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Original article

Evaluation of the prevalence and specificities of asymptomatic paranasal sinus aspergillosis: Retrospective study of 59 cases



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ARTICLE INFO

Keywords:

Fungus ball
 Asymptomatic
 Prevalence
 Chronic sinusitis
 Endonasal surgery
Aspergillus
 Root canal treatment
 Paranasal sinus aspergillosis

ABSTRACT

Study objectives: To calculate the prevalence of asymptomatic localized paranasal sinus aspergillosis (or fungus ball) in the general population and to compare asymptomatic and symptomatic fungus balls (FB) in order to determine their specificities.

Material and method: Retrospective study including 59 patients operated for FB between 2006 and 2011 in a single unit. Patients were divided into two groups: asymptomatic patients (group 1, $n = 10$), and symptomatic patients (group 2, $n = 49$). All patients in group 1 were identified by systematic screening for a site of infection prior to cataract surgery during this period ($n = 6198$). All patients were treated by endonasal surgery. Calculation of the prevalence of asymptomatic FB was based on standardization of the source population (normal distribution, 95% confidence interval). The two groups were then compared (clinical context, age, history of root canal treatment, topography, recurrence rate), after randomization test by Student's test and Chi² test.

Results: The prevalence rate of asymptomatic FB in our study was 1.6/1000 in the population over the age of 55 years. A statistically significant difference was demonstrated between the two groups in terms of the following parameters: more advanced age for patients of group 1, constant history of root canal treatment in group 1, constant maxillary topography in group 1, and higher recurrence rate in group 2. Mean follow-up was 18.7 months (range: 3–49 months).

Discussion: This study, the first to determine the prevalence of asymptomatic FB, suggests the existence of very slowly progressive, minimally symptomatic forms, raising the problem of the surgical indications in these patients.

Conclusion: The prevalence of asymptomatic fungus balls is 1.6/1000. Prospective studies are necessary to justify conservative management in these patients.

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1. Introduction

Localized paranasal sinus aspergillosis (or fungus ball) is a form of chronic sinusitis due to fungal infection caused by certain species of *Aspergillus*. According to the Société française d'ORL (SFORL) guidelines, fungus ball (FB) generally requires surgical treatment [1]. However, radiological images suggestive of FB are fairly commonly detected on imaging examinations performed in the context of screening for sites of infection prior to immunosuppressive therapy, prosthetic surgery or dental implants. The discovery of such images in a patient with no sinonasal symptoms raises the question of the need for surgical treatment.

All patients eligible for cataract surgery in the Institut Arthur-Vernes Ophthalmology department between 2006 and 2011 underwent systematic screening for a site of infection including radiological assessment (Waters' view) and an otorhinolaryngology consultation (clinical interview and nasal endoscopy) to detect paranasal sinus infection. This systematic screening was performed in order to detect asymptomatic aspergillosis, which was treated surgically to eliminate this site of infection prior to cataract surgery.

The objectives of this study were to:

- analyse the group of patients detected by routine screening in order to determine the prevalence of asymptomatic FB;
- compare this group with patients with symptomatic FB managed in the department during the same period in order to identify the specific clinical and radiological features and clinical course of this form of aspergillosis.

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2. Material and methods

2.1. Patients

This retrospective study was based on a series of 59 patients operated for fungus ball (FB) in the Institut Arthur-Vernes Otorhinolaryngology department between January 2006 and December 2011. The diagnosis of FB was suspected on clinical and CT findings. Only patients with histological confirmation of the diagnosis were included. This series comprised 16 men and 43 women with a mean of age of 60.1 years (range: 24 to 84 years). None of these patients had diabetes, HIV infection or immunosuppressive treatment at the time of the operation.

The otorhinolaryngology consultation systematically comprised of:

- clinical interview looking for signs of sinonasal dysfunction (anterior and/or posterior purulent rhinorrhoea, localized headache, facial pain, cacosmia);
- nasal endoscopy looking for purulent discharge.

Patients were divided into two groups:

- a group of asymptomatic patients, i.e. not reporting any symptoms and with no signs of purulent discharge on nasal endoscopy; these patients were identified by systematic screening prior to cataract surgery (group 1; $n = 10$);
- a group of symptomatic patients, reporting one or more of the above symptoms; these patients were derived from the otorhinolaryngology department (group 2; $n = 49$).

The group of patients identified by systematic screening (group 1) was submitted to statistical analysis with respect to the total source screening population ($n = 6198$). This source population comprised a total of 6198 patients undergoing cataract surgery during the same period and submitted to systematic screening for sites of paranasal sinus infection by Waters' view X-rays and an otorhinolaryngology consultation (clinical interview and nasal endoscopy). Data concerning the source population undergoing screening prior to cataract surgery ($n = 6198$) were derived from the PMSI database.

In the presence of suggestive radiographic signs (presence of calcifications and/or a sinus foreign body), nonenhanced CT scan of the sinuses was performed. Paranasal sinus surgery was proposed to the patient in the presence of suggestive CT features (tissue opacity associated with diffuse microcalcifications and/or metal density foreign body).

These two groups of patients were compared in order to detect differences between the group of patients derived from systematic screening and those with symptomatic aspergillosis.

This comparison was based on the following criteria:

- clinical context: age, gender;
- history of root canal treatment;
- site of FB;
- surgical technique used;
- postoperative course and recurrence rate.

2.2. Treatment

According to the Société française d'ORL (SFORL) guidelines, fungus ball generally requires surgical treatment [1]. All asymptomatic patients consented to endonasal resection of FB, which constitutes the standard treatment for FB and in order to eradicate a potential site of infection prior to cataract surgery, in agreement with

Normal age distribution of patients undergoing cataract surgery

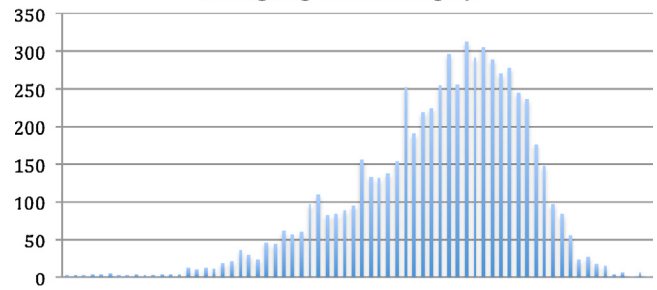


Fig. 1. Normal age distribution in the source population.

the ophthalmologists. All 59 patients included (symptomatic and asymptomatic) therefore underwent sinus surgery.

Patients with maxillary FB were treated by endonasal middle meatal antrostomy using a 30° endoscope, associated with a Caldwell-Luc procedure in 3 cases. The surgeon sometimes had to use a 70° endoscope at the end of the operation. No patient was treated exclusively by Caldwell-Luc procedure. Patients with sphenoid FB were treated by endonasal sphenoidotomy using a 30° endoscope and a neuronavigation system. Postoperative care consisted of irrigation of the nasal cavities with physiological saline several times a day for 3 weeks.

All patients were reviewed by their surgeon and evaluated by nasal endoscopy on postoperative day 8. Subsequent follow-up was ensured either by the surgeon or by the otorhinolaryngologist who referred the patient. Patients followed outside of the department were contacted by telephone to determine their long-term postoperative course (clinical interview to identify any symptoms). Patients who could not be recontacted or who were not reviewed after 3 months were considered to be lost to follow-up. Follow-up CT scan was only performed when recurrence was suspected.

2.3. Data analysis

Prevalence is an indicator of morbidity and constitutes an epidemiological tool to identify health problems and define public health priorities. It is defined as the number of subjects affected by the disease in a population at a given point in time. The prevalence rate is the prevalence observed in the mean population during the observation period [2].

Based on the hypothesis that, according to current medical knowledge, susceptibility to paranasal sinus aspergillosis is the same in patients with cataract and in the general population, standardization of the source population (patients operated for cataract, $n = 6198$) should be possible. This standardization was based on the normal distribution of the age pyramid of the source population with a 95% confidence interval (Fig. 1).

A randomization test was performed prior to comparison of the groups of asymptomatic patients (group 1) and symptomatic patients (group 2) in view of the different sample sizes (group 1, $n = 10$; group 2, $n = 49$). The various parameters were then compared by Student's test for values, and Chi² test for other variables.

3. Results

3.1. Prevalence of asymptomatic FB

The source population, i.e. all patients undergoing screening for the presence of paranasal sinus infection, comprised 6198 patients (over a 5-year period). The mean age of the source population was 74.1 years with a standard deviation of 9.67 years. The age

Table 1
Mean age and sex ratio, 95% CI.

	Group 1 (asymptomatic patients)n = 10	Group 2 (symptomatic patients)n = 49	Total number of patients	t value	P
Mean age (years)	69.6	58.1	60.1	2.14	< 0.05
Gender					
Male	3	13	16		> 0.05
Female	7	36	43	7	

distribution of this source population was considered to be normal (Fig. 1), allowing standardization of the population from the mean and standard deviation.

Standardization of this population, based on the hypothesis that susceptibility to paranasal sinus aspergillosis was the same in patients with cataract and in the general population with a 95% confidence interval, resulted in an age interval $I = (1.96 \times 9.67) = 19.1$ around the mean age (74.1 years). Our source population was therefore representative of the standardized general population between the ages of 55.2 and 93.1 years.

Ten patients presented asymptomatic FB in this source population of 6198 patients, allowing estimation of the prevalence rate of asymptomatic FB: 1.6/1000 in the population over the age of 55 years.

3.2. Comparison between symptomatic and asymptomatic FB

Comparison of the groups of asymptomatic patients (group 1) and symptomatic patients (group 2) demonstrated a significant difference ($P < 0.05$) in terms of age, as patients in the asymptomatic group (group 1) were older. A significant female predominance was observed in both groups of patients (groups 1 and 2). In contrast, no statistically significant difference was observed for the male/female distribution between the two groups ($P > 0.05$) (Table 1).

A history of root canal treatment was reported by 42 of the 59 patients, i.e. 71% of cases. In every case, root canal treatment concerned the maxillary region. No history of root canal treatment was reported in the subgroup of patients with sphenoid sinusitis. All patients of group 1 had a history of root canal treatment versus only 32 patients (65%) in group 2 (statistically significant difference). Two patients in group 2 also presented an oro-antral communication versus no patients in group 1.

Table 2 shows the topography of FB in the two groups. The most common site was isolated maxillary sinusitis, followed by equal numbers of sphenoid and ethmoidomaxillary sinusitis. No case of frontal sinusitis was observed in this series. The group of asymptomatic patients exclusively presented maxillary sinusitis.

Ninety-four percent of patients with maxillary sinusitis were operated exclusively by endonasal middle meatal antrostomy. Three patients were treated by a combination of middle meatal antrostomy and Caldwell-Luc procedure, including 2 patients with a history of ipsilateral sinus surgery. No immediate postoperative complication was observed.

Five cases of recurrent aspergillosis were observed after a mean interval of 18.8 months after surgery. All recurrences were observed in the group of symptomatic patients (group 2) and consisted of:

- three cases of recurrent maxillary sinusitis requiring repeat meatal antrostomy, at 13, 15, and 37 months, respectively;
- two cases of recurrent sphenoid sinusitis requiring repeat sphenoidotomy at 4 and 25 months, respectively.

These 5 cases of recurrences were suspected following the return of symptoms of chronic sinusitis (rhinorrhoea, cacosmia, pain), leading to CT scan and surgical revision. In every case, histological examination demonstrated persistence of aspergillosis. No recurrence was observed in the asymptomatic group (group 1). None of the patients presented any signs of short-term or long-term postoperative sinonasal dysfunction.

Overall, 80% of the patients of this series were reviewed with a mean follow-up of 18.7 months (range: 3 months to 4 years) and 12 patients were lost to follow-up.

4. Discussion

In view of their severity and the small number of patients affected, several studies have evaluated the incidence and prevalence of invasive fungal rhinosinusitis [3]. The prevalence of sinus aspergillosis in the population of patients operated for chronic sinusitis is also known [4]. In contrast, the prevalence of asymptomatic fungus balls has never been studied and consequently remains unknown. The present study is therefore the first study to evaluate the prevalence of asymptomatic fungus balls.

The essential problem is to determine the real value of surgical treatment in these patients, as the prevalence demonstrated in this study indicates that a significant number of patients with aspergillosis will probably never experience any symptoms or complications. A prospective study comparing the outcome of patients treated surgically or by simple watchful waiting would provide an answer to this question.

The Société française d'ophtalmologie has not issued any specific guidelines, at the present time, concerning screening for sites of infection prior to cataract surgery. Aseptic technique and prophylactic antibiotics have been identified as factors allowing a reduction of the incidence of postoperative endophthalmitis (0.3%), a rare nosocomial infection [5].

Unenhanced CT scan of the paranasal sinuses appears to be the reference imaging examination for the diagnosis of fungus ball according to current data [6]. Waters' view X-ray of the sinuses, a rapid examination, less irradiating than CT scan, was useful for screening purposes in our study. However, this examination, less sensitive than CT scan, may be associated with a significant number of false-negative results, i.e. patients with asymptomatic FB either not visible or only barely visible on standard X-rays, suggesting that the real prevalence rate of asymptomatic FB in the population over the age of 55 years could therefore be higher than 1.6/1000.

The asymptomatic nature of the FB detected in this study as well as our intraoperative findings (absence of pus, slightly inflammatory mucosa) are not in favour of superinfection by pyogenic bacteria. As *Aspergillus* cannot be responsible for endophthalmitis, the need to perform cataract surgery therefore cannot constitute per se an argument for surgical management of asymptomatic fungus ball.

Table 2
Sites of paranasal sinus infection.

	Group 1	Group 2	Total
Maxillary	10	39	49
Ethmoidomaxillary	0	5	5
Sphenoid	0	5	5
Frontal	0	0	0

This review of the patients' medical charts was based on a fairly large sample size compared to the retrospective series published in the literature (Braun, 35 cases; Serrano, 45 cases) [4,7]. Mycological examination was not performed in view of its poor sensitivity compared to histological examination [4,5,8,9].

A significant difference ($P < 0.05$) in terms of age was observed between the symptomatic (58.1 years) and asymptomatic groups (69.6 years) in this series. This difference can be partly explained by the fact that the asymptomatic group was derived from systematic screening performed in an older source population (patients undergoing cataract surgery). However, a latent or asymptomatic form of FB could possibly be more frequent in the elderly population, in view of the classically fairly slow course of FB [1]. A marked female predominance of FB was observed in the 2 groups, as also reported in the literature [4,6,7]. The hypothesis of more frequent root canal treatment in the female population could explain this difference.

It has been clearly established in the literature that root canal treatment is a predisposing factor to maxillary sinus aspergillosis [7,10]. A strong association was observed in the present study between a history of root canal treatment and maxillary sinusitis (71% of cases in the overall population, 100% in the asymptomatic group). As the interval between root canal treatment and onset of sinus aspergillosis could not be determined, it is therefore difficult to establish a formal cause-and-effect relationship. Various hypotheses have been proposed in the literature to explain the dental origin of sinus aspergillosis (marker of dental disease or predisposing to the development of sinus aspergillosis?) [4,10,11].

This study was also unable to explain the pathophysiology of sphenoid FB, which has rarely been studied in the literature. Asymptomatic forms of sphenoid aspergillosis have been reported, but X-rays with Waters' view are unable to detect these forms, explaining why no cases of sphenoid FB were observed in group 1. This element can constitute a bias in comparison of the two groups due to underestimation of asymptomatic forms of sphenoid FB. However, all sites of FB were included in group 2 in order to maintain a homogeneous population, allowing comparison with published series, which systematically include sphenoid FB.

According to the SFORL report on ENT fungal infections, "all of the publications indicate a consensus in favour of exclusive surgical treatment of FB, without associated medical treatment by the local or systemic antifungal therapy"; this treatment is designed to "clean" the affected sinus and obtain samples to confirm the diagnosis [1].

In the present series, surgery was performed via an endonasal approach in every case (associated with Caldwell-Luc procedure in 3 cases). Endonasal middle meatal antrostomy appears to be the technique of choice at the present time, as it is less invasive than the vestibular approach [1,5,12,13]. However, it is more difficult to control the floor of the maxillary sinus via the endonasal route than via the vestibular route. Inferior meatotomy can also be performed in combination with middle meatal antrostomy, facilitating control of the base of the sinus and allowing irrigation under endoscopic control, but this technique raises the problem of persistence of a non-physiological enlarged inferior meatal orifice that can lead to ostiomeatal complex dysfunction.

Two of these 3 cases of FB treated by endonasal surgery combined with Caldwell-Luc procedure in this series presented recurrent maxillary FB previously treated by exclusive middle meatal antrostomy. At last follow-up, no recurrence has been observed in these 3 patients. As suggested by Serrano [4], Caldwell-Luc procedure should therefore possibly be reserved for certain types of recurrence.

The minimally invasive endoscopic approach to the canine fossa, based on the principle of the Caldwell-Luc procedure but adapted to minimally invasive surgery, has the advantage of preserving the

ostiomeatal complex. In this series, the 10 cases of asymptomatic FB of the maxillary sinus discovered on systematic screening presented a functional ostiomeatal complex (by definition absence of sinonasal dysfunction), which raises the problem of the treatment of these minimally symptomatic or asymptomatic forms by middle meatal antrostomy, which induces surgical modification of a functional ostium, as emphasized by Jankowski and Chobillon in 2004 [14]. The minimally invasive approach to the canine fossa, supported by these authors, needs to be more extensively evaluated.

It may appear somewhat paradoxical to perform this surgery in minimally symptomatic forms of FB, but none of our patients presented sinonasal dysfunction on medium-term or long-term follow-up.

Three recurrences (5%) of maxillary FB were observed in these series following endonasal meatotomy, very probably related to incomplete resection of the base of the sinus. This low recurrence rate is in line with the data of the literature [7,13,15]. All of these recurrences were observed in the symptomatic group, more than 12 months after surgery (mean interval: 18.8 months), which tends to suggest the need for prolonged postoperative follow-up in view of the slow progression of this disease. All patients operated for recurrent FB were asymptomatic at last follow-up. The mean follow-up was 18.8 months, but a large number of patients were lost to follow-up (12 patients), partly explained by the fairly long period of this retrospective study (5 years).

5. Conclusion

This study was designed to define the prevalence of asymptomatic FB in a source population submitted to systematic screening. The statistical tools used in this study estimated the prevalence rate at 1.6/1000 in the population over the age of 55 years.

The secondary objective of this study was to compare this group of asymptomatic patients with patients presenting symptomatic aspergillosis, managed in the department over the same period, in order to identify the specific clinical features and clinical course of this form of aspergillosis. More advanced age, exclusively maxillary site and a systematic history of root canal treatment were shown to be significantly different between the two groups.

This prevalence and these differences suggest the existence of a very slowly progressing form of aspergillosis, which, in some patients, may never induce symptoms or complications, which therefore raises the question of the value of surgical treatment in these patients. A prospective study comparing the course of operated versus nonoperated patients could address this issue.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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