoscopy revealed no abnormalities eliminating a tumor from the nasal cavity. The biology was without abnormalities. Non contrast computed tomography CT scan of the facial bone was performed showing total filling of the sphenoid sinus, hyperdense, heterogeneous and not enhanced by the injection of PDC, with the presence of central calcifications without evidence of bone lysis. A magnetic resonance imaging MRI was also practiced. It showed left intrasphenoidal polypoid formation in hyposignal T1, T2 not enhanced after injection without intracranial or orbital extension. We decided to perform surgery through an endoscopic approach.

The intervention took place under general anesthesia, the patient was placed in the supine position, Intraoperative exploration found a sphenoidal sinus completely filled with a friable blackish formation, there were no signs of fungal a aggressiveness and invasions and these findings were in line with the imaging constatations it. An endoscopic sphenoidotomy was performed allowing a complete removal of the mass then careful cleaning of the sinus cavity.

Microscopic examination was consistent with the diagnosis of sphenoidal aspergillosis.

As we judged surgical debridement was complete and taking into account the anti-fungal's treatment side effects, we did not recommend antifungal treatment following intervention. Nevertheless, the patient received antibiotic coverage for 48 h associated with analgesics and care of the nasal cavities after stripping. The patient shows clinical and radiological improvement with total disappearance of headaches and no recurrence after a regular follow up of 4 years based on clinical examination especially endoscopic examination at the outpatient consultations.

3. Discussion

Aspergillosis is known as a fungal infection caused by a ubiquitous germ of the genus *Aspergillus* with a prevalence of fumigatus and flavus species [5]; *Aspergillosis* commonly involve the maxillary and frontal sinuses. The sphenoidal site, however, is exceptional [3].

Different forms of sphenoidal aspergillosis were described: the noninvasive form, the invasive form that includes chronic invasive sinusitis and fulminant sinusitis that may have serious consequences [6].

Thery A in his work reported that the mean age of the patients of his study was 57 years and 75 % of the population was over the age of 50 which was consistent with our case [1].

Typically, fungal sphenoid sinusitis occurs in immunocompromised subjects and without having any nasal complaints. In fact, cases of sphenoid sinus fungal infection, reported in the literature, without immunocompromise are very common [7], and seems to be related to the chronic noninvasive forms described in the current investigation.

On the other hand, many authors have identified a set of risk factors and predisposing medical disease which associated to developing sphenoid aspergillosis more than others, such as patients having allergy, alcoholism, long-term corticosteroid therapy, diabetes, AIDS, the use of anti-tuberculosis drugs or following solid organ transplantation [2,3].

Hypercoticism also has been associated with an increased incidence of aspergillosis [3].

In our study, our patient presented with diabetes and a long term corticotherapy for his rheumatoid polyarthritis.

A female predominance is described by some studies [1] while Zainine et al. found a sex ratio of 1 with no male or female predominance [3]. However, our patient is male. There is no available data that could explain any gender influence.

Most often patients presented with headache without nasal complaints then the first line of consultation will be neurological or general doctors. These elusive and nonspecific symptoms could explain the misdiagnosis of this entity and the long delay taken to diagnosis and management.

Indeed, the sphenoidal sinus is difficult to access for simple clinical examination, which explains the normality of the clinical examination in our patient. Usually the complications are inaugural of the infection when the invasion hits the structures adjacent to the sinus. The clinical presentation can be neurological, rhinological or even ophthalmological.

The sphenoidal location of aspergillosis and the proximity of the neuro-vascular structures are a source of ophthalmological and endocranial complications. These phenomena are explained by mycelial growth and production of cytotoxic metabolites responsible for soft tissue and bone destruction [6].

Intracranial complications involve skull base osteomyelitis, meningitis, meningoencephalitis, brain abscess, and cavernous sinus thrombosis, involvement of orbital apex, infarcts, and rarely mycotic aneurysm [7].

Starting with neurological signs, headache represents one of the most common signs of sphenoidal aspergillosis reported between 67 and 85 % according to different studies [1]; its main characteristics are being retro-orbital or occipital, most often unilateral and often resistant to usual analgesic treatments as was the case with our patient. These characteristics are explained by the innervation of the sphenoid sinus, which is derived from both cranial nerves V1 and afferent fibers, via the sphenopalatine ganglion [8].

As for ophthalmological signs, mainly explained by orbital extension and cavernous sinus invasion, they are often observed in association with invasive forms [2,3]. They are reported to be the second most common complex symptom in sphenoid diseases. The patients may complain from diplopia often subjective or more commonly secondary to ophthalmoplegia due to multiple nerve palsy [9]. Ptosis was reported in up to 46 % of published cases [10], exophthalmos, ophthalmoplegia or loss of visual acuity ranging from mild to total blindness [8].

The rhinological signs are dominated by anterior and/or posterior purulent rhinorrhea and nasal obstruction, which are very nonspecific. However A. Thery et al. described blood-streaked nasal discharge to be much more specific [1]. Irritation of the sinus mucosa by the aspergilloma or, at a more advanced stage, bone destruction of the sinus wall can explain this bleeding [1].

In our case, the patient had no associated ophthalmological or rhinological signs.

Radiologically, the standard images appear normal they are currently neglected in terms of invasive sinusitis [2]. Indeed CT scan and MRI represent the most sensitive diagnostic means to highlight an *Aspergillus* sinusitis by demonstrating ferromagnetic substances [10]. Actually, CT scan is known to be more specific in detecting bone lesions [11]. We need CT in axial and coronal sections 3 mm thick [3]. The most characteristic aspect is the presence of a total filling of the sinus by dense, non-raising material after injection of iodine and comprising a calcium or metal density image corresponding to calcium salts and other heavy metals (lead, copper, iron, manganese) produced by mycosis [2,7]. This aspect was found in our patient. Intrasinus calcifications are observed in 50 % of cases according to Boutarbouch et al. [10].

As for the MRI, it is rather specific for the detection of an extra sinus extension outside the sinus, it is known for its superiority in detecting and evaluating ophthalmological or intracranial extension of the disease [2,3,11]. It appears as a heterogeneous lesion on T1-weighted sequences and T2 not enhanced after injection of gadolinium, including a very hypo-intense zone on the T1-weighted sequences and T2 exactly as described in our patient [11,2].

Despite the technical and diagnostic advances in imaging, the diagnosis is still made during surgery or postoperatively. The confirmation is essentially based on the mycological study of the *Aspergillus* pus and the anatomopathological examination [12].

The Management of this pathology is still controversial regarding the surgery approach and the anti-fungal drug's basis. In all cases, therapeutic management should be discussed case-by case considering the medical statute of the host and the pharmacological behavior of medical treatment. Anyway, surgery still and with no doubt the mainstay

treatment. Indeed its quality will dictate the subsequent attitude, hence the prognostic value of the surgical intervention [3].

The surgery approach is an endoscopic sphenoidotomy which allows evacuation of intrasinus purulent fluid with macroscopic removal of the disease with a generous margin of healthy tissue to ensure resumption of sinus ventilation [3,8]. A complete excision and debridement that allow a radical removal of the diseased tissue determines the prognosis and helps to avoid residual tissue and recurrences [13].

Lee DH and al insists on the importance of the debridement even an aggressive one which should be performed in front of a fungal agent, in order to be curable. Nevertheless, we should be careful in the sphenoid sinus because its sinus wall includes important neurovascular structures [8].

External approach has also a place but, according to some authors, only in particular situations especially when orbits are included [7]. This option is figured out essentially when it is an invasive form. Then surgery become more extensive and could lead to complications such as inadvertent injury to the internal carotid artery, cranial nerves and cavernous sinus. Besides, sometimes we are faced to decide of an exenteration if the lesions reach posterior orbital structures (retro bulbar, apical).

Actually, the suitable treatment for noninvasive chronic aspergillosis is surgery with extrusion of the fungal mass [13]. Regarding antifungal treatment it is not well defined because some authors administrate it to improve the surgical outcome while others admit that a surgery considered radical spares a complementary post-operative treatment [7]. Besides, administration of intravenous antifungal treatment for immunocompetent patients is not consensual [7].

When it is about the invasive form of sphenoidal aspergillosis, surgery should be followed by antifungal treatment [13].

The antifungal compromises triazole (itraconazole, voriconazole, posaconazzole), polyenes (amphotericin and its lipid formulations) and other class agents [8].

Amphotericin B has a broad spectrum. However Ariane Baumann et al. described a successful use of voriconazole in combination with a sphenoidotomy that preserves the mucosa as an effective treatment in 4 cases with invasive sphenoidal aspergillosis and was better tolerated than amphotericin B in a recent study [13].

Amphotericin B, not being available for oral application, is associated with a high rate of nephrotoxicity and infusion reactions. Voriconazole, in contrast, is generally well tolerated and distributes well into all tissues including brain and bone, with tissue concentrations that may exceed plasma concentration [14]. This property is important in the treatment of invasive sphenoidal aspergillosis, which often erodes bone and may invade both meningeal and brain. For the treatment of invasive aspergillosis in hematopoietic cancer patients, voriconazole was even shown to have superior efficacy and survival rates compared to amphotericin B [15].

In our study, despite the association of diabetes and long-term corticosteroid therapy, our patient did not receive medical treatment after surgery; regular follow up based on clinical and radiological criteria didn't show any fungal residual or recurrence. This could be explained by a good cleaning of the sinus by endoscopic way.

According to the literature, mortality is essentially associated with invasive forms, which is observed in 50 % of cases. A regular follow up is recommended to avoid recurrences, which includes nasal cleaning by douches and nasal endoscopy [3]. Our patient was free of disease without any surgical complication after 4 years of follow-up.

4. Conclusions

Sphenoidal aspergillosis is one of the differential diagnoses of sphenoidal tumors in the immunocompetent. The prognosis of invasive fungal sphenoiditis is extremely poor despite aggressive treatment, which emphasizes the importance of early diagnosis and appropriate treatment. Because invasive fungal sphenoiditis can occur even in immunocompetent patients, a high index of suspicion should be maintained for early diagnosis. The treatment is essentially surgical with very good results. The addition of a systemic antifungal is controversial. In addition to correcting the immunosuppressive state, new treatment strategies including new antifungal agents need to be developed.

Consent

Written informed consent was obtained from the 2 patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

What this adds to the existing literature and clearly detail learning points

With the rise of fungi, we are currently seeing a microbiological revolution. Multiple factors, including likely external ones, promote these infections, which explains why various authors report varied numbers of instances. To improve the quality of international literature, we wished to share our experiences.

Ethical approval

This is a case report study and ethical approval not required.

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Meherzi Abir: conception and design of the study
Omri Malika, Bellakhdher Mouna, HwassJihen: acquisition of data
Meherzi Abir, Jemli Safa: article drafting
Wassim Kermani, Mouna Bellakhdher, Mohamed Abdelkefi: final approval of the version to be submitted.

Declaration of competing interest

None declared.

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