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# Fungus Ball of the Paranasal Sinuses: Experience in 160 Patients Treated With Endoscopic Surgery

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**Objectives/Hypothesis:** Herein we present our experience in the management of fungus ball (FB) of the paranasal sinuses. Preoperative imaging strategy and findings, surgical technique, and pathologic and microbiologic results are discussed.

**Study Design:** Retrospective chart review of patients with FB of the paranasal sinuses who underwent endoscopic surgery at the Department of Otorhinolaryngology of the University of Brescia, Italy.

**Methods:** From January 1990 to December 2006, 160 patients with sinonasal fungus ball were treated with a purely endoscopic approach. All patients underwent preoperative computed tomography (CT) and/or magnetic resonance (MR) imaging; an endo-oral dental x-ray or orthopantomography and odontological evaluation were also performed in patients with maxillary sinus localization. All removed material was sent for pathologic and microbiologic evaluation. All patients were prospectively followed with endoscopic control every 2 months during the first postoperative year and subsequently every 6 months.

**Results:** The patient cohort included 118 females and 42 males, with an age from 19 to 85 years (mean, 52.7 years). FB was located in the maxillary sinus in 135 (84.4%) patients; in two cases both sinuses were affected. Sphenoid and ethmoid involvement was observed in 23 (14.4%) and 1 (0.6%) patients, respectively. Simultaneous ethmoid and sphenoid involvement was found in one (0.6%) case. In all patients complete removal of fungal debris was obtained through wide sinusotomy. No recurrence was observed.

**Conclusions:** Endoscopic surgery is a safe and effective treatment for paranasal sinuses FB. A proper imaging study by MR and/or CT can address diagnosis, which is based upon detection of fungal hyphae at histology.

**Key Words:** Fungus ball, fungal rhinosinusitis, endoscopic surgery, paranasal sinuses.

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## INTRODUCTION

Fungi are normally found as saprophytes in the nasal cavities and paranasal sinuses of healthy subjects.[1] Nevertheless, fungi may cause specific sinonasal diseases. In 1998, DeShazo proposed a classification of sinonasal fungal infections based on the presence or absence of sinonasal mucosa invasion, separating noninvasive from invasive forms.[2] The former included mycetoma and allergic fungal rhinosinusitis, whereas the latter comprised acute fulminant rhinosinusitis, chronic invasive fungal rhinosinusitis, and granulomatous fungal rhinosinusitis. Refinements in the knowledge of pathophysiology of noninvasive forms has recently led to an update of terminology by recommending the use of term "fungus ball" (FB) instead of "mycetoma" or "aspergilloma," and to differentiate "allergic" from "eosinophilic" rhinosinusitis based on the presence or absence of hyperreactivity to fungal allergens.[3,4] FB, which generally affects immunocompetent and nonatopic subjects, is localized in the maxillary sinus in more than 80% of patients.[5] It is characterized by a mass of inspissated fungal debris and mucus progressively growing into the sinus cavity, without involvement of the underlying mucosa. Endonasal removal by a purely endoscopic approach is unanimously considered the treatment of choice.[5–8]

We herein review our experience in the treatment of a series of 160 patients with sinonasal FBs. Imaging, surgical technique, pathologic findings, and possible etiologic correlation with dental procedures are also analyzed.

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## MATERIALS AND METHODS

From January 1990 to December 2006, 160 patients with FB of the paranasal sinuses were observed and treated with a purely endoscopic approach at the Department of Otorhinolaryngology of the University of Brescia.

### *Diagnostic Work-Up*

All patients were preoperatively evaluated with rigid endoscopy and computed tomography (CT) or, less frequently, with magnetic resonance (MR) imaging. Furthermore, 120 patients with maxillary FB underwent dental evaluation with endo-oral dental x-ray or orthopantomography to identify possible residual communication between the tooth root apex and the maxillary sinus secondary to dental extraction, periodontal destruction, or previous endodontic treatments.

### *Surgical Indications and Technique*

Surgery was performed under general or local anaesthesia; the latter was employed only in recent years in cases when nasal anatomy was favorable (i.e., no septal deviation), the patient was compliant, and the FB was easily accessible (maxillary sinus rather than sphenoid or ethmoid sinus).

The patients were positioned in a slightly reversed Trendelenburg position. The nasal cavity was decongested with cottonoids soaked in oxymetazoline solution and left in place for 10 minutes. One percent lidocaine with 1:100,000 epinephrine was subsequently injected at the level of the middle turbinate root and uncinate process. If local anaesthesia was selected, a 2 mg midazolam solution was intravenously injected, followed, if required, by a bolus of 1 mg of the same solution every 10 minutes (up to a maximal dose of 5 mg) to maintain sedation. A cottonoid (K.I.S.S., Medtronic Xomed Jacksonville, FL) was placed in the nasopharynx to prevent aspiration of local anaesthetic, blood, and secretions.

When the FB was localized in the maxillary sinus, an inferior uncinectomy was performed. Subsequently, a minimal middle antrostomy was created, sparing or just trimming the head of the middle turbinate, to perform sinus irrigations with saline solution using an angled suction cannula connected to a 20 mL syringe. The use of a high-pressure, turbulent flow through a small antrostomy eased fragmentation of FB and outflow of fungal debris from the sinus. The antrostomy was then widened to explore the sinus with rigid endoscopes (45° and 70° lens), to better visualize possible residual FB fragments scattered along the inflamed mucosa and to permit their removal with further irrigations, angled malleable cannulae, and Heuwieser antrum grasping forceps.

In the case of ethmoid localization, a complete anterior and posterior ethmoidectomy was performed, leaving the maxillary ostium and the frontal recess untouched.

Finally, when the FB involved the sphenoid sinus, a transnasal sphenoidotomy was performed whenever the sphenoethmoidal recess was easily accessible; otherwise, a transethmoidal approach was preferred. Also in sphenoid FB, we generally used a high-pressure sinus irrigation technique, except when focal areas of bony resorption of the sinus were clearly evident at CT examination.

All fungal material removed was sent for pathologic examination in all cases, and microbiologic cultures were obtained in 118 (73.8%) cases. A sample of mucosa of the involved sinus was also sent for pathologic examination to rule out an invasive form of mycosis. At the end of the procedure, the nasal cavity was packed with Lyofoam (Seton Health Care Group PLC, Oldham, UK), which was removed the day after surgery before discharge.

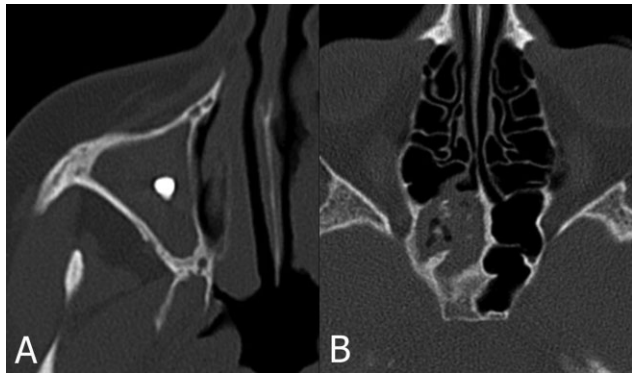


Fig. 1. (A) Axial computed tomography (CT) showing an iron-like density within the right maxillary sinus, filled by material with nonspecific CT findings. Thickening of the sinus walls suggests chronic inflammation. (B) Axial CT in a fungus ball located within the right sphenoid sinus. Microcalcifications are scattered within the material filling the sinus cavity. Thickening of the right sphenoid sinus wall is also present.

### *Perioperative Management*

Patients were treated with amoxicillin-clavulanate at a dose of 1 g twice a day for 7 days as a prophylaxis for postoperative infection. Nasal irrigations with saline solution twice a day were recommended for at least 1 month.

All patients were prospectively followed by endoscopic control every 3 months during the first postoperative year and subsequently every 6 months.

### *Statistical Analysis*

Prevalence of an "iron-like signal," microcalcifications, and bone remodeling at CT in maxillary and nonmaxillary FBs was evaluated and univariate comparison between the two groups was performed using a Fisher exact test. A $P$ value $<.05$ was considered statistically significant.

## RESULTS

The study group included 118 females and 42 males, with an age from 19 to 85 years (mean, 52.7 years). Only one patient had previously undergone endonasal surgery for sinonasal polyposis. The maxillary sinus was the most frequently affected site (135/160 patients, 84.4%), with bilateral involvement in two cases. Twenty-three (14.4%) patients presented with FB in the sphenoid sinus, whereas ethmoid and spheno-ethmoid involvement was found in one (0.6%) case each.

All patients with maxillary, spheno-ethmoid, and ethmoid FB, and 21 of the 23 cases with sphenoid localization underwent preoperative CT of the paranasal sinuses, whereas in 10 patients with sphenoid FB an MR scan was obtained. In two patients, the examination was performed because CT revealed the presence of a bone resorption at the sphenoid lateral wall, and we wished to better delineate the relationship between extracranial and intracranial interface, whereas in the remaining eight cases the imaging study had been requested by a neurologist before otolaryngologic consultation for progressively worsening headache localized to the vertex.

At CT, a metal-dense spot, also called an iron-like signal (Fig. 1A), was detected in 97/135 (71.9%) patients

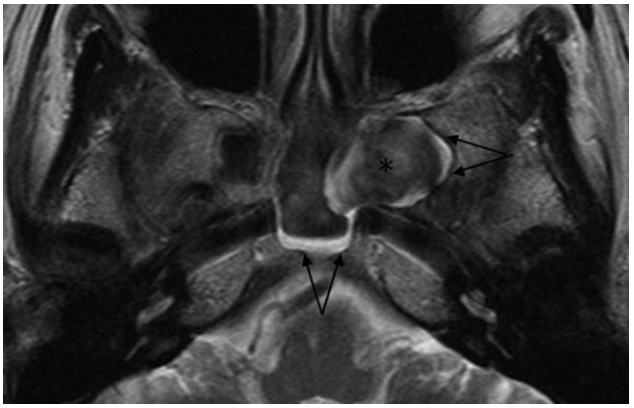

Fig. 2. A fungus ball located within the left sphenoid sinus characterized by a hypointense signal on the T2-weighted magnetic resonance image (asterisk). Thickened mucosa lining the sinus wall is visible as a continuous hyperintense signal (arrows).

with maxillary FB, and among the 23 nonmaxillary cases only in one (4.3%) patient with sphenoid FB. CT also showed a heterogeneous hyperdensity within the involved sinus in association with microcalcifications in 22/135 (16.3%) maxillary and 9/21 (42.9%) sphenoid FB (Fig. 1B), respectively. Bony wall remodeling, including erosion and/or thickening and sclerosis, was found in 51/135 (37.8%) maxillary and 11/21 (52.4%) sphenoid FB (Fig. 1A, B). The prevalence of iron-like signal in the maxillary sinus was significantly higher than in nonmaxillary FB ($P < .0001$), whereas microcalcifications in nonmaxillary FB were significantly higher than in maxillary cases ($P = .0045$). Conversely, there was no statistically significant difference between the two groups in relation to bone remodeling.

In 10 patients with sphenoid FB who underwent MR, the imaging study demonstrated a hypointense lesion bordered by hyperintense (T2-weighted sequence) and enhancing (T1-weighted sequence) mucosa (Fig. 2), whereas the pathognomonic "void signal" was observed in 5 (50%) cases.

The presenting complaints generally varied according to FB localization. In 135 patients with maxillary sinus involvement, the signs and symptoms, mimicking those of a chronic rhinosinusitis, included nasal discharge in 87 patients (64.4%), facial pain in 83 (61.5%), nasal obstruction in 73 (54.1%), headache in 58 (43%), cacosmia-hyposmia in 36 (26.7%), and palpebral edema and premaxillary swelling in two each (1.5%). Patients with sphenoid FB complained of vertex headache, nasal obstruction, and visual disturbance in 13 (56.5%), four (17.4%), and two cases (8.7%), respectively. The patient with spheno-ethmoidal FB complained only of vertex headache. In 12/135 (8.9%) cases of maxillary, in one (4.3%) case of sphenoid, and in the case of ethmoid FB, CT scan performed for unrelated reasons identified findings suggestive for FB in patients without typical FB symptoms.

Nasal endoscopy showed nonspecific mucosal changes in all patients with maxillary and ethmoid FBs. In 65/135 (48.2%) maxillary FB and in both (100%) cases with ethmoid involvement, a slight edema and hyperemia of the uncinate process mucosa and the lateral wall of the middle turbinate, associated with purulent discharge from the middle meatus, were observed. With the exception of a mild mucosal hyperemia of the ostiomeatal complex observed in 7 (5.1%) patients, a normal endoscopic appearance was reported in the remaining 88/160 (55%) patients.

Dental evaluation was obtained in 120/135 (88.9%) patients with maxillary FB, revealing previous endodontic treatments to the ipsilateral upper jaw tooth in 104/120 (86.7%) patients.

All patients underwent removal of FB through an exclusively endoscopic approach. Among the 135 patients with maxillary FB, only 11 (8.1%) were operated under local anaesthesia with intravenous sedation. A selective transnasal para-septal approach was performed in 10 patients with sphenoid sinus FB, whereas the remaining 13 patients were treated using a transethmoidal approach.

Histological examination of the specimens demonstrated a large amount of fungal hyphae in all cases. Histological analysis identified *Aspergillus* sp. in 21/160 (13.1%) samples; *Mucor* sp. and *Candida* sp. hyphae were detected in one (0.8%) case each. Fungal cultures showed a low sensitivity with only 24/118 (20.3%) positive specimens: growth of *Aspergillus fumigatus* and *Alternaria* sp. colonies was demonstrated in 18 (15.2%) patients and three (2.5%), respectively, whereas *Penicillum* sp., *Bipolaris* sp. and *Paecilomyces variotii* were found in one (0.8%) patient each.

No perioperative complications were observed, and all patients were discharged the day after surgery. Two patients with maxillary FB developed stenosis of the antrostomy with secondary recurrent maxillary sinus infection and were successfully treated with endoscopic revision surgery under local anaesthesia with sedation. After a follow-up varying from 18 to 196 months, no recurrence of the disease was observed.

## DISCUSSION

Even though no data on the prevalence of FB are available, during the last decades there has been an apparent increase in the diagnosis of this pathology. On one hand, this may be due to a genuine increase in the occurrence of FB that could be related to a wider use of endodontal treatments with possible sinus perforation. On the other hand, the extensive use of nasal endoscopy and CT of paranasal sinuses together with routine examination of sinus content have led to a more accurate identification of the disease. FB usually involves only one sinus, most frequently the maxillary sinus, followed by the sphenoid, ethmoid, and frontal sinus.[5,6,9,10] In our series, the maxillary sinus was also the most frequent localization, with 135 patients (84.4 %); only two patients had bilateral involvement. Another interesting finding was the predominance for female gender (2.97:1), which supports the idea that hormonal factors may be involved in the pathogenesis of FB.[11] Another observation, first reported by Dufour et al.,[10] indirectly confirmed a possible hormonal influence is the absence of FB in children before puberty; in the present series, there were no patients under the age of 19. Of course, it

can be also hypothesized that the absence of FB in young patients may be due to the rarity of endodontal treatments in this age group.

Presenting symptoms of FB are nonspecific.[4,5,10] Maxillary and ethmoid localizations frequently mimic chronic rhinosinusitis. Patients complain of long-standing unilateral nasal obstruction, purulent rhinorrhea with cacosmia, and facial pain scarcely responsive to anti-inflammatory or antibiotic agents. In our series of sphenoid FB, the most frequent presenting symptom was vertex headache, sometimes associated with postnasal drip, which was the most frequent complaint in a recently reported series of 12 patients with sphenoid FB.[12]

The pathogenesis of FB is still unclear. In 1969, Milosev published his experience with 17 patients affected by *Aspergillus flavus* infection of the paranasal sinuses and proposed the "aerogenic theory."[13] According to the author, the inhaled spores of fungus deposit in the sinuses, commonly the ethmoid, becoming pathogenic when conditions in the sinuses begin to be relatively anaerobic. Another theory[14] suggested that functional obstruction of sinus ostium may act as an inducing factor, and that fungal growth may be favored by hypoxic or anaerobic conditions. Moreover, decreased ventilation would lower the pH and favor growth of fungal hyphae. Recently, Tsai et al. posed some criticism to this hypothesis.[15] In fact, in their study the authors compared the Lund-McKay scores for the anterior ethmoid and frontal sinus of two groups of patients suffering from unilateral rhinosinusitis and maxillary fungus ball, respectively. By analyzing the radiologic scores, they demonstrated that obstruction of the ostiomeatal complex plays a relevant role in the onset of rhinosinusitis, whereas a similar finding was not clearly demonstrable in the onset of a maxillary fungus ball. A few years after the findings of Stevens[14] were published, Stammberger[16] hypothesized the predisposing role of chronic sinonasal infection in promoting fungus ball development. According to his report, the growth of the hyphae may extend over a long period of time with episodes of proliferation alternating with longer periods of inactivity. Bacterial or viral superinfections may lead to episodes of acute sinusitis, and the resulting purulent secretion provides the fungi with ideal nutrient conditions for further growth.[16]

In 1986, Beck-Mannagetta first postulated that dental amalgam from tooth apex together with the anaerobic habitat of the sinus could promote the growth of fungal elements.[17] Since then, other authors[18–20] supported the theory addressing the passage of dental sealers containing zinc oxide into the maxillary sinus as an important factor in inducing inflammatory and necrotic alterations of the mucosa, which favor fungus growth. Sinus perforation, mainly due to endodontic treatment, seems to be essential to supply inhaled spores with a favorable environment for growth. A recent case-control study published by our group[21] confirmed the increased risk of maxillary FB in 101 patients who had received endodontic treatment compared to 306 control-group patients. In support of this hypothesis, in the present series 104/120 (86.7%) patients with maxillary sinus FB had undergone previous endodontic treatment on the upper jaw tooth. This theory, however, does not explain the occurrence of FB in the ethmoid, sphenoid or frontal sinuses, or in the maxillary sinus of previously untreated patients.

One of the cornerstones of preoperative diagnostic workup is imaging studies. Both CT and MR findings of FB are strictly related to the content of heavy metals (iron and manganese) and calcium within fungal hyphae. As a result, FB appears spontaneously hyperdense at CT; microcalcifications, possibly scattered within the lesion, may also be observed.[12] Though extremely specific, these signs lack sensitivity. The MR pattern may often be misleading; in reality, the magnetic susceptibility of iron and manganese, combined with the reduced water content of FB, account for shortening of both T1 and T2. Consequently, on both sequences, MR may show a sinus filled with a hypointense content bordered by hyperintense (T2) and enhancing (T1, after contrast administration) mucosa. In some cases, T1 and T2 signal shortening may be so marked that it results in a signal void, making discrimination between FB and intrasinusal air very difficult, particularly if an improper windowing (brightness and contrast) is used. Chronically infected sinuses often show bony changes (focal or diffuse) that encompass both remodeling or erosion and areas of thickened, osteitic-like bone.

In our series, the iron-like signal prevalence was significantly higher in maxillary than in nonmaxillary FB (71.9% vs. 4.3%; $P < .0001$); these data are in agreement with those published in a recent paper[10] that confirms the high rate (61%) of maxillary FB displaying metallic density. In contrast, our rate of microcalcifications (42.9%) in sphenoid FB is lower than the value (64%) reported in a recent publication focusing on isolated sphenoid FB.[12]

Some speculations on the variability of the CT pattern between maxillary and nonmaxillary FB may be offered. First of all, the iron-like signal may reflect the metallic content of dental sealers that have possibly penetrated into the sinus. Following another theory,[16] considering that fungal masses may be responsible for these focal hyperdense areas, FB of maxillary sinus, which is much larger than the others, may require a longer time to become symptomatic. Consequently, greater amount of fungal material is usually found in the maxillary sinus. Moreover, according to the last theory, a higher incidence of microcalcifications into nonmaxillary compared with maxillary FB could be related to the lower quantity of fungal content within the sinus.

The treatment of choice for FB is surgery,[10] which removes fungal debris from the affected sinus and reestablishes proper ventilation and drainage. Any external approach (i.e., lateral rhinotomy, Caldwell-Luc approach) for treating FB, which is a noninvasive fungal contamination, is no longer justified.

Surgical goals may be effectively reached using a purely endoscopic approach, which should be considered the gold standard in treatment of paranasal sinus FB.[7,8] In fact, endoscopy combines easy access to the affected sinus, perfect visualization into the sinus itself, and low morbidity.[6]

According to some authors,[22] endoscopy may be combined with a canine fossa approach to better visualize the anteroinferior part of the maxillary sinus and the lacrimal

recess and to remove residual fungal and/or foreign elements. Chobillon and Jankowski[11] also proposed an exclusive endoscopic approach through the canine fossa in patients affected by maxillary FB without any signs of opacification of other paranasal sinuses. This technique is subject to some criticism. The canine fossa approach may cause persistent facial numbness, pain, and/or tingling due to the damage of anterior superior alveolar nerve and its branches.[23] Moreover, the absence of a middle antrostomy precludes postoperative endoscopic follow-up. Finally, in those patients presenting with swollen inflamed mucosa, which in our experience is a very common finding in maxillary FB, the absence of a patent middle antrostomy represents, in our opinion, an impairment to normal ventilation and drainage of the maxillary sinus and consequently to healing of the antral mucosa.

As an adjunctive observation based on our experience in maxillary sinus FB, high pressure lavage of the antrum through an initial smaller middle antrostomy, subsequently enlarged, appears critical to obtain fragmentation and detachment of fungal masses from the sinus mucosa. Moreover, the use of a 70°-angled scope, angled suction tube, and curved antrum forceps also allows visualization of the anterior wall of the maxillary sinus and removal of residual fungal debris, respectively, without the need for other approaches. Recently, Chao and Liu[24] proposed combining endoscopy with a so-called gauze-assisted technique, which attempts to expel fungal debris from the anterior corner of the maxillary sinus by pushing a gauze into it.

Histologic examination, by assessing the presence of fungal hyphae in the concretions and ruling out mucosal invasion, is essential for diagnosis of FB. Microbiological evaluation is useful to identify fungal species. It is, however, well known that, upon culture, growth of fungal elements is difficult to obtain, with a positivity rate ranging between 23% and 50%[2,9]; our results, with only 20% of positive cultures, were even lower.

According to the literature, the possibility of observing a recurrent FB after endoscopic surgery is very low,[9] and in the present series no recurrence was seen. Middle antrostomy stenosis, associated with recurrent bacterial sinusitis, was observed in two cases (1.1%). Revision antrostomy, performed under local anaesthesia, led to complete resolution of symptoms.

## CONCLUSION

Clinical presentation and endoscopic findings of FB are nonspecific. Imaging evaluation with CT and/or MR may lead, through characteristic findings, to a correct diagnosis, which is based upon histological identification of fungal hyphae. Our experience in a large cohort of patients reinforces the concept that a purely endoscopic approach including a wide sinusotomy is successful in managing FB. Because FB is a noninvasive form of fungal rhinosinusitis, systemic antifungal therapy is not indicated.

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