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Anatomical Variations Associated With Maxillary Sinus Fungal Ball

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Abstract

Objective: We investigated the anatomical and dental factors associated with unilateral maxillary sinus fungal ball (MSFB). Also, we evaluated the effect of combinations of those factors on the incidence of MSFB. **Methods:** Three hundred patients were divided into MSFB, normal, and chronic rhinosinusitis (CRS) groups. We reviewed paranasal computed tomography scans for the presence of deviated nasal septum, concha bullosa (CB), Haller cells, and various dental factors. Also, we measured the ethmoid infundibulum, maxillary natural ostium, and CB. **Results:** Maxillary sinus fungal ball showed a more significant association with CB compared to the other 2 groups (37%, $P < .05$). The MSFB group had a lower rate of Haller cells than the normal group (10% vs 22%, respectively; $P < .05$). Also, the MSFB group had a wider maxillary sinus ostium than the normal group (7.07 $\pm$ 1.8 vs 5.48 $\pm$ 1.3 mm; $P < .01$). Moreover, the combination of CB and Haller cells was significantly associated with a decreased rate of the fungal ball ($P = .047$, odds ratio = 0.694). The dental factors were more prevalent in the MSFB and CRS groups (73% and 75%, respectively) than in the normal group (32%, $P < .001$). **Conclusions:** Maxillary sinus fungal ball is significantly associated with CB, Haller cells, an increased maxillary sinus ostium size, and dental factors.

Keywords

fungal ball, natural ostium, anatomic variation

Introduction

Fungal rhinosinusitis is classified as invasive or noninvasive; the latter includes a fungal ball, which is defined as a fungal growth in any nasal sinus without invasion of the mucosa.[1] The most commonly involved sinus is the maxillary sinus, and most cases are unilateral.[2] There are 2 main hypotheses regarding the origin of maxillary sinus fungal ball (MSFB). The first hypothesis is that MSFB develops because of the anaerobic condition of the maxillary sinus, possibly caused by obstruction of the drainage system by anatomical factors. The second hypothesis is that MSFB has a dental origin.[3]

The relationship between sinonasal anatomical variations and MSFB has been investigated; however, there is reportedly no correlation between a deviated nasal septum (DNS) and a fungal ball.[4-7] Moreover, the presence of Haller cells in cases of MSFB is controversial.[4,6-8] Concha bullosa (CB) is typically present on the same side as MSFB.[5,7,8] Regarding the osteomeatal complex (OMC), a fungal ball is associated with a narrow and long ethmoid infundibulum.[7] Also, immunocompetent patients with MSFB have a wide natural ostium.[9]

We hypothesize that MSFB is associated with anatomical variations or combinations thereof and dental factors. Since prior studies of MSFB only evaluated factors in isolation, rather than their combined effects, we investigated the effect of anatomical

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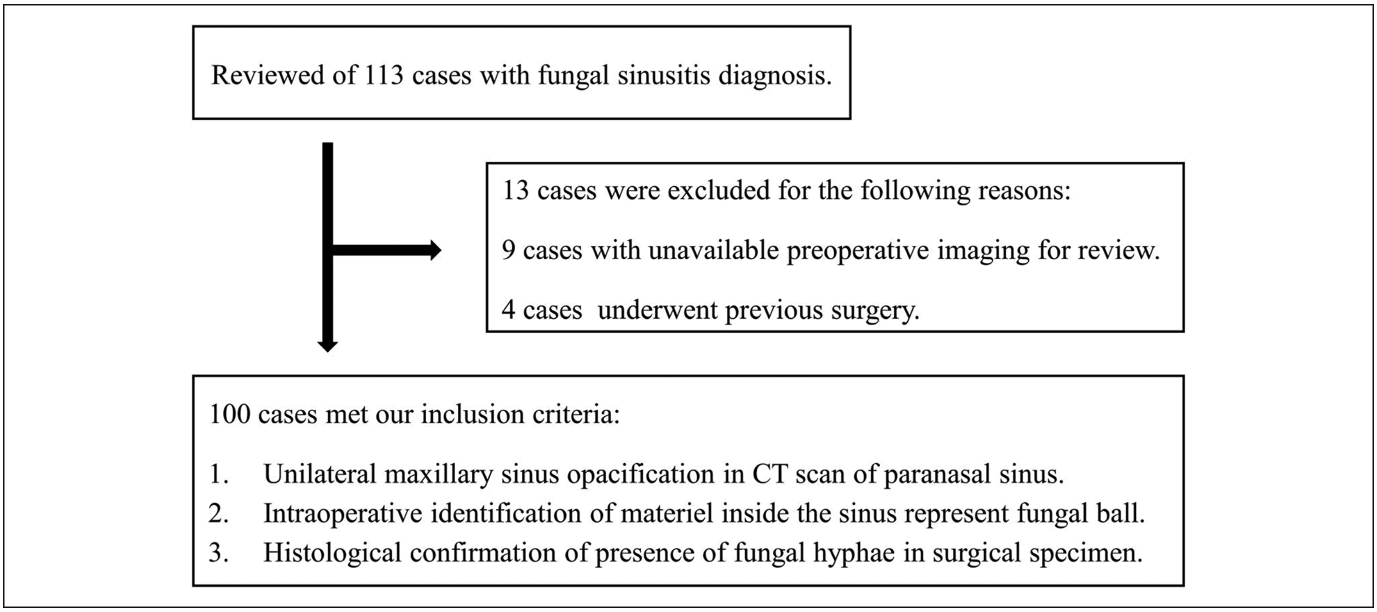

Figure 1. Flowchart of the inclusion criteria of maxillary sinus fungal ball group.

variation alone and dental factors as well as the combined effect of anatomical variations in the development of MSFB.

Materials and Methods

Study Population

This study and the associated chart review were approved by the institutional review board of the Catholic University of Korea, Seoul. St. Mary's Hospital, College of Medicine (approval no. KC20RISI0758). Patients who underwent endoscopic sinus surgery in our hospital from July 2014 to March 2019 were retrospectively reviewed. We identified 113 patients of MSFB and only 100 patients met our inclusion criteria (Figure 1). The patients with revision surgery, bilateral sinus disease, trauma, and other sinus diseases (eg, benign or malignant neoplasm) were excluded. Additionally, we identified another 200 patients as a control group within this period. We divided 300 patients into MSFB, normal, and chronic rhinosinusitis (CRS) groups (n = 100 each). The MSFB group comprised patients with radiologically confirmed unilateral MSFB and histopathology indicative of fungal hyphae.[1-3] The normal group consisted of patients who underwent transsphenoidal pituitary surgery and had a normal-appearing sinus, and the CRS group comprised patients without polyps, unilateral sinusitis revealed by computed tomography (CT), and histopathology suggestive of chronic inflammation.

Data Collection

We analyzed the following anatomical and dental factors related to the maxillary sinus: DNS, CB size, Haller cells, ethmoid infundibulum, and maxillary natural ostium. Also, we reviewed the patients' medical histories, smoking status, allergy status [based on the multiple allergen simultaneous test (MAST)], and eosinophil count. Regarding dental factors, we analyzed dental procedures (eg, extractions, root canal treatments, and implantations) and checked for apical lesions on the diseased side. We assessed only the second premolar and first and second molars.

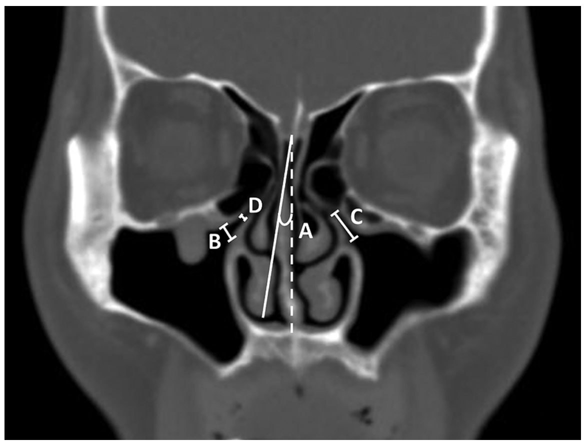

Figure 2. Measurement of anatomical variation. (A) Angle of the deviation of the septum; (B) size of the maxillary natural ostium; (C) EI length; and (D) EI width. EI indicates ethmoid infundibulum.

We reviewed the anatomical and dental factors on 0.6-mm thick axial paranasal CT images reconstructed into 1-mm thick coronal images. Deviated nasal septum was defined as a deviation toward the diseased side of more than 10°, in a vertical line from the crista galli to the nasal floor.[7] We measured the CB, ethmoid infundibulum, and maxillary natural ostium (Figure 2).[7] The measurements were conducted using the measurement tool in the Picture Archiving and Communication System

(Marotech). We measured the width and length of the ethmoid infundibulum on the disease-free side in the MSFB and CRS groups, because the evaluation of those parameters on the diseased side is problematic due to opacification (Figure 2). A previous study with a population similar to ours showed the insignificant difference between ethmoid infundibulum dimensions on both sides in normal people.[7] In the normal group, because both sinuses were disease-free, we used computer software to select the side to be included in the analysis. We calculated the mean of 2 measurements of the ethmoid infundibulum and natural ostium.

Statistical Analysis

Numerical variables are expressed as means ± standard deviations. The Student *t* test was conducted to compare the size of the CB, natural ostium, and ethmoid infundibulum among the groups. Chi-square and Fisher exact tests were used to compare categorical variables (gender, underlying disease, anatomical variations, allergy, and dental factors). We employed binary logistic regression to identify independent predictors of a fungal ball or chronic sinusitis. One-way analysis of variance was also used to test for group differences. Post hoc Student *t* test was applied using a significance level established by the Bonferroni method. A P value <.05 was considered to indicate statistical significance. The statistical analysis was performed using SPSS software (version 24.0; IBM Corp).

Table 1. Patient Demographic Data.

Characteristic	MSFB group	Normal group	CRS group
Age (years)	61 ± 12[a,b]	52 ± 16	50 ± 17
Proportion of females	76%[a,b]	55%	54%
Smoking history	8%	4%	3%
Hypertension	36%[b]	25%	19%
Diabetes mellitus	18%[b]	10%	6%
Asthma	2%	0%	1%
Hematological disorders	24%[a,b]	8%	12%

Abbreviations: CRS, chronic rhinosinusitis; MSFB, maxillary sinus fungal ball.
[a]*P* value <.05 compared to the normal group.
[b]*P* value <.05 compared to the CRS group.

Table 2. Allergy Status and Eosinophil Count Data of the 2 Groups.

Variable	MSFB group	CRS group	*P* value
Allergy[a]	43%	50%	.321
Eosinophil count	118 ± 120	150 ± 130	.07
ECP	15.4 ± 15	18.3 ± 26	.342

Abbreviations: CRS, chronic rhinosinusitis; ECP, eosinophil cationic protein; MSFB, maxillary sinus fungal ball.
[a]Based on a positive MAST test.

Results

The proportion of females was significantly higher in the MSFB group than in the normal and CRS groups (76%, 55%, and 54%, respectively; $P = .002$). Also, patients in the MSFB group were older than those in the normal and CRS groups (mean age, 61 ± 12, 52 ± 16, and 50 ± 17 years, respectively, $P < .001$). Other demographic parameters are shown in Table 1. The MSFB group had an allergy frequency similar to that of the CRS group (43% and 50%, respectively; $P = .321$; Table 2). We did not perform the MAST test in the normal group. The MSFB group had an eosinophil count comparable to those of the normal and CRS groups (118 ± 120, 167 ± 193, and 150 ± 130, respectively; $P = .07$).

Concha bullosa was present in 37% of the patients in the MSFB group, which was significantly higher than the rate in the normal and CRS groups (23% and 21%, respectively; $P =$ .031 and .013). Haller cells were seen in 10% of the MSFB group patients and in 22% of the normal group ($P = .021$). However, the prevalence of Haller cells was not significantly different between the MSFG and CRS groups ($P = .071$; Table 3). The MSFB group had a wider natural maxillary ostium than the normal group (7.07 ± 1.8 vs 5.48 ± 1.3 mm; $P < .001$). Table 3 lists the findings for other anatomical variations. Dental factors were more frequent in the MSFB and CRS groups (73% and 75%, respectively) than in the normal group (32%, $P < .001$). The prevalence of dental factors was more frequent in the MSFB and CRS groups (73% and 75%, respectively) than in the normal group (32%, $P < .001$). The mean number of teeth

Table 3. Anatomical Data of the 2 Groups.

Variable	MSFB group	Normal group	CRS group
Left side	57%	58%	52%
DNS toward the diseased side	24%	25%	25%
Haller cells	10%[a]	22%	19%
Concha bullosa	37%[a,b]	23%	21%
Concha bullosa size	1.54 ± 2.2 mm	1.1 ± 1.9 mm	0.93 ± 1.9 mm
Ethmoid infundibulum length	7.72 ± 1.56 mm	8.2 ± 1.5 mm	7.24 ± 1.79 mm
Ethmoid infundibulum width	2.49 ± 0.76 mm	2.33 ± 0.57 mm	2.56 ± 0.81 mm
Natural ostium size	7.07 ± 1.8 mm[a]	5.48 ± 1.3 mm	7.17 ± 1.9 mm

Abbreviations: CRS, chronic rhinosinusitis; DNS, deviated nasal septum; MSFB, maxillary sinus fungal ball.
[a]*P* value <.05 compared to the normal group.
[b]*P* value <.05 compared to the CRS group.

with the dental factors was more in the MSFB and in the CRS groups (1.42 ± 1.12 and 1.47 ± 1.07, respectively) compared to the normal group (0.56 ± 0.92; $P < .001$).

All 3 groups were divided into CB + Haller cells, CB + DNS, CB + DNS + Haller cells, and Haller cells + DNS subgroups. The CB + Haller cells subgroup had a significantly lower rate of fungal ball compared to the other subgroups (odds ratio = 0.694; $P = .047$). However, DNS and DNS + Haller cells did not significantly affect the rate of fungal ball, irrespective of the presence of CB ($P = .470$ and .604, respectively).

Discussion

Maxillary sinus fungal ball accounts for 85% of all fungal ball cases.[10] Similar to other types of fungal sinus balls, with which it shares radiological findings, MSFB is characterized by a female predominance and mainly affects older people.[11] Among the patients in our MSFB group, 76% were female ($P = .002$), and their mean age was 61 ± 12 years ($P < .001$), in agreement with prior reports.[4-7] The underlying mechanisms of MSFB are unknown but may be related to puberty and hormonal changes; no pediatric case of the fungal ball has been reported.[12]

Compared to CRS, MSFB showed a stronger association with diabetes mellitus (18% of cases; $P < .001$) and hypertension (36% of cases; $P < .001$). This could be due to the relatively young age of patients with CRS. The rate of hematologic diseases (eg, aplastic anemia and leukemia) was significantly higher in the MSFB group (24% of cases) than in the other 2 groups ($P < .001$). Shin et al reported similar findings in a larger population—the fungal ball was associated with asthma, hypertension, diabetes mellitus, and thyroid disease ($P < .001$).[7]

In this study, the frequency of allergy was nonsignificantly lower in the MSFB group than in the CRS group (43% and 50%, respectively). Ahn et al reported that 38.2% of patients with unilateral fungal ball had a positive MAST test.[13] In this work, the MSFB group had a nonsignificantly lower eosinophil count than the normal and CRS groups (118 ± 120, 167 ± 193, and 150 ± 130, respectively; $P = .07$). Similarly, Kim et al reported a higher eosinophil count in patients with CRS than in those with a fungal ball (249.3 ± 263.0 and 151.0 ± 132.2, respectively; $P < .001$).[10]

The association of anatomical factors with MSFB is controversial. Shin et al reported a significant difference in CB at the site of MSFB compared to the control group ($P = .006$).[7] One study that reported 538 cases of FB found 26% of patients are associated with CB; however, there was no correlation between site of sinus affected and presence of CB.[14] This study and others compared the disease side with nondisease side in the same patient, not to a control group.[4,8,14,15] In our study, CB was present in 37% of the patients in the MSFB group ($P = .013$ vs the other 2 groups). The high prevalence of CB in MSFB group could suggest a role of this anatomical abnormality in the pathogenesis. Concha bullosa modifies the nasal airflow and this may facilitate the deposition of spores into the maxillary sinus.[16]

Neither Haller cells nor DNS was associated with MSFB in several other studies.[4,5,7,14] Oshima et al reported that fungal ball was significantly more likely to be on the concave side of the nasal septum in male patients ($P = .006$) but not in the entire study population. Also, they reported the presence of Haller cells in an affected site is similar to the unaffected side.[8] In our study, the frequency of Haller cells was significantly lower in our MSFB group than in the normal group (10% and 22%, respectively; $P = .021$), and nonsignificantly lower in the MSFB group than the CRS group ($P = .07$). Some authors suggest that a wide OMC facilitates the deposition of fungal spores into the affected sinus.[4]

In this study, the average ethmoid infundibulum length and width were not significantly different among the groups, despite the longer ethmoid infundibulum in the normal versus MSFG group (8.2 and 7.72 mm, respectively; $P = .08$). This finding could be explained by the fact that 22% of the patients in the normal group were positive for Haller cells, which can narrow and lengthen the ethmoid infundibulum. Indeed, Shin et al reported that MSFB is associated with a narrow and long infundibulum ($P < .001$) compared to the control group.[7] They suggested that this can lead to a decrease in clearance of fungus from the affected sinus and cause hypoventilation. However, our study did not find the same results, and MSFB was not related to the narrowing of the maxillary sinus drainage system.

We found that the natural ostium was significantly wider in the MSFB group than in the normal group (7.07 and 5.48 mm, respectively; $P < .001$) but not compared to the CRS group. Robey et al detected a wider natural ostium in immunocompetent patients with MSFB compared to those immunodeficient patients ($P = .019$).[9] This finding could be explained by the fact that fungal ball is associated with changes in the medial maxillary sinus wall. Shin et al suggested that anaerobic conditions such as anatomical obstruction of sinus ostium are more prone to increase the growth of fungus; however, there was no narrowing in the dimension of infundibulum and ostium in MSFB compared to the 2 groups in our study.[7]

The frequency of dental factors was significantly different between our MSFB and normal groups (73% and 32%, respectively; $P < .001$), but not between the MSFB and CRS groups (73% and 75%, respectively). Mensi et al reported that 89.2% of patients with the fungal ball had undergone endodontic treatment compared to 36.9% of controls (patients with an opacification-free maxillary sinus on radiological imaging; $P < .00$).[17] Park et al also reported a significant difference in the rate of endodontic treatment between patients with the fungal ball and those with CRS (36.3% vs 16.1%, respectively; $P = .001$) but not in the rate of tooth extraction.[18]

We hypothesized that various anatomical factors would be associated with MSFB. Concha bullosa is implicated in MSFB[5,7,8]; in our subgroup analysis, CB + Haller cells were significantly associated with a lower rate of fungal ball ($P = .047$, odds ratio = 0.694), but DNS and DNS + Haller cells exhibited no such relationship ($P = .470$ and .604, respectively) irrespective of the presence of CB. This finding of lower incidence of MSFB with CB+ Haller cells does not agree with the anaerobic theory or difficult to pass the fungal material from the maxillary sinus.[7] Although we had small numbers, this finding could support that the presence of Haller cells and CB which narrow the opening of the sinus lead to decrease spores deposition into the sinus.[4] It is considered that the presence of the Haller cells would minimize the role of CB in the development of MSFB. However, further study with larger numbers is needed to explain this finding.

To our knowledge, this is the first study of MSFB involving 3 large groups of patients, and the first to analyze the effects of several factors in combination. However, the retrospective design precluded the detection of causal relationships. The 2 sinuses of the same individual are reportedly similar[7]; however, we did not measure the length and width of the ethmoid infundibulum on the disease side because of technical difficulties. Further studies should investigate the effects of other anatomical features of the maxillary sinus and middle turbinate on MSFB.

Conclusion

Maxillary sinus fungal ball is significantly associated with CB, Haller cells, natural ostium size, and various dental factors. Concha bullosa could increase the incidence of occurrence of the fungal ball in association with other factors like dental factors in support of the mix theory of the pathogenesis of MSFB. Also, the presence of CB and Haller cells was associated with a lower incidence of MSFB. Further studies should investigate the pathogenesis of MSFB according to the OMC area.

Authors' Note

Mohammed Basurrah and Il Hwan Lee contributed equally to this article. Mohammed Basurrah contributed to design of study, collected data, data analysis, drafted manuscript; Il Hwan Lee contributed to collected data, data analysis, drafted manuscript; Do Hyun Kim contributed to guided design of study, revised manuscript; Sung Won Kim contributed to guided design of study, data analysis; Soo Whan Kim contributed to guided design of study, revised manuscript, and final approval. This study and the associated chart review were approved by the Institutional Review Board of the Catholic University of Korea, Seoul St. Mary's Hospital College of Medicine (approval no. KC20RISI0758). The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/J1rA

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