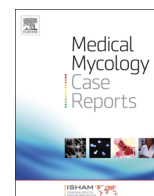




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Sinusitis caused by *Scopulariopsis brevicaulis*: Case report and review of the literature



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ARTICLE INFO

Article history:

Received 10 March 2014
Received in revised form
28 May 2014
Accepted 28 May 2014

Keywords:

Fungus ball
S. brevicaulis
Immunocompetent
Sinusitis

ABSTRACT

We report a case of non-invasive sinusitis caused by *Scopulariopsis brevicaulis* in a 70-year-old immunocompetent patient who had an antibiotic-resistant suppurative tooth infection evolving for seven months. The sinus endoscopy highlighted a foreign body at the bottom of the sinus, which led to the hypothesis of fungal ball sinusitis. Culture of excised tissue was positive for *S. brevicaulis*.

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1. Introduction

The *Scopulariopsis* genus comprises cosmopolite and common saprophytic filamentous fungi. They have been isolated from soil and from a wide range of plants and organic substrates.

In immunocompetent patients, *Scopulariopsis* is associated with nail infections, but can also occasionally cause cutaneous lesions, mostly following trauma or surgery.

The invasive infections caused by *Scopulariopsis* species are very rare and occur mostly in immunocompromised patients. In fact, only a few cases have been described, with reports of different tissues or organs infected (brain, lung, heart and especially sinus) [1–3].

Invasive fungal sinusitis is a severe and potentially fatal infection, affecting mainly immunocompromised patients, such as those affected by primary immunodeficiency or hematological malignancies, receiving intensive chemotherapy, or undergoing hematopoietic stem cells transplantation. A wide range of responsible fungi have been

described, *Aspergillus* and Mucorales being the most common agents. Fungal sinusitis can also occur in immunocompetent patients; however, the reported cases are extremely rare. Contrary to immunocompromised patients, the sinusitis is mostly non-invasive and has a good prognosis [1,2,4].

We report here the case of a non-invasive fungal sinusitis caused by *S. brevicaulis* in an immunocompetent patient. This case describes a very rare medical condition and represents the first *Scopulariopsis* sinusitis in France.

2. Case

On November 13th 2012 (Day 0), a 70-year-old immunocompetent woman without any associated impairment saw her dentist for a recurrent and antibiotic-resistant suppurative tooth infection evolving for seven months. The infection was located at the second maxillary premolar on the left side. After examination, the dentist decided to perform the tooth extraction.

One month later, on December 13th 2012 (Day 30), the patient was referred to an otolaryngologist because she was complaining of a gum suppuration associated with pain at palpation of the left maxillary sinus. A CT-scan was performed and showed mucosal thickening of the left maxillary sinus (Fig. 1). The sinus endoscopy highlighted a foreign body at the bottom of the sinus, which led to

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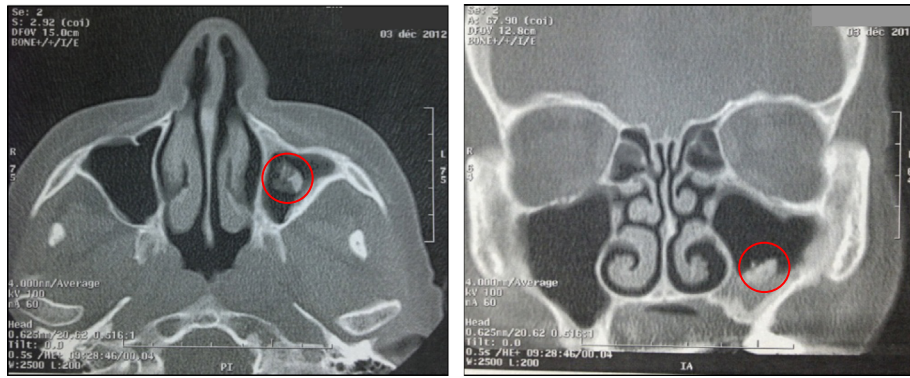


Fig. 1. CT-scan showing evidence of mucosal thickening at the bottom of left maxillary sinus.

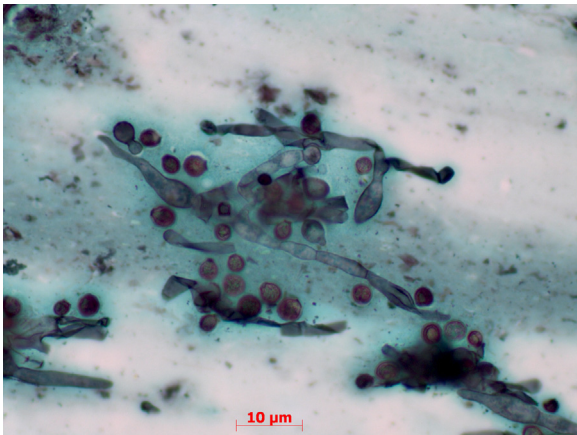


Fig. 2. Direct examination of the fungal ball: evidence of septate hyphae and globose to pyriform truncate spores evoking *Scopulariopsis* spp. (Gomori-Grocott methenamine silver stain; magnification $\times 1000$).

the hypothesis of a probable fungal ball sinusitis. Therefore, on Day 68 the patient was hospitalized in the department of maxillo-facial surgery in order to undergo the foreign body resection the following day (Day 69).

Once the foreign body removed, the surgeon described a lesion with well-defined edges and without tissue invasion.

The laboratory analysis of the excised tissue revealed many hyaline septate hyphae and globose to pyriform truncate spores at direct examination, which confirmed the fungal nature of the ball and evoked *Scopulariopsis* spp. (Fig. 2).

Then, culture on Sabouraud-chloramphenicol agar and Malt extract agar was positive for *S. brevicaulis*. The colonies were initially white, and then became buff or cinnamon-colored with a powdery or granular appearance. On the reverse side of the media, *S. brevicaulis* gradually turned from honey-colored to brown. Microscope examination showed septate, hyaline hyphae and chains of round to ovoid, finely to coarsely rough spores with a distinctly truncate base [1,5,6].

The diagnosis was confirmed by double strand sequencing of the ITS (internal transcribed spacer) region of the ribosomal DNA (primers ITS1/ITS4). The aligned sequence was compared to the GenBank and CBS databases.

Antifungal susceptibility testing of the isolate by the Etest[®] method showed the fungus to have MICs (minimum inhibitory concentrations) above 32 $\mu\text{g}/\text{ml}$ for all of the antifungal drugs tested: amphotericin B, voriconazole, posaconazole, itraconazole and caspofungin.

The patient was discharged the day after the intervention on December 22nd 2012 (Day 70), without antifungal treatment.

The absence of immunodeficiency and tissue invasion did not justify the need of an associated antifungal therapy.

On February 12th 2013 (Day 91), the surgeon saw the patient for a first check-up. She noted that the operation site had healed well and that the patient did complain neither of any pain nor of any suppuration. At the twelve months follow up, the patient had remained asymptomatic, without any complications with regards to her sinusitis.

3. Discussion

Eight *Scopulariopsis* species have been reported to be associated with human diseases: *S. acremonium*, *S. asperula*, *S. brevicaulis*, *S. brumptii*, *S. candida*, *S. flava*, *S. fusca* and *S. koningii* [5,7]. In immunocompetent patients *S. brevicaulis* is the main causative agent. In addition to *S. brevicaulis*, other *Scopulariopsis* have also been described in these infections, mainly *S. candida* and *S. acremonium* [1,2,5,8].

A literature review on sinonasal infections caused by *Scopulariopsis* spp. reveals only seven articles referring to this kind of infection [1,2,4,9–12]. For each of these cases, the reference and clinical data are described in Table 1.

Sinonasal infections caused by *Scopulariopsis* spp. have already been described in both adults and children. Regarding the *Scopulariopsis* species, the reports include 2 patients infected by *S. acremonium*, one by *S. candida*, one by *S. brevicaulis*, and 3 by *Scopulariopsis* spp. All but one patient were immunocompromised, mainly suffering from a hematological malignancy. The patients were treated mainly by an association of antifungal drugs and surgery (4 out of 7 patients). One patient was treated only with antifungal drugs, and 2 patients underwent surgery alone.

Only one patient died due to the fungal infection. The patient underwent hematopoietic stem cell transplantation because of multiple myeloma. She developed the sinusitis 485 days after the transplant, while she was treated for a graft-versus-host disease. Death was due to brain ischemia and hemorrhage secondary to disseminated fungal infection. There was a delay in diagnosis, and she received antifungal treatment alone [2].

Generally, sinonasal infections caused by *Scopulariopsis* spp. seem to have a good outcome in immunocompromised patients, and even more so if a rapid and appropriate treatment is used.

Concerning *Scopulariopsis* fungal balls with other localization (except for sinonasal ones, described above), 7 cases have been reported in the literature [13–19] and the data are presented in Table 2.

We note that male and female patients have been affected equally by this kind of infection. Most of the articles (6 out of 7) report prosthetic valve endocarditis, on aortic valve as well as on mitral valve. The responsible species was *S. brevicaulis* except for

Table 1
Case reports of *Scopulariopsis* sinonasal infection.

Age (gender)	Underlying disease	Pathogen	Treatment	Type of infection	Infection outcome	Reference
17 (M)	Acute lymphoblastic leukemia	<i>S. brevicaulis</i>	Intravenous voriconazole and surgery	Invasive	Survived	[1]
50 (F)	Multiple myeloma	<i>S. acremonium</i>	Intravenous amphotericin B+oral voriconazole	Invasive	Died	[2]
35 (M)	Hypogamaglobulinemia	<i>Scopulariopsis</i> spp.	Repeated maxillary punctures	Non invasive	Survived	[4]
52 (F)	Acute myeloblastic leukemia	<i>S. acremonium</i>	Intravenous amphotericin B+intravenous itraconazole and surgery	Invasive	Survived	[9]
72 (M)	None	<i>Scopulariopsis</i> spp.	Surgery	Invasive	Survived	[10]
12 (F)	Non-Hodgkin's lymphoma	<i>S. candida</i>	Intravenous amphotericin B+oral itraconazole and surgery	Invasive	Survived	[11]
17(M)	Chronic myelocytic leukemia	<i>Scopulariopsis</i> spp.	Intravenous amphotericin B and surgery	Invasive	Not cured (died due to underlying disease)	[12]

Table 2
Case reports of *Scopulariopsis* fungal ball (except for sinonasal localization).

Age (gender)	Localization	Pathogen	Treatment	Infection outcome	Reference
36 (M)	Prosthetic mitral valve	<i>Scopulariopsis</i> spp.	Valve replacement and intravenous amphotericin B	Survived	[13]
Not specified	Prosthetic aortic valve	<i>S. brevicaulis</i>	Valve replacement and intravenous amphotericin B+oral fluconazole	Died (fungal sepsis after endocarditis recurrence, 17 months after first operation)	[14]
67 (M)	Prosthetic aortic valve	<i>S. brevicaulis</i>	Valve replacement and intravenous amphotericin B+oral fluconazole	Died (acute myocardial infarction during third fungal endocarditis recurrence)	[15]
67 (F)	Middle pulmonary lobe	<i>Scopulariopsis</i> spp.	Lobectomy and oral fluconazole	Survived	[16]
38 (F)	Prosthetic mitral valve	<i>Scopulariopsis</i> spp.	Valve replacement and intravenous caspofungin	Survived	[17]
67 (F)	Prosthetic mitral valve	<i>S. brevicaulis</i>	Valve replacement and intravenous amphotericin B+oral voriconazole	Survived	[18]
58 (M)	Prosthetic mitral valve	<i>S. brevicaulis</i>	Valve replacement and oral voriconazole	Survived	[19]

one case (*Scopulariopsis* spp.). The fungal identification was performed after culture of the removed valve and/or on embolus. It is interesting to note that blood cultures were almost always negative (positive for one patient). The treatment was based on valve replacement associated to antifungal therapy. Four patients had a good outcome and 2 died after fungal endocarditis recurrence [14,15].

One *Scopulariopsis* fungal ball was described in a 67-year-old patient, case in which the infection was localized in the middle pulmonary lobe. The fungal culture post-lobectomy revealed *Scopulariopsis* spp. The patient was treated postoperatively with fluconazole for one month and had a good outcome [16].

Finally, although our patient did not receive any antifungal therapy, it is interesting to note that the antifungal susceptibility testing by the Etest[®] method showed our *S. brevicaulis* isolate to have high MICs for all the antifungal drugs tested, namely amphotericin B, voriconazole, posaconazole, itraconazole and caspofungin.

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) and The Clinical and Laboratory Standards Institute (CLSI) Subcommittee on Antifungal Susceptibility Testing have generated documents describing standardized methods for broth- and agar-based antifungal susceptibility testing. However, these methods can be time consuming, so simpler and more economical methods, like Etest[®], are often used in routine testing [3,5]. The difficulty with Etest[®] against non-*Aspergillus* filamentous fungi

remains the absence of interpretative breakpoints. The clinical utility and relevance of testing molds also remains uncertain. For many molds, good correlations have been shown between the MICs obtained by both Etest[®] and CLSI [20].

Many publications have indeed described multiresistance of *S. brevicaulis* against antifungals. High in vitro MICs were shown against amphotericin B, itraconazole, posaconazole, voriconazole, caspofungin and terbinafine [5,21]. Some studies show that voriconazole was more effective than amphotericin B and itraconazole [2,7] and that caspofungin could be used in synergy with amphotericin B, voriconazole or posaconazole [3,7,21].

4. Conclusion

Sinonasal infections caused by *Scopulariopsis* spp. are very rare, associated mainly with immunocompromised patients. Fungal sinusitis occurring in immunocompetent patients has been described, but the cases reported are extremely rare. In these patients, contrary to the immunocompromised ones, the sinusitis is mostly non-invasive and has a better prognosis.

To our knowledge this is the second case of sinusitis caused by the species *S. brevicaulis*. It also represents the second *Scopulariopsis* sinusitis described in an immunocompetent patient, and the first case of a *Scopulariopsis* sinusitis reported in France.

Conflict of interest

There are none.

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