INTRODUCTION AND OBJECTIVES: The fungus ball is the most frequent type of fungal rhino-sinusitis. The objective of this study is to analyse the clinical and surgical features of our patients.

METHODS: Retrospective analysis of 35 patients with fungus ball treated in our centre between 2006 and 2014.

RESULTS: Mean age was 55 years old. 49% were men and 51% women. 75% involved the maxillary sinus, whereas 25% involved the sphenoid. 69% of our patients showed microcalcifications in the CT study. All the patients were surgically treated, with no cases of recurrence.

CONCLUSIONS: Clinical manifestations of fungus ball are non-specific, therefore endoscopy and image study are mandatory. The definitive diagnosis is made by histopathological study of the lesion. Endoscopic sinus surgery is the treatment of choice, with opening of the diseased sinus and complete removal of the fungus ball. The frequency of complications is very low. No oral or topical antymycotic treatments are necessary.

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Métodos: Se analizaron retrospectivamente 35 pacientes con bola fúngica tratados en nuestro centro entre 2006 y 2014.

Resultados: La edad media fue de 55 años. El 49% de los pacientes fueron varones y el 51% mujeres. El 75% se localizaron en el seno maxilar y el 25% restante en el seno esfenoidal. La clínica más frecuente fue obstrucción nasal, rinorrea y algias craneofaciales. El 69% de pacientes mostró microcalcificaciones intrasinusales en la tomografía computarizada. Todos los pacientes fueron intervenidos quirúrgicamente, sin registrarse recidivas.

Conclusiones: Las manifestaciones clínicas de la bola fúngica son muy inespecíficas, por lo que el diagnóstico de sospecha se hace mediante endoscopia y estudio de imagen. El estudio histopatológico confirma el diagnóstico. La cirugía endoscópica nasosinusal es la base del tratamiento de la bola fúngica, limitándose a la apertura del seno (o senos) afecto, y exéresis completa de la lesión. La tasa de complicaciones postoperatorias es muy baja, y no es necesario tratamiento antifúngico oral o tópico concomitante.

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Introduction

Fungi are micro-organisms which, apart from yeasts, reproduce by producing spores. These spores are ubiquitous and are considered saprophytes of the mucosa of the entire upper aerodigestive tract. Despite the enormous diversity of species, only a few cause disease in human beings. The species most commonly involved in sinonasal disease are: *Aspergillus*, *Alternari*, *Pseudallescheria*, *Bipolaris* and *Rhizopus*. Fungal rhino-sinusitis (FRS) is classified into two large categories; invasive and non-invasive (NIFRS). The former is determined by histological evidence of invasion of the mucosa, submucosa, blood vessels or underlying bone, and occurs in immunosuppressed patients. By contrast, with NIFRS there is no evidence of tissue invasion and it is typical in immunocompetent patients. The fungus ball (FB) is a form of NIFRS which is defined as an agglomeration of detritus and hyphae inside a paranasal sinus. This is the most common form of FRS, and in most cases is located in the maxillary sinus, followed by the sphenoid sinus. The pathogenesis of the FB remains a matter of debate. Treatment of this disorder is surgical with a view to resecting the entire lesion and ventilating the affected sinus, without the need for adjuvant antifungal therapy. The objective of our study is to describe our experience in the surgical treatment of the FB, analysing the main epidemiological and clinical characteristics, and the outcomes of surgery in our patients.

Methods

A retrospective study was made of 35 cases of FB-type NIFRS diagnosed and treated in our centre between 2006 and 2014. The diagnosis was confirmed by the presence of hyphae in histological analysis of the intrasinusal mass. All the patients presented intact immunological function. The clinical features and semiology of the disease, associated pathology, distribution per age and sex, and location were analysed. The mean age was compared between the males and females using the Student’s t-test. All the patients were studied preoperatively with computerised tomography (CT scan) to assess the location and extension of the disease, and the existence of microcalcifications. The study was complemented with magnetic resonance (MRI) in cases where the location was the sphenoid sinus. The type of surgical approach and its complications were also studied, and recurrence of the disease. Mean follow-up was 10 months.

Results

Forty-nine percent of the patients were male (17/35) and 51% females (18/35). The mean age at the time of diagnosis was 55, with a range of between 22 and 79 years of age. The mean age was analysed per age subgroups; 48 being the mean for the female group and 62 for the male (P=.003). All the cases were unilateral, except for one patient (3%) who presented a bilateral maxillary sinus FB. Seventy-five percent of the FB (27/36) were located in the maxillary sinus, whereas the remaining 25% (9/36) were located in the sinus. The most frequent clinical symptom of maxillary sinus FB was nasal obstruction (76.9%), followed by purulent rhinorrhea (61.5%) and facial or cranial algias (46.1%). In the cases of sphenoid sinus FB the most common symptoms were cranial or facial algias (77.8%) followed by purulent rhinorrhea (66.7%) and cacosmia, only 11.1% of the patients presented a sensation of nasal obstruction (Table 1). Oedema of the mucosa or the presence of purulent exudate in the middle meatus or sphenethmoidal recess was found in 69% of the FB (25/36). The proportion of pathological findings on endoscopy, according to the location, was 75% in the maxillary sinus FB and 66% in the sphenoid sinus FB.

CT scan showed intrasinusal microcalcifications in 69% of cases (25/36). In the case of sphenoidal FB, the proportion of microcalcifications was 33%, less than the 83% found in the maxillary sinus FB. All the cases were operated using an endoscopic endonasal approach, with wide opening of the...
affected sinus, extraction of the fungal material for histological analysis and the removal of any remnant of hyphae and detritus by irrigating the sinus. Postsurgical care consisted of nasal washes with isotonic saline solution. Topical or systemic antifungal agents were not prescribed in any case after surgery. None of the patients in this series presented recurrence of the disease. Two cases of mild postoperative epistaxis were recorded that were correctly managed by non-absorbable nasal packing, and there were 2 cases of synechia between the middle nasal concha and the septum, with no functional implications.

Discussion

Fungal rhinosinusitis comprises between approximately 4% and 10% of surgical interventions in the region of the paranasal sinuses. Between 4.5% and 26.8% of chronic rhinosinusitis affecting the sphenoid sinuses are mycotic. In recent years, an increase in the diagnosis of this pathology has been described, possibly due to the extensive use of complementary tests such as the CT scan and endoscopy. It has been suggested that the use of endodontics with a high affinity for fungi might explain in part the increased cases of FB located in the maxillary sinuses. The pathological spectrum of mycoses in the region of the paranasal sinuses is broad, and is divided according to the presence of tissue invasion. There is considered to be invasion when the presence of hyphae can be seen microscopically in the mucosa or submucosa, bone or blood vessels. In 1997, de Shazo proposed classifying FRS as non-invasive, which include the FB and allergic fungal rhinosinusitis, and invasive FRS, of which three forms are distinguished: acute, chronic and granulomatous. The FB is considered a non-invasive form which presents in immunocompetent individuals in whom the presence of allergic mucin has been ruled out. It is defined as an agglomeration of material or fungal hyphae inside a paranasal sinus. The first case of an FB in the paranasal sinuses was described by Mackenzie in 1894. However, current knowledge on the pathophysiology of this disorder has resulted in its terminology being updated and the term FB is recommended. This term also enables this nasosinusial disorder to be distinguished from mycetoma, which is a typical disorder in tropical regions comprising a granulomatous infection which affects the skin of the lower limbs. The term aspergilloma is not recommended either, because in addition to Aspergillus, other fungal species have been isolated in FB such as Mucor, Alternaria and Bipolaris. The pathogenesis of FB is unknown. In 1969, Milosev proposed the aerogenic theory, which suggests that the spores, ubiquitous, are deposited in the mucosa by inhalation, and acquire pathogenic capacity when anaerobic conditions are created inside the affected sinus. Other authors indicate osteomeatal complex obstruction as the cause. Stammberger postulated the possible predisposing role of chronic rhinosinusitis such that, at times of superinfection, purulent exudate provides an ideal growth medium for the fungi. Some authors have found a history of dental procedures on the upper ipsilateral jaw in more than 85% of patients with FB. However, this theory does not explain the cases of FB which affect the sphenoid sinus.

Many predisposing factors have been proposed, such as living in a rural area, diabetes, oestrogens, previous surgical interventions on the sinonasal area or anatomical variants. FB is typical in adult patients, and anecdotal in children and adolescents. In our series there is no case under the age of 20. In their series of 160 cases, Nicolai et al. found no patients under the age of 19. The authors themselves suggest that this lack of cases might be explained by the lack of a history of dental procedures in paediatric patients. There is also consensus that there is a slight female predominance, the extent of which depends on the series consulted. Some authors attribute this predominance to the greater life expectancy of women. Most series highlight the maxillary sinus as the most common location (83%–88%). The sphenoidal sinus represents between approximately 5% and 15%, and the ethmoidal sinus between 1% and 15%. In most cases the disorder is unilateral, and rarely affects more than one sinus. There are anecdotal cases of locations such as the nostril, the concha bullosa, the superior meatus or the frontal sinus. In our series there were no cases of FB located in the frontal sinus, ethmoidal sinus or in the nostril. There are few clinical manifestations of FB, and sometimes none at all; they are occasionally an incidental finding in imaging tests. Most patients present symptoms that are compatible with chronic unilateral rhinosinusitis, which does not respond to medical treatment. The various series published highlight rhinorrhoea as the most common symptom, in up to 86% of patients, followed by nasal respiratory failure and algias in the craniofacial region. In sphenoid sinus FB, the most common manifestation is retro-orbital or occipital headache (86%), followed by purulent rhinorrhoea (79%) and blurred vision, diplopia or decreased visual acuity in up to 20%. Endoscopic exploration can show some non-specific signs, such as oedema and rhinorrhoea in the area of the affected sinus, although it can occasionally be normal. Some authors maintain that more than 60% of patients present inflammatory changes in the mucosa and/or the presence of purulent rhinorrhoea in the middle meatus or sphenoethmoidal recess. This proportion is confirmed in our series, at 69% of patients with pathological endoscopic findings. However, other authors confirm that endoscopy does not show changes in the majority of patients. On the CT scan we observed a hyperdense image inside the affected

### Table 1 Clinical Symptoms of the Fungal Ball According to Its Location.

<table>
<thead>
<tr>
<th>Location</th>
<th>NRF</th>
<th>Cacosmia</th>
<th>Anosmia</th>
<th>Rhinorrhea</th>
<th>Craniofacial algias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxillary sinus</td>
<td>85</td>
<td>54</td>
<td>9</td>
<td>65</td>
<td>46</td>
</tr>
<tr>
<td>Sphenoid sinus</td>
<td>11</td>
<td>33</td>
<td>11</td>
<td>67</td>
<td>78</td>
</tr>
</tbody>
</table>

NRF: nasal respiratory insufficiency.
sinus (Fig. 1) in 75% of the patients.1,3 These microcalcifications are due to the high content in manganese, zinc, iron and calcium of fungal hyphae. Studies of sphenoid sinus FB indicate that hyperdense material is found less frequently in this location, in between 14% and 56% of cases.2,26,27 In our series, 33% of the sphenoid sinus FB and 83% of the maxillary sinus FB presented microcalcifications. Other less common radiological findings with this disease include disorders of the bony walls of the sinus such as sclerosis, erosion or thickening, possibly secondary to chronic local inflammation. Karkas et al.,28 in their series of 28 patients with sphenoid sinus FB, found bone erosion in 18% of cases. However, Nicolai et al., found bone erosion in a higher percentage; 54.2% of patients with sphenoid sinus FB and 37.8% of patients with maxillary sinus FB.1 A differential diagnosis of intrasinusal microcalcifications should be made with inverted papilloma, carcinoma, polyps, rhinoliths, antroliths, osteoma or chondroma, odontoma and inflammatory diseases such as syphilis and TB.19

The use of MR to complement tomography is indicated in cases where malignancy is suspected, untreatable headache, the presence of erosion on the CT scan and in cases with clinical symptoms of visual disturbances, in order to rule out major complications or tumour pathology. In our series, we complemented the study with MR imaging in all the patients with sphenoid sinus FB. The usual appearance of FB on MRI is an intrasinusal mass which is isointense or hypointense on T1 and markedly hypointense on T2, with peripheral enhancement secondary to inflammation of the surrounding mucosa.1,10,31 Despite the usefulness of radiological tests, a firm diagnosis is made by biopsying the lesion and the surrounding mucosa obtained during surgery (Fig. 2). Culture of the fungal material is usually negative, since it is considered that hyphae inside the mycetoma are non-viable. The various series highlight that culture is positive in less than 20% of patients,13,27 In our centre we do not systematically request fungal culture of the sinusal material, because it provides little diagnostic yield, and we confirm diagnosis by anatomopathological study. In 1999, DeShazo proposed the clinicopathologic criteria for diagnosis22; these are summarised in Table 2. Treatment for FB is surgical,15 and requires the affected sinus to be opened and complete removal of the fungal ball. This presents as a brownish mass, similar in appearance to clay, which is found inside the affected sinus during surgery (Fig. 3). Microscopic analysis of this mass shows an accumulation of hyphae with no evidence of tissue invasion, granuloma or allergic mucin. Postoperative outcomes are quite homogeneous in most series; there is less than 5% recurrence,1 and the patients' quality of life improves by more than 80%.27 Postoperative complications are anecdotal, mild in the majority, such as epistaxis or synechia. In our series, no case of recurrence was recorded.
in the 10 months of mean follow-up; there were 2 cases of mild epistaxis and 2 cases of synechia.

Klossek et al.,\(^{16}\) and DeShazo et al.\(^{32}\) consider that antifungals are not indicated in the treatment of sinus fungal balls, since there is a low rate of recurrence reported in the published series of patients treated exclusively with surgery. Furthermore, there are clinical trials which have evaluated the adjuvant perioperative use of these substances. However, some authors indicate perioperative treatment with antifungals (for example: itraconazole, amphoterin B) in immunosuppressed patients, in patients with diabetes mellitus or in whom the sphenoid sinus is affected.\(^{34-36}\) Furthermore, topical corticosteroids are prescribed for specific cases where there is evidence of major inflammation of the mucosa. Likewise, a short course of oral antibiotics is recommended if there is evidence of abundant purulent exudate.

**Conclusion**

The FB is a type of non-invasive fungal rhinosinusitis, typical in immunocompetent patients. Its clinical manifestations are very non-specific; therefore studies by CT scan and endoscopy are compulsory. Histopathological study confirms the diagnosis of this disease. Endoscopic sinonasal surgery is the basis of treatment for FB, limited to opening the affected sinus (or sinuses) and the complete removal of the lesion. It has a very low rate of postoperative complications and it is not necessary to add oral or topical antifungal treatment after surgery.

**Conflict of Interests**

The authors have no conflict of interests to declare.

**References**


