Differential Diagnosis between Fungal Maxillary Sinusitis and Odontogenic Sinusitis Using CT Images

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Abstract
Objectives The purposes of this study were to investigate image findings and clinical symptoms of fungal maxillary sinusitis and odontogenic sinusitis, and to assessment of usefulness of differential diagnosis between fungal maxillary sinusitis and odontogenic sinusitis.

Study Design The study included 32 patients (16 fungal sinusitis, 16 odontogenic sinusitis) with a confirmed histopathologic diagnosis of fungal sinusitis or odontogenic sinusitis. Computed tomography (CT) images were used to evaluate such as 1) location and shape of mucosal thickening, 2) calcification, 3) osteolysis, 4) osteosclerosis and 5) thickening of bony wall. Moreover, we investigated clinical symptoms of all patients.

Results There were significant differences between fungal sinusitis and odontogenic sinusitis in sex difference, shape of mucosal thickening, calcification, osteosclerosis, thickening of bony wall and clinical symptoms.

Conclusions This study suggested that these findings are useful for differential diagnosis between fungal maxillary sinusitis and odontogenic sinusitis.

Introduction
Occurrence of fungal infection in the paranasal sinusitis is relatively rare (1). There are four clinicopathologic classifications of mycotic sinonasal disease acute invasive fulminant disease, chronic invasive infection, noninvasive mycotic colonization (mycetoma) and allergic mycotic sinusitis. These four types of infection can be seen with any fungus but are most commonly a result of Aspergillus infection. Aspergillus species are opportunistic fungi and widely distributed in the environment (1–4).

Odontogenic sinusitis primarily results from multiplication of bacteria invading from the mouth or the focus of a dental infection. It is very important to differential diagnosis between fungal sinusitis and odontogenic sinusitis because there have different treatment methods (1–3, 5). However, it is often difficult to differentiate because fungal sinusitis and odontogenic sinusitis also occur unilaterally in the maxillary sinus (6, 7). Furthermore, a history of previous endodontic treatment is also common among patients with fungal balls. Root-filling materials based on zinc oxide-eugenol is considered to be a growth factor for fungal sinusitis (2, 8, 9). That further makes it difficult to differentiate between fungal sinusitis and odontogenic sinusitis.

The purposes of this study were to investigate image findings and clinical symptoms of fungal maxillary sinusitis and odontogenic sinusitis, and to assessment of usefulness of differential diagnosis between fungal maxillary sinusitis and odontogenic sinusitis.

Materials and methods

Human rights statements and informed consent
All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. This study

Keywords:
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was approved by the Ethics Committee of the University School of Dentistry (No. EC12-009), and all patients signed an informed consent agreement for the Computed tomography (CT) examination.

Patients

From April 1, 2006 to December 31, 2016, 83 patients with detection of fungal hyphae at histopathological examination of tissues excised at surgery were included in the study (Fig. 1). 16 patients were identified as fungal sinus disease at CT in the Department of Radiology, Nihon University School of Dentistry at Matsudo. The group included 14 females and 2 males. Their age ranged from 32 to 76 years (mean, 62.4 years). Similarly, 16 patients with histopathological confirmation of odontogenic sinusitis who underwent CT imaging from April 1, 2006 to December 31, 2016, were included in this study (Fig. 2). Maxillary sinusitis near the apical periodontitis or advanced periodontal bone loss on the CT image was diagnosed with odontogenic sinusitis (Fig. 3). The group included 9 males and 7 females. Their age ranged from 29 to 85 years (mean, 56.8 years). Patients with squamous cell carcinoma and metal artifacts precluding visualization of the maxillary sinus were excluded from this study.

Image protocol

CT imaging was performed with a 64-Multi-detector row CT (MDCT) system (Aquilion 64; Toshiba Medical Systems, Tokyo, Japan). All patients were scanned using the routine clinical protocol for cranio-maxillofacial examination at our hospital as follows: tube voltage, 120 kV; tube current, 100 mA; field of view, 240 × 240 mm; helical pitch, 41. The imaging included axial (0.50 mm) and multiplanar (3.00 mm) images. The MDCT images were interpreted using a medical liquid crystal display monitor (RadiForce G31; Eizo Nanao, Ishikawa, Japan).

All images were independently evaluated by over 5 years experienced two oral radiologists. The kappa statistic was used to assess the agreement between fungal sinusitis and odontogenic sinusitis for the imaging findings (shape of mucosal thickening, calcification, osteolysis, osteosclerosis and thickening of bony wall). Kappa values were classified as poor (0.0–0.19), fair (0.2–0.39), moderate (0.4–0.59), good (0.6–0.79) and excellent (0.8–1.00).

Assessment

CT images were used to evaluate fungal sinusitis and odontogenic sinusitis such as 1) location and shape of mucosal thickening, 2) calcification, 3) osteolysis, 4) osteosclerosis and 5) thickening of bony wall (10–13). Analysis of shape of mucosal thickening was performed on the CT images. The shape characteristics of fungal sinusitis and odontogenic sinusitis were evaluated using coronal slices. The shape of mucosal thickening of fungal sinusitis and odontogenic sinusitis were differentiated into two groups (Fig. 4): (a) conform to maxillary sinus shape and (b) mucosal thickening of maxillary sinus walls (1). Analysis of calcification was evaluated using coronal slice. The calcification was into four groups (Fig. 5): (a) fine punctate; (b) linear; (c) nodular; and (d) eggshell. When the calcification was similar to dotted or sandy, it was classified as fine punctate. When the calcification was similar to a straight or
Fig 3. Maxillary sinusitis with the following CT findings were diagnosed as odontogenic sinusitis: (A) maxillary sinusitis near the apical periodontitis (arrows); and (B) maxillary sinusitis near the advanced periodontal bone loss (arrows).

Fig 4. The shape of fungal sinusitis and odontogenic sinusitis were differentiated into two groups: (A) conform to maxillary sinus shape (arrows); and (B) mucosal thickening (arrows).

Fig 5. The presence of calcification was into four groups: (a) fine punctate (arrowheads); When the calcification was similar to dotted or sandy, it was classified as fine punctate. (b) linear (arrowheads); When the calcification was similar to a straight or curved line, it was classified linear. (c) nodular (arrowheads); When the shape of calcification was similar to a polygon or rectangular, it was classified as nodular. (d) eggshell (arrowheads); When the shape was globular, round, or rimlike, it was classified as eggshell.
curved line, it was classified linear. When the shape of calcification was similar to a polygon or rectangular, it was classified as nodular. When the shape was globular, round, or rimlike, it was classified as eggshell (14). Analysis of the osteolysis, osteosclerosis and thickening of bony wall were evaluated using axial slice (Fig. 6). Osteolysis was defined as absorption of maxillary sinus wall. Osteosclerosis was defined as having high density region in the anterior wall or the posterior wall of maxillary sinus compared with the opposite side. Thickening of bony wall was defined as the increase of maxillary sinus wall compared with the opposite side (10).

Symptoms were evaluated from retrospective review of the medical charts. Symptoms of fungal sinusitis and odontogenic sinusitis were evaluated such as 1) rhinorrhea, 2) pain, 3) nasal obstruction 4) neurological symptoms (10).

**Statistical analysis**

The statistical significance of differences in data was determined by a two-sided Mann-Whitney U test. Differences with values of \( P < 0.05 \) were considered significant. SPSS software for Windows (version 21; IBM Japan Inc., Tokyo, Japan) was used for the analysis.

**Results**

Fungal sinusitis was diagnosed in the surgical specimens of 16 of 83 patients. Location of all sinusitis was the maxillary sinus. Fungus species of all fungal sinusitis was aspergillus in this study. Evaluation of calcification of fungal sinusitis in the following findings: 9 calcifications were fine punctate (56.3%), 2 calcifications were linear (12.5%), 3 calcifications were nodular (18.8%) and 2 calcifications were eggshell (12.5%). All calcifications of odontogenic sinusitis were fine punctate (3/3). Histopathologically, findings of infection with aerobic bacteria, anaerobic bacteria or both were found in all odontogenic sinusitis.

Demographic characteristics on patients with fungal sinusitis and odontogenic sinusitis are shown (Table 1). Sex difference were significantly different between fungal sinusitis and odontogenic sinusitis (\( P=0.02 \)). Ages were not significantly different between fungal sinusitis and odontogenic sinusitis (\( P=0.27 \)).

Image data on patients with fungal sinusitis and odontogenic sinusitis are shown (Table 2). Evaluation of the different shape of mucosal thickening of sinusitis resulted in the following findings: 15 fungal sinusitis (93.8%) and 8 odontogenic sinusitis (50.0%) had a conform to maxillary sinus shape, 1 fungal sinusitis (6.3%) and 8 odontogenic sinusitis (50.0%) had a mucosal thickening of maxillary sinus.
walls (P < 0.01). Preoperative imaging data of patients with fungal sinusitis and odontogenic sinusitis resulted in the following findings: 15 fungal sinusitis (93.8%) and 3 odontogenic sinusitis (18.8%) were detected of calcification (P < 0.01), 3 fungal sinusitis (18.8%) and 1 odontogenic sinusitis (6.3%) were detected of sinus wall osteolysis (P=0.29), 9 fungal sinusitis (31.3%) and 3 odontogenic sinusitis (18.8%) were detected of osteosclerosis (P = 0.03) and 10 fungal sinusitis (62.5%) and 2 odontogenic sinusitis (12.5%) were detected of thickening of bony wall (P<0.01).

Clinical symptoms on patients with fungal sinusitis and odontogenic sinusitis are shown (Table 3). Clinical symptoms were observed in all fungal sinusitis (100.0%) and 9 odontogenic sinusitis (56.3%), (P<0.01). Analysis of clinical symptoms of all fungal sinusitis patients and odontogenic sinusitis showed that 9 fungal sinusitis (56.3%) and 6 odontogenic sinusitis (66.7%) were observed rhinorrhea (P= 0.36), 8 fungal sinusitis (50.0%) and 3 odontogenic sinusitis (33.4%) were observed pain (P=0.11), 6 fungal sinusitis (37.5%) and 0 odontogenic sinusitis (0.0%) were observed nasal obstruction (P=0.02) and 4 fungal sinusitis (25.0%) and 0 odontogenic sinusitis (0.0%) were observed neurological.

### Table 1. Comparison of demographic characteristics on patients with fungal sinusitis and odontogenic sinusitis: Two-sided Mann-Whitney U test

<table>
<thead>
<tr>
<th></th>
<th>Fungal sinusitis</th>
<th>Odontogenic sinusitis</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n=11)</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Female (n=21)</td>
<td>14</td>
<td>7</td>
<td>0.02*</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(Mean ± SD), years</td>
<td>62.4 ± 11.3</td>
<td>56.8 ± 17.0</td>
<td>0.27</td>
</tr>
</tbody>
</table>

* = P<0.05

### Table 2. Comparison of image data on patients with fungal sinusitis and odontogenic sinusitis: Two-sided Mann-Whitney U test

<table>
<thead>
<tr>
<th></th>
<th>Fungal sinusitis</th>
<th>Odontogenic sinusitis</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shape of sinusitis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conform to maxillary sinus shape (n=23)</td>
<td>15</td>
<td>8</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td>Mucosal thickening of maxillary sinus walls (n=9)</td>
<td>1</td>
<td>8</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td><strong>Calcification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence (n=18)</td>
<td>15</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Absence (n=14)</td>
<td>1</td>
<td>13</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td><strong>Osteolysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence (n=4)</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Absence (n=28)</td>
<td>13</td>
<td>15</td>
<td>0.29</td>
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<tr>
<td><strong>Osteosclerosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence (n=12)</td>
<td>9</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Absence (n=20)</td>
<td>7</td>
<td>13</td>
<td>0.03*</td>
</tr>
<tr>
<td><strong>Thickening of bony wall</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence (n=12)</td>
<td>10</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Absence (n=20)</td>
<td>6</td>
<td>14</td>
<td>&lt;0.01**</td>
</tr>
</tbody>
</table>

* = P<0.05, ** = P<0.01
symptoms (P = 0.07).

The agreement between fungal sinusitis and odontogenic sinusitis was good (k = 0.79) for shape of sinusitis. The agreement between fungal sinusitis and odontogenic sinusitis was excellent (k = 0.94) for calcification. The agreement between fungal sinusitis and odontogenic sinusitis was good (k = 0.79) for osteolysis. The agreement between fungal sinusitis and odontogenic sinusitis was good (k = 0.78) for osteosclerosis. The agreement between fungal sinusitis and odontogenic sinusitis was excellent (k = 0.93) for thickening of bony wall.

**Discussion**

In our study, all fungal sinusitis occurred in the maxillary sinus. Moreover, Fungus species of all fungal sinusitis was aspergillus in this study. According to Michel et al., the most frequent sinus in fungal sinusitis was the maxillary sinus, then the sphenoid sinus, the frontal sinus, the ethmoid sinus (1). Aspergillus, Schizophyllum commune and Alternaria are known as fungal species of fungal sinusitis (15, 16).

Additionally, they reported that fungus sinusitis can be seen with any fungus but are most commonly a result of aspergillus infection (1–3, 15, 16). Acute and chronic invasive fungal sinusitis often develops as an opportunistic infection in patients with reduced immunity due to the use of adrenocortical steroids, immunosuppressants, antineoplastic agents. It is also easy to become severe when blood is inclined to ketoacidosis due to diabetes or kidney dialysis (1, 2). In this study, patients with these general conditions were not included. These frequencies location and fungus species of the fungal sinusitis are similar to our results. Also, the shape of mucosal thickening had a significant difference between fungal sinusitis and odontogenic sinusitis. It is considered better to suspect fungal sinusitis in the case of conform to maxillary sinus shape.

Thery et al. reported that analysis of clinical sign of aspergillosis was 14 pain (93.3%), 3 nasal obstruction (20%), 3 rhinorrhea (20%), 2 oculomotor disorders (13.3%) and 5 neurological symptoms (33.3%) (11). From our result, Analysis of clinical symptoms of all fungus sinusitis showed that 9 rhinorrhea (56.3%), 8 pain (50.0%), 6 nasal obstruction (37.5%) and 4 neurological symptoms (25.0%). There was a difference in results between past reports and our research. It was considered that this is probably because our research is only chronic noninvasive fungal disease, and the past report was Aspergillus including acute infiltrative mycosis. In addition, since our study was only performed on surgery, it seems that all patients had clinical symptoms.
Michelle AM. reported that clinical symptoms of odontogenic sinusitis was pain, cacosmia and mucopurulent discharge (1). Similarly, Simuntis R et al. reported that of clinical symptoms of odontogenic sinusitis were pain, foul smell and dental pain. Further, they said these symptoms did not distinguish odontogenic sinusitis from other causes of sinusitis (17). However, from our study showed that nasal obstruction and neurological symptoms were found only fungal sinusitis. Therefore, they were considered that the presence or absence of nasal obstruction and neurological symptoms are useful for differentiating between fungal sinusitis and odontogenic sinusitis.

From our result, there was a significant difference in sex difference between fungal sinusitis and odontogenic sinusitis. Fungal sinusitis occurred in female predominance. There was no sex difference in odontogenic sinusitis. Michelle et al. reported that there was sex difference in fungal sinusitis, and it occurred in female predominance (1). This report is same as our result. However, there are reports that there was no sex difference in fungal sinusitis, and it is considered that there is a difference in sex difference among races (17, 18).

Yoon et al. reported that the intrasinus calcification was found in 20 (51%) of 39 patients with fungal sinusitis and in 16 (3%) of 471 patients with nonfungal sinusitis. From our results, the intrasinus calcification was found in 15 (93.8%) of 16 patients with fungal sinusitis and 3 (18.8%) of 16 patients with odontogenic sinusitis. It was considered that it is very useful the presence or absence of calcification in differential diagnosis between fungal sinusitis and odontogenic sinusitis (14). The form of calcifications of fungal sinusitis were 9 fine punctate (56.3%), 2 linear (12.5%), 3 nodular (18.8%) and 2 eggshell (12.5%). Also, all calcifications of odontogenic sinusitis were fine punctate (3/3). These findings suggested that form of calcification of liner, nodular and eggshell may be a peculiar form of fungal sinusitis.

Osteosclerosis and thickening of bony wall are typical findings of chronic sinusitis (1). Because all fungal sinusitis in this study were noninvasive mycotic colonization, findings similar to chronic sinusitis considered to be obtained. In addition, odontogenic sinusitis is mostly acute inflammation. Therefore, it was considered that chronic sinusitis-like findings such as osteosclerosis and thickening of bony wall were few in odontogenic sinusitis. However, in the case of long-term odontogenic sinusitis, it is suspected that chronic sinusitis-like findings are observed.

Osteolysis is a characteristic finding of invasive fungal sinusitis and is atypical in noninvasive mycotic colonization and odontogenic sinusitis (1). Therefore, it was considered that there was no significant difference in Osteolysis in this study. However, in the case of invasive fungal sinusitis, it is suspected that there is a significant difference with dental sinusitis.

In our study, there were significant differences in sex, shape of mucosal thickening, osteosclerosis, thickening of bony wall and symptoms in addition to calcification between fungal sinusitis and odontogenic sinusitis. These findings are thought to be useful for differential diagnosis between fungal maxillary sinusitis without calcification and odontogenic sinusitis.

Conclusions

The present study showed that the characteristics of fungal sinusitis and odontogenic sinusitis. In addition to calcification, there were significant differences in many findings between fungal maxillary sinusitis and odontogenic sinusitis.

This study suggested that these findings are useful for differential diagnosis between fungal maxillary sinusitis and odontogenic sinusitis.

References