Diagnosis of a Maxillary Sinus Fungus Ball Without Intralesional Hyperdensity on Computed Tomography

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Objectives/Hypothesis: Maxillary sinus fungus ball (MSFB) is the most common type of noninvasive fungal rhinosinusitis. Surgical removal of the ball achieves good outcomes. Making a rapid and accurate diagnosis is important to avoid unnecessary medical therapy. Intralesional hyperdensity (IH) on computed tomography (CT) is reportedly a good indicator. The aim of this study was to evaluate the diagnostic features of MSFB without IH on preoperative CT images.

Study Design: Retrospective database review.

Methods: Two hundred fifty-eight patients with histopathological evidence of a sinus fungal ball were retrospectively investigated. Forty-one patients with MSFB did not show IH on preoperative CT images and were enrolled in the MSFB group. Forty-one patients with unilateral nonfungal chronic rhinosinusitis were enrolled in a control group. CT features previously reported to have diagnostic significance were evaluated.

Results: Sclerosis of the lateral sinus wall, erosion of the inner sinus wall, and irregular surface of the material were more than 80%. In the subgroup with partial opacification, the sensitivity, specificity, and positive and negative predictive values for erosion of the inner sinus wall were more than 90%. In the subgroup with partial opacification, the sensitivity, specificity, and positive predictive value of an irregular surface of the material were more than 80%.

Conclusions: We have devised an algorithm to help diagnose MSFB without IH on preoperative CT images. Use of this algorithm would improve the diagnostic accuracy and ensure appropriate treatment.

Key Words: Aspergillus, computed tomography, fungus ball, maxillary sinus, rhinosinusitis.

Level of Evidence: 4

Laryngoscope, 129:1041–1045, 2019

INTRODUCTION

Sinus fungal ball (SFB), usually found in the maxillary sinus (MSFB), is the most common form of noninvasive fungal rhinosinusitis (FRS) seen in clinical practice. A single sinus is involved in 94% of cases, and a unilateral lesion is seen in 99%. Endoscopic sinus surgery (ESS) to eradicate the fungus ball usually achieves good outcomes, including low recurrence and high symptom-free rates. Therefore, rapid and accurate diagnosis of SFB is important to avoid unnecessary medical therapy and treatment delays.

According to the criteria developed by deShazo et al.,5 the only opportunity for preoperative diagnosis of SFB is a radiologic finding of sinus opacification with or without associated calcifications. Computed tomography (CT) of the sinuses is the first choice for preoperative diagnosis of chronic rhinosinusitis and for planning ESS because of its ability to delineate the fine bone structures of the sinuses, orbital lamina, and skull base. Several studies have reported the CT features of MSFB, which include intralesional hyperdensity (IH), calcification spots, erosion of the inner sinus wall, irregular surface of the material, and sclerosis of the lateral sinus wall.

However, it is still difficult to diagnose MSFB preoperatively if IH or calcification spots are not present on CT images of the sinuses. In this study, we retrospectively investigated patients who underwent ESS and were diagnosed to have SFB based on clinical and histopathological analyses. The aims of the study were to evaluate the diagnostic features of MSFB without IH on the preoperative sinus CT images and to increase the accuracy of preoperative diagnosis of MSFB.
MATERIALS AND METHODS

Patients
A search of the pathology database at Chang Gung Memorial Hospital identified 258 patients with histopathological evidence of SFB after ESS between January 2007 and August 2017. The preoperative CT images of the sinuses for these patients were reviewed. Fourteen patients with bilateral chronic rhinosinusitis, 18 with sphenoid SFB, three with ethmoid SFB, and one with frontal SFB were excluded. Forty-seven of the remaining 222 patients had MSFB that did not show IH or calcification spots in the maxillary sinus on CT images and were enrolled for further analysis. Forty-one consecutive patients with a clinical and histopathological diagnosis of nonfungal unilateral chronic rhinosinusitis (UCRS) between June 2015 and August 2017 were enrolled as a control group.

Evaluation of CT Features

CT features that have been previously reported to have diagnostic significance (i.e., sclerosis of the lateral sinus wall, erosion of the inner sinus wall, and irregular surface of the material) were evaluated (Fig. 1). Lateral wall thickness was measured at the midpoint of the maxillary antral wall at the level where the inferior turbinate attaches to the maxillary sinus wall on the axial CT images. The lateral wall ratio was calculated by dividing the thickness of the lateral wall of the diseased sinus by that on the contralateral side. Sclerosis of the lateral sinus wall was defined as a lateral wall ratio ≥ 1.2. Erosion of the inner sinus wall was defined as absence of part of the medial wall of the maxillary sinus. Irregular surface of the material was defined as a soft tissue lesion with a rough surface in the sinus cavity. All CT images were interpreted by two otolaryngologists and a radiologist who were blinded to the histopathologic diagnosis. This study was approved by the institutional review board of Chang Gung Memorial Hospital (approval number 201801040B0). All study procedures were performed in accordance with the relevant guidelines and regulations. The requirement for informed consent was waived in view of the retrospective nature of the research and anonymity of the data.

Statistical Analyses
Proportions were compared between the groups using the $\chi^2$ test. Continuous variables were evaluated between the groups using the Student $t$ test. Logistic regression models were used to investigate associations between variables. The data are presented with the odds ratio (OR) and 95% confidence interval (CI). The statistical analyses were performed using SPSS version 24.0 software (IBM Corp., Armonk, NY). A $P$ value <.05 was considered statistically significant.

RESULTS
The demographics of the 222 patients who had MSFB (175 with IH and 47 without IH) and the 41 patients with nonfungal UCRS are shown in Table I. The patients with MSFB were older than those with UCRS ($P = .001$). There

![Fig. 1. Computed tomographic features of maxillary sinus fungus ball. (A) Calcification spot, (B) intralesional hyperdensity, (C) sclerosis of the lateral sinus wall, (D) erosion of the inner sinus wall, (E) irregular surface of the material, and (F) mucosal thickness.](image-url)
TABLE I. Characteristics of the Study Population.

<table>
<thead>
<tr>
<th></th>
<th>MSFB, Total</th>
<th>MSFB With IH</th>
<th>MSFB Without IH</th>
<th>Nonfungal UCRS</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, n</td>
<td>222</td>
<td>175</td>
<td>47</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>57.9 ± 13.8</td>
<td>58 ± 13.9</td>
<td>57.7 ± 13.3</td>
<td>47.6 ± 14.8</td>
<td>&lt;.001†</td>
</tr>
<tr>
<td>Male:female, n</td>
<td>80:142</td>
<td>54:121</td>
<td>26:21</td>
<td>26:15</td>
<td>.444</td>
</tr>
</tbody>
</table>

*Comparison between MSFB without IH and nonfungal UCRS
†P < .05.
IH = intralesional hyperdensity; MSFB = maxillary sinus fungal ball; UCRS = unilateral nonfungal chronic rhinosinusitis.

TABLE II. Features of MSFB on Computed Tomographic Images.

<table>
<thead>
<tr>
<th></th>
<th>MSFB, Total</th>
<th>MSFB With IH</th>
<th>MSFB Without IH</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IH, n (%)</td>
<td>175 (78.8)</td>
<td>175 (100)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Sclerosis of lateral sinus wall, n (%)</td>
<td>203 (91.4)</td>
<td>162 (92.6)</td>
<td>41 (87.2)</td>
<td>.305</td>
</tr>
<tr>
<td>Lateral wall ratio</td>
<td>2.1 ± 0.8</td>
<td>2.1 ± 0.7</td>
<td>2.2 ± 0.8</td>
<td>.053</td>
</tr>
<tr>
<td>Erosion of inner sinus wall, n (%)</td>
<td>131 (59.0)</td>
<td>108 (61.7)</td>
<td>23 (48.9)</td>
<td>.114</td>
</tr>
<tr>
<td>Irregular surface, n (%)</td>
<td>84 (37.8)</td>
<td>64 (36.6)</td>
<td>20 (42.6)</td>
<td>.453</td>
</tr>
<tr>
<td>Total opacification, n (%)</td>
<td>118 (53.2)</td>
<td>95 (54.3)</td>
<td>23 (48.9)</td>
<td>.514</td>
</tr>
<tr>
<td>Partial opacification, n (%)</td>
<td>104 (46.8)</td>
<td>80 (45.7)</td>
<td>24 (51.1)</td>
<td>.514</td>
</tr>
</tbody>
</table>

*Comparison between MSFB with and without IH.
IH = intralesional hyperdensity; MSFB = maxillary sinus fungal ball.

was no significant difference in sex or the side affected between the two study groups. The CT features of lateral wall sclerosis, erosion of the inner sinus wall, and irregular surface of the material of these 222 patients were analysed and are described in Table II. In spite of the difference of IH, the other radiologic features were not different between MSFB with and without IH.

The CT features in the MSFB without IH and UCRS groups as well as the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each CT feature are shown in Table III. Sclerosis of the lateral sinus wall (P = .032), erosion of the inner sinus wall (P < .001), and irregular surface of the material (P < .001) were significantly more common in the MSFB without IH group than in the UCRS group. The lateral wall ratio was also higher in the MSFB without IH group than in the UCRS group (P < .001). Erosion of the inner sinus wall and an irregular surface of the material had the highest specificity (95.1% and 92.2%, respectively) and the highest PPV (92% and 83.3%, respectively). Total opacification of the sinus was found in 48.9% of patients in the MSFB without IH group and in 58.5% of those in the UCRS group; the remainder showed partial opacification. No significant difference in the degree of sinus opacification was found between the MSFB without IH and UCRS groups.

In the subgroup of patients with total opacification of the maxillary sinus, erosion of the inner sinus wall showed increased sensitivity, specificity, PPV, and NPV (all more than 90%). In the subgroup with partial opacification of the maxillary sinus, irregular surface of the material had a sensitivity, specificity, and PPV of more than 80%; this feature seemed to be the best indicator for diagnosis of MSFB in this subgroup.

In the univariate regression analysis, sclerosis of the lateral sinus wall, a high lateral wall ratio, erosion of the inner sinus wall, and irregular surface of the material were significantly associated with MSFB (Table IV). Further analysis in a multivariate regression model revealed that a high lateral wall ratio (OR: 5.1), erosion of the inner wall of the sinus (OR: 19.5), and irregular surface of the material (OR: 69.7) were significant predictors of MSFB (Table IV). Furthermore, erosion of the inner sinus wall in the sinus with total opacification (OR: 83.4) and irregular surface of

TABLE III. Features of MSFB Without IH and UCRS on Computed Tomographic Images.

<table>
<thead>
<tr>
<th></th>
<th>MSFB Without IH, n = 47</th>
<th>UCRS, n = 41</th>
<th>P Value</th>
<th>Specificity %</th>
<th>Sensitivity %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerosis of lateral sinus wall, n (%)</td>
<td>41 (87.2)</td>
<td>28 (68.3)</td>
<td>.032*</td>
<td>31.7</td>
<td>87.2</td>
<td>59.4</td>
<td>68.4</td>
</tr>
<tr>
<td>Lateral wall ratio</td>
<td>2.2 ± 0.8</td>
<td>1.7 ± 0.7</td>
<td>.001*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Erosion of inner sinus wall, n (%)</td>
<td>23 (48.9)</td>
<td>2 (4.9)</td>
<td>&lt;.001*</td>
<td>95.1</td>
<td>48.9</td>
<td>92</td>
<td>61.9</td>
</tr>
<tr>
<td>Irregular surface, n (%)</td>
<td>20 (42.6)</td>
<td>4 (9.8)</td>
<td>.01*</td>
<td>90.2</td>
<td>42.6</td>
<td>83.3</td>
<td>57.8</td>
</tr>
<tr>
<td>Total opacification, n (%)</td>
<td>23 (48.9)</td>
<td>24 (58.5)</td>
<td>.371</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sclerosis of lateral sinus wall, n (%)</td>
<td>21 (91.3)</td>
<td>16 (66.7)</td>
<td>.02*</td>
<td>33.3</td>
<td>91.3</td>
<td>56.8</td>
<td>80</td>
</tr>
<tr>
<td>Erosion of inner sinus wall, n (%)</td>
<td>21 (91.3)</td>
<td>1 (4.2)</td>
<td>&lt;.001*</td>
<td>95.8</td>
<td>91.3</td>
<td>95.5</td>
<td>92</td>
</tr>
<tr>
<td>Irregular surface, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Partial opacification, n (%)</td>
<td>24 (51.1)</td>
<td>17 (41.5)</td>
<td>.371</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sclerosis of lateral sinus wall, n (%)</td>
<td>20 (83.3)</td>
<td>12 (70.6)</td>
<td>.339</td>
<td>29.4</td>
<td>83.3</td>
<td>62.5</td>
<td>55.6</td>
</tr>
<tr>
<td>Erosion of inner sinus wall, n (%)</td>
<td>2 (8.3)</td>
<td>1 (5.9)</td>
<td>.770</td>
<td>97.6</td>
<td>4.3</td>
<td>66.7</td>
<td>47.1</td>
</tr>
<tr>
<td>Irregular surface, n (%)</td>
<td>20 (83.3)</td>
<td>3 (17.6)</td>
<td>&lt;.001*</td>
<td>82.4</td>
<td>83.3</td>
<td>87.0</td>
<td>77.8</td>
</tr>
</tbody>
</table>

*P < .05.
IH = intralesional hyperdensity; MSFB = maxillary sinus fungal ball; NPV = negative predictive value; PPV = positive predictive value; UCRS = unilateral nonfungal chronic rhinosinusitis.
the material in the sinus with partial opacification (OR: 27.3) were strongly associated with MSFB.

**DISCUSSION**

FRS is usually classified as invasive or noninvasive. In contrast to invasive FRS, noninvasive FRS is characterized by an absence of invasion of nasal tissue by fungal hyphae and consists mainly of SFB (an intertwined mass of fungus) and allergic FRS (characterized by the presence of allergic mucin and a marked inflammatory reaction). SFB is the most common type of noninvasive FRS and can be eradicated completely if removed surgically. Therefore, a rapid and accurate diagnosis of SFB is important in terms of reducing the likelihood of unnecessary medical treatment. IH or calcification represents the presence of heavy metals (iron, zinc, and manganese) and calcium within fungal hyphae and has been reported to be the most reliable diagnostic feature of SFB on preoperative CT images. The prevalence of IH reported in the recent literature ranges from 66% to 82% and is 78.8% (175/222) in the present study.

In this study, we evaluated the diagnostic features of MSFB on CT, focusing on patients without IH, and found that sclerosis of the lateral sinus wall, erosion of the inner sinus wall, and irregular surface of the material were significantly more common in the MSFB without IH group than in the UCRS group. Erosion of the inner sinus wall and irregular surface of the material had the highest specificity and PPV. In the subgroup of patients with total opacification of the maxillary sinus, the sensitivity, specificity, PPV, and NPV of erosion of the inner sinus wall were all higher than 90%. In the partial opacification subgroup, the sensitivity, specificity, and PPV of irregular surface of the material were all higher than 80%. We have devised a diagnostic algorithm for MSFB (Fig. 2). When reading the preoperative CT images of the sinus as a first step, unilateral opacification of the maxillary sinus with IH or calcification is suggestive of a diagnosis of MSFB. Erosion of the inner sinus wall is a good indicator of MSFB when there is total opacification of the maxillary sinus. However, irregular surface of the material can be used to distinguish MSFB from UCRS if there is partial opacification of the maxillary sinus.

Erosion of the inner sinus wall results from expansion and thinning of the bony wall of the sinus because of pressure from the growing SFB and has been reported in 33.3% to 72.9% of patients with MSFB. In our present study, erosion of the inner sinus wall occurred in 48.9% of patients in the MSFB without IH group and in up to 91.3% of patients in the subgroup with total opacification of the maxillary sinus. There was a significant difference in the frequency of erosion of the inner sinus wall between the MSFB without IH and UCRS groups (48.9% vs. 4.9%, respectively; P < .001); this feature was strongly associated with MSFB (OR: 19.5, 95% CI: 2.5–152.4).

Irregular surface of the material referred to the rough, unsmooth surface of the clay-like SFB in the maxillary sinus, in contrast to smooth mucosal swelling or air-fluid level in UCRS. In this study, irregular surface of the material was found in 42.6% of patients in the MSFB without IH group and in up to 83.3% of patients in the subgroup with partial maxillary opacification. There was also a significant difference in the frequency of irregular surface of the material between the MSFB without IH and UCRS groups (42.6% vs. 9.8%, P < .001); this feature had a significant association with MSFB (OR: 66.7, 95% CI: 10.2–474.9). Similar results were reported by Yoon et al., who reviewed 538 cases of SFB and found irregular surfaces in 88.5% of cases with partial opacification.

There was a significant difference in the frequency of sclerosis of the lateral sinus wall between the MSFB without IH and UCRS groups but not in the subgroup with partial opacification. Multivariate regression analysis did not show a statistically significant between-group difference in the frequency of sclerosis of the lateral sinus wall. However, we did find a statistically significant between-group difference in the lateral wall ratio this.
sclerotic change might reflect bone remodeling in response to the chronic inflammation associated with both MSFB and UCRS, and is likely to have been present for longer in the MSFB subgroup with total opacification. Jun et al.\textsuperscript{17} reported bony changes in unilateral MSFB in a study in which they quantified wall thickness as an indicator of sclerotic remodeling and compared the values obtained between the diseased sinus and the healthy contralateral sinus. They also reported that the difference in wall thickness was greatest in the lateral sinus wall. Similarly, the difference in wall thickness became statistically significant when we focused on the lateral wall.

Studies have shown that SFB mostly occurs in older individuals and with a female predominance. The average age at presentation has been reported to be 49 to 61.1 years, with women accounting for 60.1% to 76.7% of cases.\textsuperscript{3,4,7–9,18} The findings in the 222 patients with MSFB in the present study were similar in that the mean age was 57.9 years and 64.0% were women. The mean ± standard deviation age of our patients with MSFB that did not show IH was 57.7 ± 13.3 years, which was older than the patients in the UCRS group but comparable with that in the literature. However, there was no difference in sex distribution between the study groups. The patients with MSFB who did not show IH were possibly a subgroup with relatively early-stage MSFB or a short disease duration and inadequate fungal metabolic metal deposition in the SFB. Our relatively high proportion of partial maxillary opacification in comparison with the reports in the literature (51.1% vs. 33.8%)\textsuperscript{7} support this hypothesis. Ferguson\textsuperscript{19} and Nomura et al.\textsuperscript{18} suggested that the longer life expectancy of women may be a possible reason for the female predominance, although this interpretation remains controversial.\textsuperscript{7} These may be why a female predominance was not observed in our cases of MSFB without IH.

This study has several limitations that warrant consideration. First, we only enrolled patients with histopathological evidence of SFB after ESS. Therefore, neither the study group nor the control group included patients who did not undergo surgery, which may have introduced a degree of selection bias. Second, all cases with clinical and histopathological diagnosis of nonfungal UCRS in the same period (between January 2007 and August 2017) should have been included in the control group to prevent bias in sampling. However, nonfungal UCRS is a common condition, so it was difficult to enroll all the cases between January 2007 and August 2017 because of lack of a specific diagnostic term for unilateral lesion in our pathology database. It was also difficult to review the large number of patients’ medical records and sinus CT scans in the same period. Therefore, we only reviewed the data of 41 consecutive patients with nonfungal UCRS between June 2015 and August 2017. This may have contributed to bias when evaluating the PPV, NPV, and OR. Third, there was no information on fungal species or culture results, although aspergillus has been reported to be the most common causative organism. Different species of fungi may have different CT imaging features. Finally, this study had a retrospective case-control design, and although blinded to all diagnostic information, the CT readers were only required to distinguish between MSFB and UCRS. In everyday clinical practice, many differential diagnoses, such as neoplasms, dental foreign bodies, and autoimmune disorders, would need to be considered. A large-scale prospective study is needed to determine the diagnostic process required for a unilateral maxillary sinus lesion.

CONCLUSION

We have devised an algorithm to help diagnose MSFB in patients without IH or calcification on preoperative CT scan images. Erosion of the inner sinus wall and irregular surface of the material were the most reliable indicators of MSFB in patients with total and partial maxillary opacification, respectively. Awareness of these CT features will allow us to improve the diagnostic accuracy for MSFB and ensure appropriate treatment.

BIBLIOGRAPHY


Laryngoscope 129: May 2019
Ho et al.: MSFB Without Intralesional Hyperdensity

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