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ORIGINAL ARTICLE

NON-*Aspergillus* FUNGAL RHINOSINUSITIS AT A TERTIARY CARE HOSPITAL AND THE FIRST REPORT OF HUMAN INFECTION BY *Trichoderma asperellum*

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ABSTRACT

We describe 27 cases of fungal rhinosinusitis, which were caused by agents other than *Aspergillus*, diagnosed at our institution during a 24-year period. Particular focus was on defining the causal fungi and the predisposing factors. Fungal cultures were obtained from 20 cases and there was no growth in seven cases. Classification of mycotic disease of the nose and paranasal sinuses as invasive and noninvasive is based on clinical, radiological, and histopathological factors. The most common pathogens were *Histoplasma capsulatum* (n=4), *Scedosporium apiospermum* (n=2), *Alternaria alternata* (n=2), *Schizophyllum commune* (n=2), *Pseudallescheria boydii* (n=1), *Penicillium* sp. (n=1), *Lichtheimia* (*Absidia*) *corymbifera* (n=1), *Xylaria enteroleuca* (n=1), *Trichoderma asperellum* (n=1), *T. harzianum* (n=1), *T. viride* (n=1), *Fusarium solani* (n=1), *Cladosporium* sp. (n=1), and *Cryptococcus neoformans* (n=1). From the ones that revealed no growth, four were classified as hyalohyphomycosis and three were mucormycosis by the histopathological findings. In addition, we describe the first well-documented case of rhinosinusitis and human infection by T. asperellum.

KEY WORDS: Sinus; sinusitis; non-*Aspergillus* rhinosinusitis; *Trichoderma asperellum*.

RESUMO

Rinossinusite fúngica não aspergilar em um hospital terciário e relato do primeiro caso de infeccão humana por *Trichoderma asperellum*

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Descrevemos 27 casos de rinossinusite fúngica causada por agentes não aspergilares diagnosticados em nossa instituição durante um período de 24 anos. O foco do estudo foi o agente causal e fatores predisponentes. Em 20 casos foi isolado o agente fúngico e, em 7, não houve crescimento. A rinossinusite foi classificada em invasiva e não invasiva com base em avaliação clínica, radiológica e histopatológica. Os agentes patogénicos mais comuns foram *Histoplasma capsulatum* (n = 4), *Scedosporium apiospermum* (n = 2), *Alternaria alternata* (n = 2), *Schizophyllum commune* (n = 2), *Pseudallescheria boydii* (n = 1), *Penicillium* sp (n=1), *Lichtheimia* (*Absidia*) *corymbifera* (n = 1), *Xylaria enteroleuca* (n = 1), *Trichoderma asperellum* (n = 1), *T. harzianum* (n = 1), *T. viride* (n = 1), *Fusarium solani* (n = 1), *Cladosporium* sp (n = 1) e *Cryptococcus neoformans* (n = 1). Os casos em que não ocorreu crescimento foram classificados, com base nos achados histopatológicos, como hialohifomicose (n = 4) e mucormicose (n = 3). Além disso, descrevemos o primeiro caso de rinossinusite humana pelo *T. asperellum*.

DESCRITORES: Seio nasal; sinusite; rinosinusite não *Aspergillus*; *Trichoderma asperellum*.

INTRODUCTION

Fungal infections of the paranasal sinuses may occur in immunocompetent and immunocompromised individuals. In immunocompetent individuals, disease is usually a localized infection of the paranasal sinuses without bone and soft-tissue invasion. However, in immunocompromised individuals, disease usually results in disseminated fungal infection and may cause bone erosion.

Three types of non-*Aspergillus* fungal infections may affect the paranasal sinuses: (I) allergic fungal rhinosinusitis, (II) invasive fungal rhinosinusitis (acute and chronic forms), and (III) fungus ball (5, 6).

Acute invasive fungal rhinosinusitis is a rapidly progressive disease occurring in patients with poorly controlled diabetes (mucormycosis) or immunosuppressed patients (e.g., histoplasmosis and cryptococcosis). In patients with noninvasive mycelial diseases of the paranasal sinuses, there are two clinical forms of rhinosinusitis: fungus ball and allergic fungal rhinosinusitis (AFS). There is no fungal invasion in the local soft tissue or bone in either of these two forms (7). They are typically caused by *Aspergillus* or *Scedosporium apiospermum/Pseudallescheria boydii*, although a number of additional fungal species are responsible for sporadic cases (e.g., pigmented and hyaline molds). We adopted nomenclature based on the genus of the fungus involved, dividing the fungal rhinosinusitis in two groups: hyalohyphomycosis and phaeohyphomycosis (1). The groups are distinguished by the presence of septate hyphal filaments without (hyalohyphomycosis) or (phaeohyphomycosis) with pigmented hyphae due to the presence of melanin in the inner aspect of the fungal cell wall and sometimes in the host tissues.

We describe a cohort of 27 fungal rhinosinusitis cases caused by fungi other than *Aspergillus*, which have been diagnosed at our institution during a 24-year period, with a particular emphasis on their etiologic agent and the predisposing

factors. Furthermore, in this series, we report the first case of rhinosinusitis and human infection by *Trichoderma asperellum*.

MATERIALS AND METHODS

This study is a retrospective analysis of 27 patients with fungal rhinosinusitis at the Mycology Laboratory of Santa Casa, Porto Alegre, RS, from 1989 to 2013. The study was conducted with the permission of the Medical Research Ethics Committee of Santa Casa (Protocol number 64705/12). The inclusion criteria for this study were as follows: positive nasal sinus cultures and/or biopsy specimens demonstrating fungal hyphae.

Clinical presentation

Criteria for the diagnosis of the type of fungal rhinosinusitis:

Allergic fungal rhinosinusitis (AFS): Presence of allergic mucin of the nasal cavity with eosinophils, Charcot-Leyden crystals, fungal elements, and absence of fungal invasion of tissue.

Invasive fungal rhinosinusitis (IFS): Histopathological evidence of hyphal forms within the sinus and invasion of mucosa and submucosa.

Fungus ball: Radiological studies demonstrating sinus opacification and tissue section demonstrating agglomeration of hyphae and absence of fungal invasion of mucosa.

Materials: A portion of the paranasal tissue obtained at surgery (Caldwell-Luc or endoscopic) was placed in 10% formalin for histopathological examination. The remaining portion of the specimen was sent to the Mycology Laboratory for fungal culture.

Methods: A portion of the biopsy tissue was mounted in 10% KOH for direct microscopic examination. The remaining tissue was inoculated on Sabouraud's dextrose agar with chloramphenicol and Mycosel agar and incubated at 25°C and 37°C, respectively. Histological examination of the specimens was done using hematoxylin and eosin (H&E), Gomori methenamine silver (GMS), and Fontana-Masson stains.

RESULTS

A total of 27 cases of non-*Aspergillus* fungal rhinosinusitis were studied. These are summarized in Table 1, listed by species in order of decreasing frequency of isolation. A total of 14 (51.9%) of the 27 cases were women, and 13 cases (48.2%) were men. The mean age of the patients was

45.3 years (range: 6-76 years).

Conventional sinus radiographs demonstrated significant opacification of the involved sinuses in 15 patients. Computed tomography (CT) scans of the sinuses of 20 patients were reviewed. The imaging studies of the other two cases were not retrievable.

Table 1: Organisms causing non-*Aspergillus* paranasal sinusitis in 27 patients

Disease manifestation	Fungus	No. of patients (%)
Invasive		
	Histoplasma capsulatum	4 (14.8)
	Mucorales	3 (11.1)
	Cryptococcus neoformans	1 (3.7)
	Lichtheimia corymbifera	1 (3.7)
Fungus ball		
	Pseudallescheria boydii	1 (3.7)
Allergic sinusitis with unusual fungi		
Hyalohyphomycosis		
	Unidentified fungal species	4 (14.8)
	Schizophyllum commune	2 (7.4)
	Xylaria enteroleuca	1 (3.7)
	Trichoderma asperellum	1 (3.7)
	T. harzianum	1 (3.7)
	T. viride	1 (3.7)
	Fusarium solani	1 (3.7)
	Penicillium sp.	1 (3.7)
Scedosporiosis	*Scedosporium apiospermum*	2 (7.4)
Phaeohyphomycosis		
	Alternaria alternata	2 (7.4)
	Cladosporium sp.	1 (3.7)

Of the 27 patients, nine were found to have evidence of invasive disease, one presented fungus ball due to P. boydii (Figures 1 and 2), and the remaining patients were found to have evidence of AFS. The primary symptoms, predisposing diseases, and associated risk factors, such as other information relating to the 27 cases, are detailed in Table 2.

Table 2: Overview of 27 cases of fungal rhinosinusitis and associated fungal etiology

Case	Age Sex	Material	Direct	Culture	Main Symptoms	Predisposing conditions/associated	Examinations Image	Treatment
1	25 / F	Secretion maxillary sinuses	Septate hyaline hyphae branched	*Schizophyllum commune*	Headache, nasal obstruction	Corticosteroid therapy, chronic sinusitis, sinonasal polyps	NI	NI
2	74 / F	Secretion maxillary sinuses	Septate hyaline hyphae branched	*Fusarium solani*	Nasal congestion, facial pain, headache, fever	SLE, COPD, immunosuppression (methylprednisone), pancytopenia, corticosteroid	X-ray/TC: paranasal sinuses: complete opacification left maxillary sinus, metallic density image.	Fluconazole Voriconazole
3	50 / M	Right maxillary sinus secretion	Fragment of septate hyphae in fungal ball arrangement	*Penicillium* sp.	Productive cough with purulent sputum	Bronchial asthma, chronic allergic rhinitis (8 years), corticoid	X-ray paranasal sinuses: complete opacification of the right maxillary sinus, metallic image	Ketoconazole
4	44 / F	Secretion ethmoid and sphenoid sinuses	Presence of septate hyaline hyphae	*Trichoderma asperellum*	Postnasal flashing green and purulent nasal congestion, rhinorrhea	Asthma, chronic allergic rhinitis, sinonasal polyps	CT sinuses: opacification of the left ethmoid and sphenoid sinuses with erosion of bony walls. Soft mass involving the left nasal cavity with obliteration of the left middle meatus.	Polypectomy Ethmoidectomy Sphenoidectomy
5	06 / M	Secretion sinuses	Non-septate broad hyphae 90º angle (mucormycosis)	*Lichtheimia corymbifera*	Fever, fatigue, epistaxis, nasal obstruction (death)	Bone marrow aplasia	X-ray: opacity of the maxillary sinus and ethmoid cells	Amphotericin B
* 6	25 / M	Fragment nasal septum	Non-septate broad hyphae 90º angle compatible with mucormycosis	Negative	Fever, nasal congestion, facial pain, seborrheic dermatitis on the face	Diabetes mellitus, HIV, alcoholic, smoking, right eye enucleation	CT: Right retro-orbital lesion with bone invasion, ipsilateral ethmoid-frontal inflammatory process, expansive process intraorbitary right medial to the eyeball	Amphotericin B
* 7	62 / F	Bone fistula face	Non-septate broad hyphae 90º angle compatible with mucormycosis	Negative	Epistaxis, bradypsychism, incoordination, dislalia, impaired gait deviation to the right labial commissure, alcoholic, embolic occlusion of the ophthalmic artery	Diabetes mellitus, hepatitis, HIV	NI	NI

8	38 / F	Maxillary sinus secretion	Hyphae septate fungal ball in arrangement	*Alternaria alternata*	Hyperthermia, bilateral nasal obstruction, purulent rhinorrhea bilateral	Lung transplant	X-ray paranasal sinuses: bilateral thickening greater than 6mm	NI
9	57 / F	Maxillary sinus secretion	Septate hyaline hyphae arrangement fungal ball (hyalohyphomycosis)	Negative	Productive cough, nasal obstruction, purulent rhinorrhea for 6 months, mitral valve prolapse	Lung transplant	X-ray/CT: paranasal sinuses: complete opacification of the right maxillary sinus, metallic density image.	NI
10	32 / M	Maxillary sinus secretion	Septate hyaline hyphae arrangement in fungal ball (hyalohyphomycosis)	Negative	Productive cough, nasal obstruction, purulent rhinorrhea	User drug (cocaine)	X-ray/CT paranasal sinuses: complete opacification of the right maxillary sinus, metallic density image; thickness greater than 6mm left maxillary sinus	NI
11	50 / F	Maxillary sinus secretion	Septate hyaline hyphae branched arrangement in fungal ball (hyalohyphomycosis)	Negative	Productive cough, nasal obstruction	Pneumonia (two months), chronic antibiotic therapy	X-ray/CT sinuses, sinus opacification of the left maxillary, metallic density image; metallic image, cells left ethmoid opacification	NI
12	74 / M	Right secretion frontal sinus	Septate hyaline hyphae branched, presence of crystals of calcium oxalate	*Cladosporium* sp.	Nasal congestion, facial pain, headache	Diabetes mellitus, chronic steroid therapy and antibiotics, former smoker	X-ray/CT breasts face: right maxillary sinus opacification opacified, with right lateral frontal sinus anterior wall erosion, ethmoid mucocele frontal maxillary and ethmoid labyrinth with thickened mucosa	Ethmoid sinusectomy
13	49 / M	Maxillary sinus secretion	Septate hyaline hyphae arrangement fungal ball (hyalohyphomycosis)	Negative	Cough productive recurrent chronic, nasal obstruction, postnasal drip	Pneumonia (6 months)	X-ray/CT paranasal sinuses: complete opacification of the right maxillary sinus, metallic image.	NI
14	14 / 10 67 F	Left maxillary sinus secretion	Septate hyaline hyphae branched	*Scedosporium apiospermum*	Nasal congestion, facial pain, headache, cough with yellow sputum	Pneumonia repetition (2 to 3x year), corticosteroids fungal sinusitis (surgery / 03)	CT sinuses: “bullous” middle turbinates, obstruction of the ostium of the left maxillary sinus with mucous secretion, calcified granules.	Itraconazole Sinusectomy ethmoid and maxillary

15	38 / M	Secretion maxillary sinuses	Negative	*T. viride*	Headache, facial edema, purulent productive cough, facial pain (death)	Kaposi's sarcoma, HIV, CMV, pansinusitis	X-ray/CT paranasal sinuses: mucosal thickening of the maxillary, right with nearly complete opacification formation of liquid level and breasts. Reduced transparency of the right frontal sinus and bilateral ethmoid, retention without bone invasion	Itraconazole Amphotericin B
16	29 / F	Fragment nasal mucosa	Non-septate broad hyphae 90º angle compatible with mucormycosis	Negative	Necrotic lesion on the nose (mucormycosis), respiratory dysfunction, fever, facial pain, nasal congestion (death)	Myelodysplasia, severe sepsis, pancytopenia, immunosuppression, antibiotic therapy	X-ray/CT paranasal sinuses: complete opacification, metallic image.	Micafungin
17	76 / M	Left sphenoid sinus secretion	Septate hyaline hyphae branched	*S. apiospermum*	Chronic headache, nasal congestion, facial pain	Septum deviation	X-ray/CT paranasal sinuses: complete opacification of the left maxillary sinus, metallic image.	Septoplasty sinusectomy ethmoid / sphenoid
18	54 / M	Mucosa nasal septum	Negative	*A. alternata*	Nasal congestion, facial pain, headache	Apical periodontitis, chronic rhinitis	X-ray paranasal sinuses: left maxillary sinus opacification, metallic image	Sinusectomy maxillary
19	29 / M	Shaved nasal lesion	Small oval yeast cells compatible with *Histoplasma capsulatum*	Negative	Nasal obstruction, nasal congestion, facial pain, cough, rhinorrhea fetid purulent nasal septum lesion, chronic headache	Sarcoidosis, tuberculosis (antibiotic treatment 6 months), smoking	CT sinuses: tortuosity of the nasal septum to the left, especially the right, by bulging soft tissue partial obstruction of the nasal passages. Normally pneumatized frontal sinuses. Possible opacification of the ethmoid cells.	Ketoconazole Septoplasty
20	31 / F	Nasal secretion	Small oval yeast cells compatible with *H. capsulatum*	*H. capsulatum* (Isolator)	Nasal obstruction, nasal discharge, facial pain, nasal congestion, headache, fever	Rhinoplasty, HIV	CT paranasal sinus: thickened and opaque mucosa, inflammatory sinus disease	Amphotericin B
21	42 / M	Fragment nasal septum	Small oval yeast cells compatible with *H. capsulatum*	Negative	Nasal obstruction (6 years), rhinorrhea, headache, nasal septum lesion	COPD, smoking, valvulopathy mitral	CT sinuses, thickened mucous, opacification, metallic image	Itraconazole

22	40 / F	Fragment lesion right maxillary sinus	Negative	*H. capsulatum*	Nasal congestion, purulent discharge, facial pain, headaches, mass maxillary region	HIV, nasal polyps, pansinusitis, cervical lymphadenopathy, neurosyphilis	CT sinuses: ostiomeatal units occluded with nasal septum in normal position. Maxillary sinuses, frontal, sphenoid and ethmoid labyrinth c / thickened and opaque mucosa, sinusitis	Itraconazole Amphotericin B
23	44 / F	Sphenoid sinus secretion	Misshapen hyphae branched septate with large numbers of crystals	*T. harzianum*	Left nasal obstruction and postnasal discharge, eliminating green discharge with dark lumps, decrease of smell, headache	Altered glucose curve, sulfa allergy, chronic rhinitis, bronchial hyperreactivity, polyposis nasosinusal	CT sinuses: maxillary opacification, ethmoid and sphenoid left with areas of attenuation in the sphenoid sinus and left ethmoid cells. Areas of demineralization of bone ethmoid and sphenoid walls of the cavities.	NI
24	41 / F	Secretion maxillary sinus and sphenoid	Hyphae septate and branched large number of Charcot-Leyden crystals	*S. commune*	Nasal congestion, headache, nasal obstruction, rhinorrhea hyaline	Allergic rhinitis, nasal polyposis	CT sinuses, mucosal thickening, sinus opacification jaws, metallic image	Ethmoid and sphenoid sinusectomy
25	42 / F	Maxillary sinus secretion	Septate hyaline hyphae branched	*Xylaria enteroleuca*	Nasal congestion, productive cough with dark sputum, facial pain, pulmonary secretions, fever	Lung transplantation, immunosuppression, renal insufficiency	CT sinuses: secretion in the sinuses, liquid level sphenoid sinuses, ethmoid partially crossed. There is no inner calcification or bone thickening	Fluconazole, amphotericin B sinusectomy maxillary
**26	66 / M	Maxillary sinus secretion	Tangle of branching septate hyphae and many annelloconidia suggestive of fungal ball *S. apiospermum*	*Pseudallescheria boydii*	Cough chronic (8 years) productive purulent, nasal congestion, facial pain, recurrent respiratory infection	Corticosteroid therapy, antibiotic therapy, chronic rhinitis, septum deviation	CT paranasal sinus: inflammatory changes of the maxillary, ethmoid and sphenoid sinuses left, post-inflammatory hyperplasia remaining paranasal sinuses. bilateral rhinitis	Septoplasty Sinusectomy maxillary
27	36 / M	Secretion maxillary sinuses	Encapsulated yeast fungal elements	*Cryptococcus neoformans*	Productive cough, chest pain, headache, facial pain, lesions in the nasal vestibule	HIV, Hepatitis A, CMV	X-Ray: no abnormalities	Fluconazole, Amphotericin B

CMV: cytomegalovirus; COPD: chronic obstructive pulmonary disease; F: female; HIV: human immunodeficiency virus M: male; NI: No information; SLE: systemic lupus erythematosus; CT: computerized tomography; * Cases previously reported (16); ** Cases previously reported (17).

Microbiology: Fungi recovered from biopsy material included *Histoplasma capsulatum* (n=4), *S. apiospermum* (n=2), *Alternaria alternata* (n=2), *Schizophyllum commune* (n=2) (Figures 3 and 4), *P. boydii* (n=1), *Penicillium* sp. (n=1), *Lichtheimia corymbifera* (n=1), *Xylaria enteroleuca* (n=1), *T. asperellum* (n=1), *T. harzianum* (n=1), *T. viride* (n=1), *Fusarium solani* (n=1), *Cryptococcus neoformans* (n=1), and *Cladosporium* sp. (n=1). Secondary bacterial colonization and/or lack of viable fungus was accompanied by negative cultures in seven cases (Fontana-Masson stain ranked four of these cases as hyalohyphomycosis, and the other three were classified as mucormycosis by direct examination).

Case report of a new causative agent of AFS: A 44-year-old woman with a history of asthma, chronic rhinosinusitis, and allergic rhinitis since childhood was admitted to our hospital. For approximately 10 years before admission, the patient presented intermittent green, purulent post-nasal discharge and nasal congestion. She was treated, without success, with several antibiotics, vaccines, and homeopathy. Family history revealed a brother with allergic rhinitis. Axial and coronal CT scan without contrast medium showed opacification of the entire sphenoid and left ethmoid sinuses, with erosion of the bony walls (Figure 5). Soft tissue mass involving the left nasal fossa, with obliteration of the osteomeatal complex and opacification of the left maxillary sinus, was observed. Nasal endoscopy revealed polypous swelling of the mucosa in the left middle meatus. Endoscopic polypectomy, ethmoidectomy, and sphenoidectomy were performed (Figure 6). Histopathological study of tissues stained with H&E revealed edematous respiratory mucosa containing chronic inflammatory infiltrate with submucosal eosinophilia in the ethmoidal and sphenoidal sinuses. There was no evidence of fungal invasion in the sections stained with GMS. Stained sections (H&E) of inspissated mucus recovered from both sinuses revealed eosinophils and Charcot-Leyden crystals. Scattered fungal hyphae (dichotomous branching with septation) were identified by GMS staining in the mucin. Fungal culture on Sabouraud's dextrose agar (at 25°C) produced a white colony that became green. The fungal mold was identified in microslide culture on potato agar as *Trichoderma*.

The isolated sample was sent to the Fungus Testing Laboratory, Department of Pathology, University of Texas Health Science Center at San Antonio, Texas, for confirmation. The *Trichoderma* was identified as *T. asperellum* (UTHSC #: R-3055).

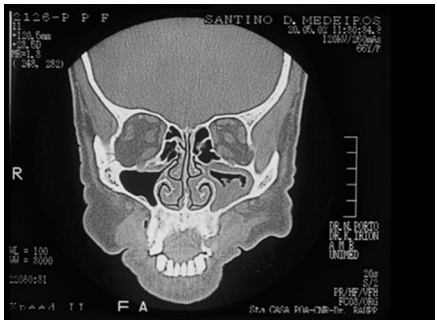

Figure 1. CT scan of the head of a patient with *P. boydii* fungus ball demonstrating opacified left maxillary sinus and clear right maxillary sinus.

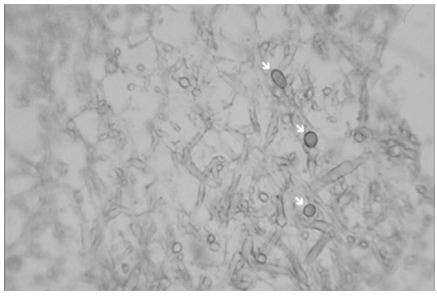

Figure 2. Tissue section of a fungus ball taken through an endoscope, showing profuse growth of septate, branched hyphae and three pyriform annelloconidia (arrows) of *P. boydii* (H&E, x400).

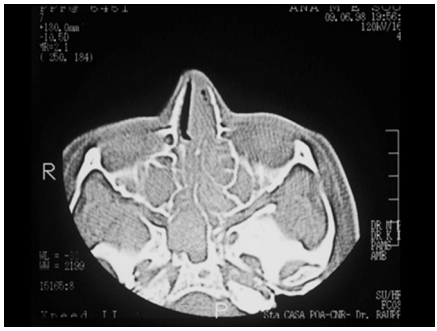

Figure 3. *S. commune* rhinosinusitis. CT scan showing soft tissue mass in ethmoid and sphenoid cavities.

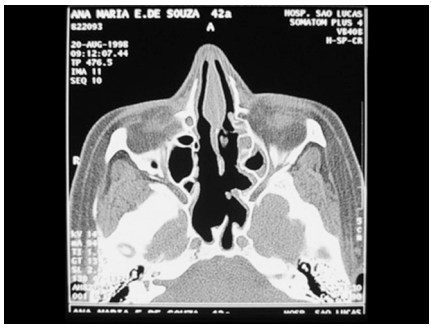

Figure 4. CT scan of the patient in Figure 3 after endoscopic treatments. Notice that the cavities were normal.

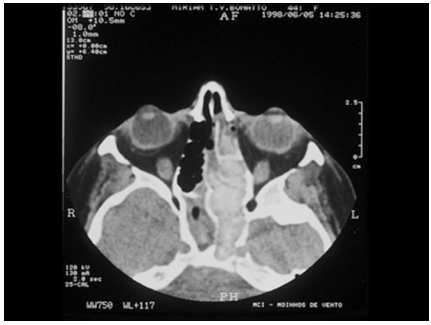

Figure 5. Axial view on CT scan in patient with *T. asperellum* rhinosinusitis showing soft tissue material in the sphenoid and ethmoid cavities.

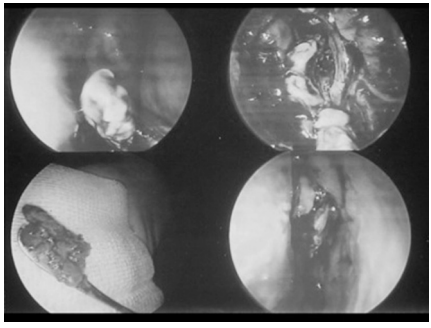

Figure 6. *T. asperellum* rhinosinusitis middle meatal antrostomy and sphenoidotomy shows a yellow-brown material that was allergic mucus.

DISCUSSION

Fungal infection of the paranasal sinuses is an uncommon disease, although it has been reported more frequently in recent years. *Aspergillus* and *Mucor* are the most commonly implicated fungal organisms in invasive rhinosinusitis. Nevertheless, numerous fungi may colonize the paranasal sinuses, and it is not surprising that many of them can cause symptomatic infections.

Based on the clinical presentation, mucormycosis may be divided into five categories: rhinocerebral, pulmonary, cutaneous, gastrointestinal, and disseminated. Rhinocerebral mucormycosis is the most common form of the disease. Three of our patients presented acute invasive Mucorales rhinosinusitis, one due to *L. corymbifera*. The initial presentation is often consistent with rhinosinusitis, including facial pain, unilateral headache, occasional proptosis, soft tissue swelling, and serosanguineous nasal discharge.

Classifying the disease as phaeohyphomycosis and hyalohyphomycosis may be considered a poor classification, since it is not a specific taxonomic classification. Important human pathogens included in the hyalohyphomycosis group are *Fusarium, Schizophyllum*, and *Trichoderma species*. Two pathogens were observed for the first time as the agent of rhinosinusitis and human infection (*X. enteroleuca* (10) and *T. asperellum*, present report). The role of *Trichoderma* species remains to be elucidated. This species is emerging as an opportunistic pathogen that rarely causes disease in humans. Few reports causing rhinosinusitis have been published, with *T. longibrachiatum* as the species most often involved causing allergic or invasive disease. The treatments used in the few cases were debridement of the lesion with antifungal association (12, 18).

The spectrum of clinical presentation by *Fusarium* species includes those seen in both the healthy and the immunocompromised hosts. Allergic fungal sinusitis caused by *F. solani* in an immunocompetent patient has been previously reported (11). Filamentous basidiomycetes are uncommon causes of human and animal disease. In our series, we found one case of AFS caused by *F. solani* in the immunocompetent group. The most frequently reported clinically important pathogen is *S. commune*, recognized as a significant cause of allergic rhinosinusitis, and we observed two cases in our cohort.

Scedosporiosis includes *S. apiospermum* and *P. boydii* infections that have been regarded as having an anamorph-teleomorph connection. However, this has been disproved based on nucleic acid sequence analysis. The taxonomy of this genus is rather complex (8, 9). In our series, we identified two cases of *S. apiospermum* causing AFS and a fungus ball, caused by *P. boydii*.

Although infections caused by dematiaceous fungi are rare, they are increasingly being recognized as the cause of human disease (15). The term phaeohyphomycosis is based on the characteristics of the fungi, as seen

in infected tissue (dark-walled). Our cohort includes three cases classified as phaeohyphomycosis, two of them caused by *A. alternata* and another by *Cladosporium* sp.

Other slowly progressive infections may be less commonly caused by dimorphic fungi such as *H. capsulatum* or encapsulated yeast cells of *C. neoformans*. We only isolated these agents in our immunocompromised group: histoplasmosis (n=4) and cryptococcosis (n=1). There is a wide spectrum of clinical manifestations of histoplasmosis, ranging from a transient pulmonary infection to more widespread disseminated disease. Mucosal ulcers are found in >60% of these patients (14). The oropharynx is often affected; however, lesions also occur on the lip and nose (2, 3, 4). It has been stated that cryptococcosis affecting the paranasal sinuses is rare (13). In our series, we describe the second case of cryptococcal sinusitis in an immunocompromised (AIDS) male.

AFS is the most common form of fungal rhinosinusitis, and diagnosis is often missed in cases of unexplained chronic rhinosinusitis. For this reason, clinicians should include AFS in the differential diagnosis of patients with chronic rhinosinusitis refractory for standard therapy. In addition, we believe that documentation of histological evidence is preferable to positive culture only because culture carries an inherent risk of contamination.

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