

Fungal sinusitis among patients with chronic rhinosinusitis who underwent endoscopic sinus surgery

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ABSTRACT:

Introduction: Fungal paranasal sinusitis can be either invasive or noninvasive. Saprophytic infections, fungus balls (FB) and allergic fungal rhinosinusitis are noninvasive (AFR).

Materials and methods: The present study examined 521 patients who underwent endoscopic sinus surgery between January 2016 and April 2017 due to chronic paranasal sinusitis at the Department of Laryngology and Laryngological Oncology of the Upper Silesian Medical Centre in Katowice. The aim of the study was to analyze histopathological and microbiological material collected intraoperatively and to determine incidence and type of fungal infections among patients treated for chronic sinusitis.

Results: Chronic fungal sinusitis was confirmed in 10 of 521 operated patients. The study group consisted of 9 females and 1 male. Histopathological examination revealed dead mycelium in 5 patients and colonies of *Aspergillus* spp. in 4, while microbiological examination revealed *Candida albicans* infection in 1 case. Allergy to inhalant allergens of fungal spores of *Alternaria* and *Penicillium* was confirmed in a 73-year-old patient, which, based on the whole clinical presentation, enabled to diagnose chronic allergic fungal sinusitis. The most common location of mycelium was maxillary sinus, followed by sphenoid sinus.

Discussion: The most common form of noninvasive fungal sinusitis is the so-called fungus ball, which was also confirmed in our report (95% of the test subjects). AFRS is more likely to occur in warm, moist climates that favor the growth of fungi.

KEYWORDS:

fungal sinusitis, fungus ball, allergic fungal sinusitis

INTRODUCTION

The presence of fungi in the mucosa of the nose and the paranasal sinuses is reported both in the population of healthy individuals and in patients with chronic sinusitis. This may be due to the widespread presence of fungal spores in the inhaled air. The most common species colonizing the mucosa of the nose and the paranasal sinuses and causing fungal sinusitis is *Aspergillus* spp., including *Aspergillus fumigatus* (90%), *Aspergillus niger*, *Aspergillus flavus* [1]. Colonization is different from an infection since not every colonized patient will

develop a fungal infection. Mutual interaction of fungi with the host's immune system determines development of the infection or its absence.

Fungal rhinosinusitis (FRS) is an inflammation of the nasal cavity and the sinuses taking an invasive or noninvasive form. Invasive rhinosinusitis may take the form of acute invasive or fulminant (AIFRS) as well as chronic invasive (CIFRS) and chronic granulomatous (CGFRS). Noninvasive form is represented by saprophytic infections (SFI), fungus balls (FB) and allergic fungal rhinosinusitis (AFRS). Histopathological examination

assessing fungal vascular invasion and the degree of bone destruction are helpful in differentiation [2,3,4]. Invasive inflammation is most common in patients with immunodeficiency and develops within 4 weeks [5]. Noninvasive forms more frequently include only the sinus mucosa in patients with normal immune system, as well as patients with chronic diseases such as diabetes [6]. AFRS is diagnosed on the basis of the characteristic sinus CT scan, clinical symptoms of chronic sinusitis, polyps, mycelium without tissue invasion and evidence of IgE (immunoglobulin E)-dependent allergy (type I), confirmed by medical history, positive skin prick tests and serological tests [7]. The aim of the study was to analyze histopathological and microbiological material obtained during endoscopic sinus surgery (ESS) and to determine the incidence and type of fungal infections among patients treated for chronic sinusitis (CRS).

MATERIAL AND METHOD

A total of 521 patients who underwent endoscopic sinus surgery between January 2016 and April 2017 due to chronic paranasal sinusitis at the Department of Laryngology and Laryngological Oncology of the Upper Silesian Medical Centre in Katowice were subjected to analysis. All patients were qualified for surgery based on physical, laryngological and endoscopic examination as well as CT scans of paranasal sinuses (according to EPOS 2012 guidelines). The extent and localization of inflammatory lesions were assessed using the Lund-Mackay score. During surgical procedures, material for microbiological (bacteriological and mycological) and histopathological examination was collected from all the patients.

A group of patients with fungal sinusitis revealed in histopathological and/or microbiological examination underwent extensive observation. The patients' medical records were analyzed. The main complaints, the presence of comorbidities (bronchial asthma, diabetes, ischemic heart disease, hypothyroidism, glaucoma), working environment, use of drugs including cigarettes were studied. The results of allergy tests for -IgE-dependent allergy to inhalant allergens of fungal spores (*Alternaria*, *Cladosporium*, *Aspergillus*, *Penicillium*), most commonly found in indoor and outdoor environments in our climatic zone, were analyzed.

RESULTS

Of all 521 operated patients, chronic fungal sinusitis was confirmed (by histopathological and/or microbiological examination) in 10 patients (i.e., 1.9%). The study group consisted of 9 females and 1 male, aged 50 to 74 years. The mean age was 63 years (+/- SD 2).

Clinical symptoms

The most commonly reported complaint in the study group before surgery was facial pain (75% of patients), followed by nasal obstruction (60%), post-nasal drip (60%), purulent nasal discharge (9%), and other complaints such as toothache, impaired smell.

Localization of lesions, imaging studies

Before surgery, all patients had a CT scan of paranasal sinuses done in three projections. MRI was performed in the case of involvement of the sphenoid sinus and bone destruction confirmed by CT. Unilateral inflammatory lesions were found in 3 patients, and bilateral ones in 7. Fungal lesions were always present within one sinus. The most common location of mycelium was the maxillary sinus (7 patients) followed by the sphenoid sinus (3 patients).

The presence of microcalcifications was found in CT scans of 4 patients, while the features of bone destruction in 3. Bilateral nasal polyps occurred in 6 patients. The Lund-Mackay score of the extent of lesions ranged from 2 to 12 points.

Histopathological and microbiological examination

Histopathological examination revealed dead mycelium in 5 patients, and colonies of *Aspergillus* spp. in 4. Microbiological examination revealed *Candida albicans* infection in 1 patient.

Comorbidities

In the group of 8 patients with comorbidities, the most common was hypertension (5 patients), followed by diabetes (3 patients), allergy (IgE-dependent allergy to allergens such as grass, dog or cat hair in 3 patients, and type IV - nickel in 1 patient), hypothyroidism (3 patients), ischemic heart disease (2 patients).

One 73-year-old female patient was diagnosed with allergic reactions to inhalant allergens of fungal spores of *Alternaria* and *Penicillium*. Amongst all, she reported the most significant symptoms to be increasing headaches (for around 6 months) of the parietal and temporal regions on the left side, progressive memory disturbances, dizziness, periodic fever. CT and MRI showed that the left sphenoid sinus was fully filled with hypodense masses. On the left side, there was bone erosion of the lateral wall of sphenoid sinus and invasion of the inflammatory process outside sphenoid sinus. The results of CT and MRI are shown in Figs. 1 and 2. Endoscopic sinus surgery (left-sided ethmosphenoidectomy) was performed. After opening the anterior and posterior ethmoid cells, the polyps obstructing the sphenoid sinus ostium were removed, and then the

Tab. I. General characteristics of the study group.

NO	AGE	SEX	LOCALIZATION OF LESIONS, SINUS:	THE LUND-MACKAY SCORE	PRESENCE OF POLYPS	HISTOPATHOLOGICAL / MICROBIOLOGICAL EXAMINATION	PRICK TESTS	MICROCALCIFICATIONS	BONE DESTRUCTION IN CT	PREVIOUS OPERATIONS	HARMFUL WORKING CONDITIONS
1	73	F	Sphenoid	3	+	Dead mycelium	+	+	+	-	-
2	72	F	Maxillary	12	+	Aspergillus	-	-	-	-	+(mine)
3	73	F	Sphenoid	10	-	Dead mycelium	-	+	-	-	-
4	50	F	Maxillary	8	+	Aspergillus	-	-	-	-	-
5	52	F	Maxillary	8	-	Dead mycelium	-	+	-	-	-
6	74	F	Sphenoid	2	-	Aspergillus	-	-	-	-	-
7	59	F	Maxillary	6	-	Dead mycelium	-	+	+	-	-
8	64	M	Maxillary	5	+	Aspergillus	-	-	-	-	-
19	52	F	Maxillary	11	+	Candida albicans	-	-	+	+	-
20	69	F	Maxillary	4	+	Dead mycelium	-	-	-	+	-

brown masses, which histopathological examination identified as dead mycelium, were removed from the left sphenoid sinus. The patient remained under observation for 12 months without relapse. Clinical presentation and additional examinations may suggest AFRS in this patient.

Environmental burden, stimulants

In the study group, 1 patient was exposed to hazardous working conditions (mining), 1 patient smoked cigarettes.

Reoperations

Of the 10 test subjects, 2 (20%) patients were previously operated for chronic sinusitis (FESS). Aetiology of fungal infection was previously identified in none of them. Two patients underwent endodontic treatment in the past.

Treatment results

The observation period in patients ranged from 6 to 12 months. In the study group, no patient had recurrences, no patient needed another surgical intervention

The general characteristics of patients are shown in Table 1.

DISCUSSION

It is estimated that fungal sinusitis constitutes around 4-13% of

all cases of chronic sinusitis. Fungus balls are the most common form of noninvasive fungal sinusitis. They are usually located one-sidedly mainly in the maxillary sinus and are more common in middle-aged and older women [8,9]. In CT, the characteristic feature is occurrence of microcalcifications within the lesion in the involved sinus. MRI shows low signal intensity in both T1- and T2-weighted images [1]. The pathogenic factor is usually *Aspergillus* spp. [1,10]. In our report, the most common form of fungal sinusitis was also the fungus ball (95% of the test subjects).

In a group of 4573 patients subjected to endoscopic surgery for chronic sinusitis in South Korea, Kim et al. confirmed the occurrence of fungus balls in 5.4% of patients [11]. Our study confirmed the presence of fungus balls in 10 patients, which accounts for less than 2% of all 521 patients operated for chronic sinusitis. This can be related to the more frequent occurrence of fungal sinusitis in warm and humid climates. Differences in histopathological and microbiological examination methodology, which is not identical in all centers in Europe and in the world, may also be relevant. According to some researchers, the risk of developing fungus balls is related to endodontic treatment (in our case, 2 patients underwent such treatment), as proven by the fact that the most common location of fungus balls is the maxillary sinus [11,12]. In the latest publications, authors point to the increased incidence of fungal sinusitis in recent years [11]. This phenomenon may be related to development of diagnostic techniques, but also to the widespread use of broad-spectrum antibiotics, increased number of patients with immunodeficiency or steroid therapy. Its more frequent



Fig. 1. CT of the paranasal sinuses of a 73-year-old patient. Mycosis of left sphenoid sinus causing destruction in sinus bone.



Fig. 2. MRI of fungal infection of left sphenoid sinus.

occurrence in middle and older age may be associated with impaired ciliary mucosal transport, resulting in abnormal sinus drainage and increased risk of developing a fungus ball [11]. The diagnostic process of fungal sinusitis is complex, based on physical, imaging, microbiological and histopathological examination. However, it is not always possible to identify fungal pathogens [13,14]. It is estimated that only 25-50% of patients with confirmed mycosis have positive results of microbiological examination [15,16]. The only reliable diagnosis of mycosis is the positive result in the course of direct preparation of clinical material in histopathological examination [17]. In our study, fungal pathogens were identified in 25% of patients, in whom the most commonly isolated species was *Aspergillus*, followed by *Candida albicans*. *Aspergillosis* was confirmed in 80% of patients with a specific fungal pathogen, which is similar to the reports of other authors such as Pagella (82%) [4].

The main complaints reported by patients are dense nasal secretion, nasal obstruction, headache, post-nasal drip [10,11,18,19]. In our work, the reported complaints were similar, but they were mostly headaches and facial pain (75%). Among comorbidities, hypertension and confirmed type 2 diabetes were predominant, which is not different from other authors' reports. In computed tomography, the common feature is the presence of so-called microcalcifications caused by the presence of

magnesium, zinc, iron and calcium contained in mycelium [18]. In Nicolai's study, microcalcifications were confirmed in about 75% of patients [10], and other authors observed them in 61-67% of cases [9,10,11,18]. In our report, microcalcifications were present in 40% of patients.

There are many factors that potentially predispose to the development of chronic fungal sinusitis. These include rural life, diabetes, previous operations. In our material, 10% of patients were exposed to harmful working conditions (mining), 10% smoked cigarettes, and 20% were previously operated due to chronic sinusitis.

Allergic fungal rhinosinusitis (AFRS) is more common than other forms of fungal sinusitis in younger, healthier patients. Its incidence is estimated at 5 to 10% in patients with chronic sinusitis treated surgically [20]. Patients complain mainly about nasal obstruction, headache and other symptoms of chronic sinusitis. AFRS is mainly present in warm, moist climates that promote fungal growth [1]. AFRS patients are more likely to develop atopy, bronchial asthma, sometimes eosinophilia, and have an elevated total fungal-specific concentration of IgE. The pathomechanism of the disease is based on mucosal hypersensitivity to fungal antigens including *Bipolaris*, *Curvularia*, *Alternaria*, *Aspergillus* and *Fusarium*. Sticky thick eosinophi-

lic secretion is produced and accumulated within the mucous membrane of the sinuses and a chronic inflammatory process develops [1,21,22]. Although this type of mycosis is not considered invasive, the untreated disease can lead to bone destruction (6-56% of cases) [23]. In our material, AFRS diagnosis was suggested in one 73-year-old patient, which may be associated with a lower incidence of this disease in our climate.

The method of choice in the case of chronic noninvasive fungal sinusitis is surgical treatment. Endoscopic surgery is the golden standard, that restores proper drainage and ventilation within the sinuses after complete removal of fungal masses. Endoscopic surgery is associated with lower trauma of the patient, faster healing and a low recurrence rate <5% [18,19]. The use of anti-fungal drugs as a supplement to surgical treatment is advocated by some researchers, but no clear statement has been made on that matter yet. Some authors recommend general steroid therapy both prior to planned surgery (prednisone at a dose of

1mg/kg) and postoperatively (prednisone - 0.5-10mg/kg/day at reduced doses for about 14 days), which reduces inflammation and improves intraoperative conditions [24,25]. In the case of allergic fungal sinusitis, immunotherapy is proposed, which, according to some reports, improves the course of disease and the quality of life of patients after surgical procedures [20,26,27].

RESULTS

1. Fungal sinusitis is rare, but it is always important to take into account mycotic aetiology in the case of unilateral lesions.
2. The golden standard for noninvasive treatment of fungal sinusitis is endoscopic surgery.
3. Previous surgery, in particular dental treatment, means that we should be alert to the possibility of occurrence of FRS.

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