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### Original Article

# Frequency of non-invasive fungal sinusitis in patients undergoing surgery for chronic rhinosinusitis

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### Abstract

**Background:** In this study, we investigated the presence of non-invasive fungal sinusitis in patients who underwent endoscopic sinus surgery with the diagnosis of chronic rhinosinusitis in our clinic.

**Methods:** A total of 283 patients who underwent functional endoscopic sinus surgery for chronic rhinosinusitis in our clinic between 2008-2018, who were at the ages of 18 or above, and who did not have invasive fungal sinusitis and tumor were included in the study. Sinus pathology was examined by routine examination using nasal endoscopy and computed tomography. Eosinophil count, total, and specific IgE levels were measured in the peripheral blood samples of the patients. Sinus surgery was performed under general and local anesthesia with the Messerklinger technique. Aspirated secretions from the sinuses and removed surgical tissues were examined microbiologically and histopathologically.

**Results:** 68 females, 215 males, totally 283 patients with a mean age of 41 had sinus surgery; 11 (40.74%) females and 16 (59.26%) males, totally 27 (9.54%) patients had non-invasive fungal sinusitis. 18 (6.36%) of the cases were microbiologically reported as allergic fungal sinusitis while 9 (3.18%) of them reported as mycetoma. Nasal obstruction (19, 70.37%) and headache (13, 48.14%) were the most common clinical findings. Eosinophilic mucus was detected in the sinus material of the patients with allergic fungal sinusitis. According to their prevalence, *Aspergillus*, *Penicillium*, and *Candida* were the most prevalent in the patients with allergic fungal sinusitis, respectively; *Aspergillus fumigatus* and *Aspergillus flavus* were the most prevalent in the patients with allergic fungal sinusitis, respectively. Radiologically, fungal balls localized at the maxillary sinuses in six patients, the sphenoid sinuses in two patients, and the ethmoid sinus in one patient. As a treatment, sinus surgery was performed as a complete evacuation of the mucus and removal of pathological and polypoid tissues. The follow-up periods of the patients ranged between 7-31 months; the mean duration of follow-ups was 17 months. Non-invasive fungal infections were not treated with antifungal therapy, no recurrence was observed.

**Conclusions:** In this study, non-invasive fungal sinus infection was detected 9.54% of patients. Nasal examination, radiological, and immunological examination should be applied to patients as additional examinations on the suspicion of pre-operative fungal rhinosinusitis; samples should be taken from the sinuses during surgery and should be examined for fungus microbiologically and histopathologically. Antifungal therapy was not administered to patients with non-invasive fungal infection. Endoscopic sinus surgery is a successful method in the treatment of non-invasive fungal rhinosinusitis.

**Keywords:** allergy, fungal infections, fungi, sinusitis

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## Introduction

The presence of paranasal fungal sinusitis in patients with chronic rhinosinusitis is one of the most frequently wondered and popular topics in the last two decades. Fungal sinusitis occurs with multi-factorial pathogenesis on the basis of chronic rhinosinusitis. These factors include chronic rhinosinusitis infection, immune resistance of the patient, anatomical variations, systemic diseases, and allergic causes. All these factors, nasal mucosa alterations, osteomeatal edema in the sinuses, impaired mucociliary activity, inadequate air circulation in the sinuses, and acidification (a transition to acidic conditions, low pH), facilitate the colonization and spreading of fungal infection. Paranasal fungal sinusitis infections are seen in two different forms as invasive and non-invasive. Invasive fungal sinusitis is observed in patients with impaired immune resistance and diabetes, whereas non-invasive form is observed in patients with normal immune resistance as allergic fungal sinusitis and mycetoma (fungus ball) [1-5].

Fungal sinusitis diagnosis can be made by microbiological and histopathological analyses of fungal infection in the aspirates of and pathological tissues taken from the sinuses. The diagnostic criteria for allergic fungal sinusitis which form non-invasive fungal sinusitis were first described and published by Millar in 1981. The diagnosis of mycetoma can be made easily by nasal examination, imaging, and histopathological methods [3-6].

The aim of this study was to investigate the presence of non-invasive fungal sinusitis in the paranasal sinuses of patients with chronic rhinosinusitis.

## Methods

This study was conducted in accordance with the Declaration of Helsinki and informed consent was obtained from all participants. A total of 283 patients aged 18 years and older with the diagnosis of chronic rhinosinusitis in our clinic during the last decade (2008-2018) were included in the study.

The patients were evaluated according to age, gender, anamnesis (asthma, diabetes, aspirin intolerance, history of allergy, nasal and sinus operations), anterior rhinoscopy and nasal examination (septal deviation, polyp, presence and nature of nasal discharge), coronal and axial paranasal computed tomography results or endoscopic sinus surgery performed with Messerklinger technique under general or local anesthesia. During the surgery, the sinus material which was aspirated under sterile conditions sent to the microbiology and pathology departments for histopathological evaluation. The samples were stained with Periodic Acid Schiff (PAS) and Hematoxylin-Eosin (HE) and histopathologically evaluated.

The diagnosis of allergic fungal sinusitis was made on the basis of deShazo [7] criteria (macroscopic appearance compatible with allergic mucin, eosinophilia, total and specific IgE elevation, histopathological hyphae, presence of allergic mucin, fungal culture positivity).

The diagnosis of mycetoma was made by anamnesis, nasal examination, radiological images (in tomography, sinus is usually seen with single, complete or incomplete opacity and central hyperdense areas), histopathological, and microbiological examination of the sinus material.

The patients with immunodeficiency, cystic fibrosis, inverted papilloma, antrochoanal polyp, invasive fungal sinusitis, and tumor were excluded from the study.

In the analysis of the data, the descriptive information about the patients included in the study was given a number, percentage distribution and average. For the statistical analysis, the SPSS (Windows 22.0) was used.

## Results

283 patients who underwent endoscopic sinus surgery for chronic rhinosinusitis in the last decade were included in the study. 68 patients were female and 215 were male; their mean age was  $41\pm 17$ ; their ages ranged between 19-64 years. 84% of the patients underwent surgery under general anesthesia while 16% of them underwent surgery under local anesthesia.

Non-invasive fungal sinus infection was detected in 27 of these patients (9.54%). In the patients with a non-invasive fungal sinus infection, 18 (6.36%) of them had allergic fungal sinusitis while 9 (3.18%) of them were with mycetoma. 11 (40.74%) of the patients were female; 16 (59.26%) of the patients were male; their mean age was  $46\pm 14$ ; their ages ranged between 26-62 (Table 1).

Nasal obstruction (19, 70.37%) and headache (13, 48.14%) were the most common clinical findings in the patients. Eosinophilic mucus was determined in the sinus materials of the patients with allergic fungal sinusitis; *Aspergillus*, *Penicillium*, and *Candida* complex were isolated according to the order of frequency. 11 of 18 patients with allergic fungal sinusitis had unilateral polyposis while 7 of them had bilateral nasal polyposis. *Aspergillus fumigatus* and *Aspergillus flavus* were the most common fungus species in patients with mycetoma. In radiological analyses, fungal balls localized in the maxillary sinus in six patients, the sphenoid sinus in two patients and the ethmoid sinus in one patient (Table 1).

In the treatments, debridement of the sinus with retention and complete evacuation of the mucus and clearance of polypoid tissues were administered. The mean duration of hospital stay was two days; the follow-up period ranged between 7-31 months; the mean follow-up duration was 17 months. Antifungal therapy was not administered to patients with non-invasive fungal infection.

**Table 1.** Details of patients with non-invasive fungal sinusitis

No	Age	Sex	Symptom	Surgery	Predisposing factors	Fungal species	Sinus mycoses types
1	43	Male	Nasal congestion	ESS+BNPS	Nasal polyp Asthma	A. flavus	Allergic FS
2	35	Male	Postnasal drip Headache	ESS+NPS	Nasal polyp Allergic rhinitis	Candida glabrata	Allergic FS
3	26	Female	Nasal congestion	ESS+BNPS	Nasal polyp Allergic rhinitis	Candida glabrata	Allergic FS
4	43	Female	Postnasal drip Headache	ESS+NPS	Diabetes	A. flavus	Allergic FS
5	49	Male	Nasal congestion	ESS+BNPS	Nasal polyp	Penicillium polanicum	Allergic FS
6	57	Male	Nasal congestion Headache	ESS+NPS	Diabetes	A. flavus	Allergic FS
7	62	Female	Nasal congestion	ESS+NPS	Diabetes	Penicillium polanicum	Allergic FS
8	33	Male	Nasal congestion Headache	ESS+BNPS	Allergic rhinitis	A. flavus	Allergic FS
9	41	Male	Nasal congestion Headache	ESS+NPS	Nasal polyp	Candida glabrata	Allergic FS
10	44	Female	Nasal congestion	ESS+BNPS	Nasal polyp Allergic rhinitis	Penicillium chrysogenum	Allergic FS
11	42	Female	Postnasal drip Nasal congestion	ESS+NPS	Nasal polyp	Candida glabrata	Allergic FS
12	37	Male	Nasal congestion	ESS+BNPS	Allergic rhinitis	Penicillium chrysogenum	Allergic FS
13	28	Female	Nasal congestion Headache	ESS+BNPS	Nasal polyp Asthma	A. flavus	Allergic FS
14	53	Male	Headache	ESS+NPS	Nasal polyp	A. flavus	Allergic FS
15	51	Female	Nasal congestion	ESS+NPS	Nasal polyp	Penicillium chrysogenum	Allergic FS
16	54	Male	Nasal congestion Headache	ESS+NPS	Nasal polyp Allergic rhinitis	A. flavus	Allergic FS
17	32	Male	Nasal congestion Headache	ESS+NPS	Nasal polyp	A. fumigatus	Allergic FS
18	52	Female	Nasal congestion	ESS+NPS	Nasal polyp	Penicillium chrysogenum	Allergic FS
19	35	Male	Nasal congestion Headache	ESS	Maxillary sinus	A. fumigatus	Mycetoma
20	62	Male	Postnasal drip	ESS	Ethmoid sinus	A. flavus	Mycetoma
21	36	Female	Headache	ESS	Maxillary sinus	A. fumigatus	Mycetoma
22	46	Male	Nasal congestion	ESS	Sphenoid sinus	A. flavus	Mycetoma
23	55	Male	Headache	ESS	Maxillary sinus	A. flavus	Mycetoma
24	28	Female	Headache	ESS	Maxillary sinus	A. fumigatus	Mycetoma
25	31	Male	Nasal congestion	ESS	Sphenoid sinus	A. fumigatus	Mycetoma
26	42	Male	Postnasal drip	ESS	Maxillary sinus	A. fumigatus	Mycetoma
27	48	Female	Nasal congestion	ESS	Maxillary sinus	A. fumigatus	Mycetoma

ESS: Endoscopic sinus surgery, NPS: Nasal polyp surgery, BNPS: Bilateral nasal polyp surgery, Allergic FS: Allergic fungal sinusitis, A. flavus: Aspergillus flavus, A. fumigatus: Aspergillus fumigatus

## Discussion

In the last two decades, the diagnosis of fungal sinusitis has been common in patients undergoing endoscopic sinus surgery on the basis of chronic sinusitis. Paranasal fungal sinusitis is usually associated with single sinus involvement in individuals with normal immunity and is mucosal and non-invasive fungal infections [1-4].

In recent studies, the incidence of non-invasive fungal sinusitis in sinus infections ranges between 5% and 12%. In cases of chronic rhinosinusitis undergoing surgery, allergic fungal sinusitis is seen as 5-12% while mycetoma rate is 3.7% [3-9]. In our study, non-invasive fungal sinusitis rate was found as 27/283 (9.54%); allergic fungal sinusitis rate was found as 6.36%; mycetoma rate was found as 3.18%. Most patients have atypical complaints. When they are symptomatic, the most common complaint is head/face pain and nasal obstruction [1-3,5,6,8-10]. In our study, the most prevalent complaints were nasal obstruction and headache with the rates of 19 (70.37%) and 13 (48.14%), respectively.

Allergic fungal rhinosinusitis is the hypersensitivity response of nasal mucosa against fungal elements. Patients are generally young adults and atopic individuals. Most of them have asthma, nasal polyps, aspirin sensitivity, and eosinophilia. In their histopathological examinations, Charcot-Leiden crystals consisting of degenerated eosinophils can be observed [3,5,9,10-13]. Bent and Kuhn [14] stated the diagnostic criteria as characteristic, adhesive allergic mucin, the observation of fungal elements in histopathological analyses or the production of fungal elements in culture, typical tomography findings, nasal polyp presence in 75-100% of patients, and type 1 hypersensitivity according to fungal skin test or in vitro tests. In our study, the presence of allergic mucus in the sinus samples of the patients diagnosed with allergic fungal sinusitis, fungal diagnosis in histopathological examinations, typical tomography findings were reported. 11 unilateral and 7 bilateral nasal polyposis were also reported in 18 patients.

In the nasal endoscopic examination, the characteristic is not observed in half of mycetoma patients. In patients with sphenoid sinus mycetoma, purulent discharge and a few numbers of polyps can be observed in the sphenoid-ethmoid resection. The prevalence of atopy in patients with a fungal ball is not different from the normal population; their skin test results and specific immunoglobulin E (IgE) levels are normal. Complete or incomplete opacity is observed in sinus imaging. The retention of the maxillary sinus is the most prevalent. Hyperdense areas are also observed in the center of retention in 25-50% of the patients. Fungus ball should be suspected in the diagnosis especially in unilateral sinusitis. In the imaging, opacities with unilateral sinus retention and hyperdense areas in the center of retention support the diagnosis. However, a definitive diagnosis is made by histopathological examination [2,4,6,8,16-18]. In our study, the fungus balls were localized in the maxillary sinus, sphenoid sinus, and ethmoid sinus of six, two and one patients, respectively according to radiological analyses in accordance with the literature.

Samples aspirated from the infected paranasal sinus are stained with HE and PAS to make the fungal elements visible. However, histopathological species cannot be discriminated. Microbiological culture is required for the discrimination of species [1,3,6,12-18]. In our study, the samples were stained with PAS and HE; the presence of invasion was investigated, but none of them had tissue invasion. Microbiological culture examinations were also performed and fungal agent species were detected.

Grigoriu et al. [19] reported that fungal infections, especially *Aspergillus fumigatus* were the cause in 81% (13.5%) of the patients in 60 maxillary sinusitis cases. Laskownick et al. [20] reported that most of the isolated fungus composed of *Penicillium* (49 cases), *Aspergillus* (30 cases), and *Candida* (20 cases).

In recent studies, the fungus species frequently isolated in the microbiological analyses of allergic fungal sinusitis were *Aspergillus*, *Alternaria*, *Curvularia*, *Exserohilum*, *Drechslera*, *Helminthosporium*, and *Fusarium*. In mycetoma, *Aspergillus*, especially *Aspergillus fumigatus* and *Aspergillus flavus* were frequently isolated [15-18,21-24]. In our study, *Aspergillus*, *Penicillium*, and *Candida* and *Aspergillus fumigatus* (most common) and *Aspergillus flavus* were the most prevalent fungus species in the patients with allergic fungal sinusitis.

In recent years, more studies reported to identify the role of antifungal therapy have been performed [25]. But antifungal therapy was not recommended to the patients with non-invasive fungal infection. In the treatment of noninvasive fungal sinusitis, endoscopic sinus surgery is sufficient in the successful treatment of infection in patients.

In conclusion, allergic fungal sinusitis and mycetomy are important in the etiology of chronic rhinosinusitis as non-invasive fungal infections. In patients with chronic rhinosinusitis with the suspicion of fungal rhinosinusitis before surgery, nasal examination and additional radiological and immunological examinations should be requested; the samples taken from the sinuses during surgery should be examined microbiologically and histopathologically. In the treatment of noninvasive fungal sinusitis, endoscopic sinus surgery is sufficient in the successful treatment of infection in patients. Postoperative hospital stay is short, antifungal therapy is not required after this application which improves life quality.

#### **Conflict of interest**

The author declares no conflict of interest.

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