Allergic fungal sinusitis and Paranasal sinus fungus ball: Are they different in management?

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Background and aims: Allergic fungal rhinosinusitis and paranasal sinus fungal balls are two distinct forms of non-invasive fungal rhinosinusitis which affect immunocompetent hosts. Each of them has its specular diagnostic features and hence treatment methods. Our study aims at comparing different ways of diagnosis of allergic fungal sinusitis and sinus fungus ball disease and evaluating methods of treatment of both diseases.

Patients and Methods: It is a prospective study carried out at ENT department, Sohag university hospitals, from March 2011 to January 2013. Forty patients were included in the study. Those patients were divided into two groups: group 1 (24 patients with allergic fungal sinusitis) and group 2 (16 patients with fungal balls). Clinical presentation, laboratory investigations, CT findings, operative findings and postoperative histopathological examination were compared between both groups using statistical analysis.

Results: Statistically significant difference was observed between both groups as regard presence of atopy, clinical presentation and disease laterality, imaging findings and laboratory data. As regard operative findings, each disease has distinct intra-operative findings. Statistical significant difference between both groups was found when we compared Post-operative histopathological examination as well as the possibility for local recurrence.

Conclusions: Both AFS and FB are two categories of fungal sinusitis affect immunocompetant patients but each has different aetiopathology and accordingly different management. Through bacteriology, immunology and CT-scanning it is possible to reach a proper diagnosis and accordingly to start a suitable treatment. A combination of surgical debridement and medical treatment consist of antiallergic drugs is the treatment of choice in AFS while surgery remains the mainstay of treatment for FB without need for medical treatment.

Keywords: allergic fungal sinusitis, fungus balls, diagnosis, histopathology, treatment.

Introduction

Fungal rhinosinusitis (FRS) has been described for many years, initially in immunocompromised patients, but since the development of nasal endoscopy, several new cases have been reported in immunocompetent patients [1]. Nevertheless, controversies still remain concerning the definition, classification, and management of these pathologies. Since De Shazo's classification in 1997, FRS has been separated into invasive and noninvasive form which include fungus ball (FB) and allergic fungal rhinosinusitis (AFS) [2].

AFS is a non-invasive disease believed to be an allergic reaction to aerosolized environmental fungi in an immunocompetent host representing an allergic hypersensitivity response to extramucosal fungi present within the sinus cavity. The traditional criteria are the demonstration of allergic mucin and the presence of noninvasive fungi in patients with chronic rhinosinusitis (CRS). FB is a noninvasive fungal colonization usually displays distinctive gross features of friable or grumous grey to brown or black material, which on microscopic examination is composed of abundant, tightly packed fungal hyphae that does not invade mucosal tissue. The distinction between mycetoma with fungal growth adjacent to tissue and chronic invasive fungal sinusitis may be problematic, but the latter condition is characterized by hyphae actually within tissue, absence of fungus balls, and presence of granulomatous inflammation [3].

There are five criteria for the diagnosis of AFS including., nasal polyposis; allergic mucin; CT scan findings consistent with chronic rhinosinusitis; histological presence of fungal hyphae, positive fungal culture; and Type I hypersensitivity (atopy) diagnosed by history, positive skin test, or serology [4]. Patients with FB presented with symptoms of unilateral or bilateral nasal obstruction, pressure feelings and nasal discharge with the detection of a

mass of mycelia embedded in mucus within the paranasal sinuses without mucosal invasion on histopathology [2]. Anatomically, the roots of the upper first premolar, second premolar, first molar and second molar are in close contact with the floor of the maxillary sinus and may protrude into the maxillary sinus in some cases [5]. Endodontic treatment is performed to cure neural damage resulting from dental caries. During the procedure, a hole is made in the target tooth first and then the nerve and vessels within the root canal are removed, followed by filling with inert materials. These filling materials can extrude during treatment and are frequently introduced into the maxillary sinus beyond the root canal, due to their close anatomical proximity. These procedural complications are common and part of everyday clinical practice. As a result, inflammatory response may involve the sinus mucosa [6]. Root-filling materials containing zinc oxide-eugenol have been reported to microbiologically promote the growth of Aspergiollosis fumigates [7]. That growth may reduce the protective function of the respiratory epithelium by paralyzing the cilia or by inducing soft tissue hypervascularization and oedema [8].

In this study, we compared different ways of diagnosis of allergic fungal sinusitis and sinus fungus ball disease and we further evaluated methods of treatment of both diseases.

Patients and methods

It is a prospective study carried out at ENT department, Sohag university hospitals, from March 2011 to January 2013. The study was approved from ethical committee and informed written consent was obtained from all the participated patients. Forty patients were included in the study underwent surgical removal of fungal contents from involved sinuses and creation a wide access to these sinuses for ventilation and postoperative care. Those patients were divided into two groups: group 1 (24 patients with AFS) and group 2 (16 patients with FB).

Preoperative evaluation was the same for all patients in both groups and included:

- Clinical evaluation: for nasal clinical presentation
- Radiological study: CT scans nose and paranasal sinuses
- Laboratory investigation
    - Total serum immunoglobulin E (LgE): Normal values are up to 200 IU/ml
    - Aspergillus fumigatus (AF specific IgE): The test was considered to be positive if the result ≥ 0.35 IU/mL
    - Aspergillus fumigatus (AF specific IgG) :> 12 U/ml was considered positive.
    - Skin prick test: The used antigens were Aspergillus fumigatus, Aspergillus flavus and Aspergillus niger.

Postoperative laboratory investigations

Biopsy, irrigation and aspiration are methods used in specimen collection from the nasal sinuses. The specimens collected were examined as follow:

- Histopathological examination of the excised fungal mass was performed for exclusion of tissue invasion by fungus
- Direct microscopic examination of specimen stained with fungal stain (Gomorimethenamine silver)
- Culture on Sabouraud's dextrose agar (SDA) with antibiotic supplemented medium

Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Science (SPSS) version 11(SPSS Inc., Chicago, IL., USA). The association and relationship between 2 qualitative variables were evaluated with Chi-square test. The results were expressed as the means and standard deviation for quantitative variables and as frequencies for categorical findings.To compare the means of 2 independent groups, Student's t test was used. All statistically significant P values were set at < 0.05.

Results

Forty patients with FRS in this study were categorized into two groups, Group A which include 24 patients with AFS (13men, 11 women) and group B which include 16 patients with FB (7 men , 9 women). The mean age± standard deviation (SD) for the group A was 26.98± 12.85 years while mean age ±SD for Group B was 41.69± 8.99 years and the difference between both groups was found to be significant difference (P< 0.05).

Atopy was assessed by the history of asthma, aspirin hypersensitivity and intolerance, level of serum total IgE, skin test reactivity and peripheral blood eosinophilia.

Using Chi square test, there were significant difference between both groups as regards total serum immunoglobulin E, Aspergillus specific IgE, Aspergillus specific IgG and skin test reactivity (P < 0.05) (Table 1).

Table 1. Atopic state among allergic fungal sinusitis (AFS) and fungus ball (FB) groups

	AFS	FB	P values
Asthmatic	6 (25%)	4 (25%)	0.640
Aspirin	2 (8.3%)	2 (12.5%)	0.529
Elevated total	16 (66.7%)	3 (18.5%)	0.003
Aspergillus specific IgE	14 (58.3%)	1 (6.25%)	0.001
Aspergillus specific IgG	11 (45.8%)	0	0.0005
Positive skin test	14 (58%)	3 (18.5%)	0.014
Peripheral blood eosinophilia	10 (41.7%)	6 (37.5%)	0.422

Clinical presentations and diseases laterality

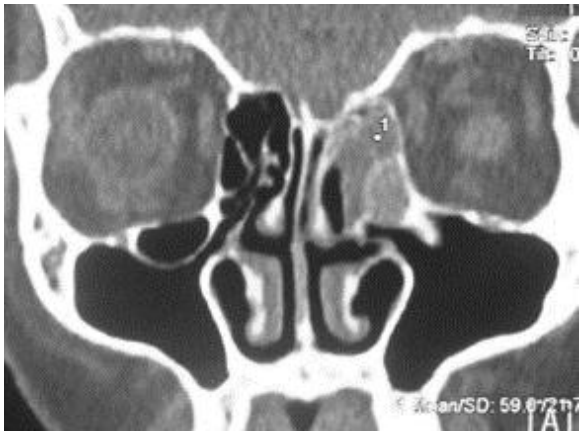
The clinical features depend upon the extension of the disease, involvement of orbital or intracranial structures and presence of the concomitant bacterial rhinosinusitis.

By using Chi square test for comparing AFS to FB group as regard clinical presentations: nasal polyps, cacosmia, previous endodontic treatment, previous sinonasal surgery, facial pain, and history of allergic rhinitis were founded to be of significant difference between both groups (Table 2).

CT scan findings

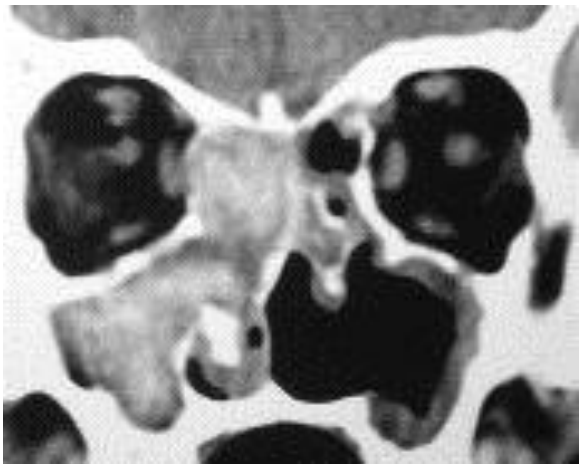
Solitary sinus affection is higher in FB group and showing significant difference between both groups (Fig 1). Ethmoidal, frontal, sphenoid sinus opacifications and bone erosion are more frequent in AFS group and shows significant difference between both groups (Figs 2,3). Metallic density is higher in FB group and showing significant difference between both groups (Table 4).

Figure 1



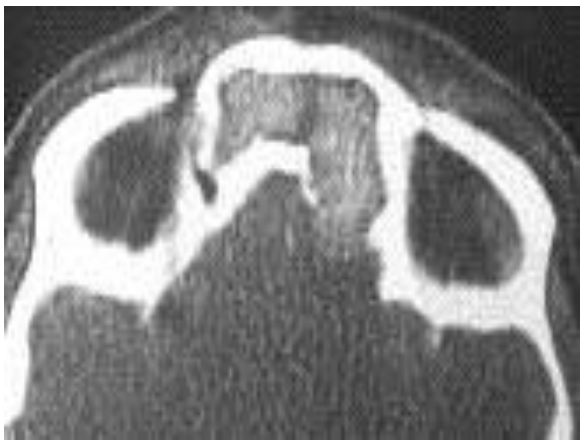
Coronal CT scan showing a heterogeneous opacity of the left ethmoid sinuses (fungus ball) without affection of the other sinuses

Figure 2



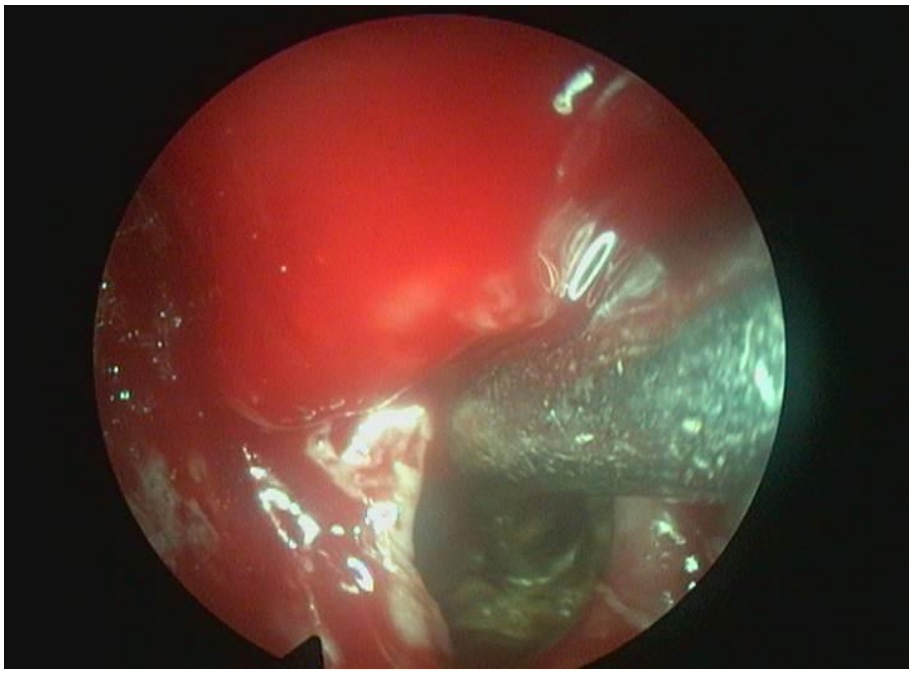
Coronal CT scans show expansion of the right ethmoid sinuses with increased attenuation in the right maxillary and ethmoid sinuses. There is characteristic hyper-attenuating material within these sinuses. Note also the smooth thinning of the lamina papyrecea, This patient had history of previous functional endoscopic sinus surgery for treatment of fungal sinusitis

Figure 3



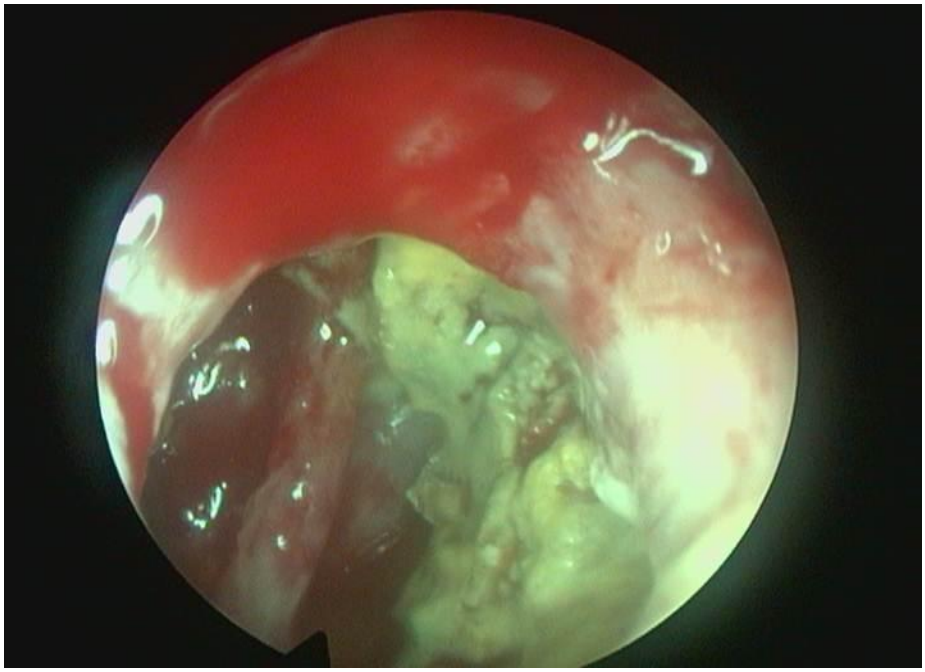
Axial CT scan shows expansion of and increased attenuation in both frontal sinuses with erosion of posterior table of the left frontal sinus

Figure 4



Endoscopic view of a case of allergic fungal sinusitis (after removal of extensive nasal polypi) showing the characteristic thick peanut-buttery tan to dark-green allergic mucin

Figure 5



Endoscopic view of a case of fungus ball showing swollen sinus mucosa with purulent discharge in the middle meatus.

Role of corticosteroid

Improvement occurred associated with decrease size of the polyps but without complete cure in 14 patients (58.3%) of AFT group while no improvement was observed in FB group (P = 0.0001).

Operative findings

Functional endoscopic sinus surgeries are usually far less damaging. The purpose of functional endoscopic sinus surgery is to remove the obstruction at the outflow tract of the sinuses while preserving all possible mucous membranes and all possible normal structures.

Operative details showed a distinct difference between groups, extensive polyposis and characteristic thick peanut-buttery tan to dark-green allergic mucin in all AFS patients (Fig4).

Swelling of the mucosa, purulent nasal discharges, a blocked ostiomeatal complex with purulent discharge in the middle meatus was found in all FB patients associated with unilateral nasal polyps in 3 patients of them (Fig5).

Histopathological Findings

By using Chi square test for comparing AFRS group to fungus ball group as regard histopathology and culture findings; eosinophilic mucin, eosinophils clustered in mucin, degenerating eosinophils in mucin, charcot-Leyden crystals in mucin and fungus seen on H&E stain were founded to be of significant difference between the two groups (Table 4).

Recurrence rate

Postoperative recurrence occurred in 9 patients (37.5%) with AFS while occurred in only 2 patients (12.5%) with FB and the difference was found to be significant (P value< 0.001).

Table 2. Allergic fungal sinusitis versus fungus ball as regard clinical presentations

Variables	AFS	FB	P value
Purulent nasal discharge	22 (91.7%)	14 (87.50%)	0.529
Chronic nasal obstruction	24 (100.0%)	14 (87.50%)	0.154
Facial pain	6 (25.0%)	11 (68.75%)	0.008
Post nasal discharge	18 (75.0%)	10 (62.50%)	0.309
Cacosmia	2 (8.3%)	9 (56.25%)	0.001
Headache	16 (66.7%)	8 (50%)	0.234
Nasal polyps	24 (100.0%)	3 (18.8%)	0.0001
History of allergic rhinitis	12 (50.0%)	2 (12.5%)	0.016
Previous endodontic treatment	3 (12.5%)	9 (56.25%)	0.005
Previous sinonasal surgery	13 (54.2%)	2 (12.5%)	0.008
Proptosis	5 (20.8%)	1 (6.25%)	0.212

Table 3 Allergic fungal sinusitis versus fungus ball as regard CT scan results

Variables	Allergic fungal sinusitis	Fungus ball	P value
Solitary sinus affection	0 (0%)	15 (93.5%)	0.0001
Maxillary sinus opacification	24 (100.0%)	13 (81.00%)	0.057
Ethmoidal sinus opacification	22 (91.7%)	2 (12.5%)	0.0001
Sphenoid sinus opacification	14 (58.3%)	1 (6.00%)	0.001
Frontal sinus opacification	16 (66.7%)	0 (0%)	0.0001
Bone erosion	11 (45.8%)	2 (12.5%)	0.029
Thickness or bone sclerosis	9 (37.5%)	6 (37.50%)	0.083
Heterogeneous opacities	17 (70.8%)	13(81.25%)	0.360
Metallic density	6 (25.0%)	11(68.75%)	0.008

Table 4 Allergic fungal sinusitis versus fungus ball as regard histopathology and culture findings

Variables	Allergic fungal sinusitis	Fungus ball	P value
Eosinophilic mucin	24 (100.0%)	0 (0%)	0.0001
Eosinophils clustered in mucin	14 (58.3%)	0 (0%)	0.0001
Degenerating eosinophils	17 (70.8%)	2 (12.5%)	0.0001
Charcot-Leyden crystals	22 (91.7%)	1 (6.00%)	0.0001
Eosinophils in mucosa (>10/hpf)	14 (58.3%)	6 (37.50%)	0.167
Plasma cells in mucosa (>10/hpf)	19 (79.2%)	16(100.00%)	0.065
Fungus seen on GMS stain	19 (79.2%)	13 (81.00%)	0.601
Positive culture	13 (54.2%)	9 (56.25%)	0.578

Discussion

AFS and FB are two categories of FRS occurred in immunocompetent patients but each has different aetiopathology. According to that the lines of management are different in both categories. This study and compare the frequency of symptoms, signs, CT findings, laboratory findings and recurrence rates between AFS and FB patients.

All patients with AFS were young with a mean age at presentation 26.9 years while in FB patients the mean age was 41.68 years.

Zakirullah et al [9]. reported that mean age of AFS at presentation was 20 years and Montone et al [10]. founded that in FB group mean age was 55 years. Pierre and Rainer [11] reported that FB is mostly encountered in older individuals with an average age at presentation being 64 years and added that no case has been reported in young children.

Regarding sex distribution, in AFS group we had slight male predominance. This is in agreeing with other reports [12,13]. In our study, the FB had a female predominance; (62.5%) were females and (37.5%) were males which match with other studies [10,14,15] but the reason of this phenomenon is still unknown.

Association with asthma, aspirin sensitivity, skin test, peripheral blood eosinophilia, and total IgE were compared between both groups. AFS Group had more presentation but with statistically insignificant difference to FB group in relation to asthma, aspirin sensitivity, and peripheral blood eosinophilia. The significant differences were founded in elevated total IgE, Aspergillus specific IgE, Aspergillus specific IgG and positive skin test reactivity; these results confirmed that AFS is related to atopy. cheng et al [16] showed statistically insignificant difference among AFS and FB group in relation to asthma, aspirin sensitivity, and total IgE. The only significant issue was the positive skin test reaction. Atopy in FB group is not more frequent than in general population. Skin test for fungi and fungal specific IgE are usually negative while Goldstein et al [17] reported history of atopy in one third of AFS patients.

Nine patients (56.25%) had history of endodontic treatment In FB group with a statistically significant difference from patients with AFS.

Ga Young et al [18] reported also significant difference between both groups as regard endodontic treatment on maxillary teeth.

Nasal obstruction, discharge, postnasal discharge, and headache were predominant symptoms in both groups. Cacosmia and facial pain showed higher incidence in FB than in AFS patients with statistically significant difference. Proptosis was present in 5 patients (20.8%) in AFS group while occurred in one patient of FB group. These results are close to the results of deShazo et al [2] who stated that proptosis is a rarer clinical presentation in FB patients. Thahim et al [13] and UR Rehman et al [19] founded proptosis in (20%) and (33.3%) respectively of AFS cases. Zakirullah et al [9] reported a high incidence of proptosis in AFS (78%), in the contrary to Zubair et al [20]. reported a low incidence (8%).

Polyps were presented in all patients of AFS group and 18.8% of patients with fungus balls. Klossek et al [21] reported that 10% of his FB patients had polyps.

Nasal polyps were also found in all patients with AFS in other studies [22-24].

CT scan is of great value in comparing AFS and FB groups. It revealed that both and solitary sinus affection and metallic density were significantly higher in FB group compared to AFS group. On the

other hand ethmoid, frontal, sphenoid sinus opacification and bone erosion were significantly frequent in AFS group. In AFS group, (70.8%) of patients had double density sign, (45.8%) of patients had pressure erosions, most commonly of the intra-ethmoidal septae and the medial wall of the maxillary sinus. Erosion of the lamina papyracea was seen in (20.8%) of patients and intracranial involvement in (4.2%) of patients. The incidence of erosion in AFS patients was in accordance with many published reports [25, 26]. Houser and Corey [24] described bone erosion in only (20%) of patients in a literature review.

Although these findings are not specific for AFS, they remain relatively characteristic of the disease and may provide preoperative information which supports the diagnosis of AFS. The most common observation in CT scan of patients with FB was Heterogeneous opacities (81.25%) with metallic density in (68.75%). These focal hyperattenuations formed by tertiary calcium phosphate or calcium sulfate and are deposited in the necrotic regions of the mycelium. They assume that these radiographic signs are a result of the mycotic metabolism and correspond to "Aspergilloma" masses or fungus balls [27-29].

Similarity of these substances to zinc oxide contained in the root filling material iatrogenically placed endodontic materials was detected [30].

The current study also provides additional insight into the morphologic spectrum for AFS. It confirms the previous reports that AFS is characterized by a special type of mucin, termed “allergic mucin.” Allergic mucin was founded in all cases of AFS. The mucin contained Charcot-Leyden crystals in 22 patients. These findings are in agree with other studies [10,31].

In FB group eosinophilic mucin or eosinophils clustered in mucin not detected, Charcot-Leyden crystals in mucin were present in one case and degenerating eosinophils in mucin were noticeable in two cases. Comparing AFS group to FB group as regard eosinophils in histopathological examination, there is significant difference between the two groups.

In AFS positive microscopic fungal hyphae in (79.2%), fungal cultures were positive in (54.2%). Positivity for fungi by microscopic and culture methods were reported to be (70.0%) and (40.0%) of AFS patients respectively [22].

In FB group positive histologic fungal hyphae were founded in (81. 25%), fungal cultures were positive in (56. 25%). Another report of positive histologic fungal hyphae in (93.6%), and positive fungal cultures in (32.1%) is present [14].

This discrepancy between microscopic examination and fungal culture has been thought to be due to occasional entrapment of the fungal hyphae in the mucus, preventing contact with the culture media or tissue sample processing such as cut into small pieces, may cause negative effects on viability of fungi so they cannot grow well, it seems. But the digest of tissue by the digestive reagents makes appropriate condition to reveal fungal elements in direct examination. In addition, it is suggested that released proteins by eosinophils in mucin are toxic for fungi in tissue.

Postoperative recurrence occurred in 9 (37.5%) patients with AFS which is significantly higher than in FB group. these results are matching with Telmesani LM [32] who reported that the rate of recurrence in AFS patients was 54.5% and Vennewald et al [33] who stated that recurrence is rare in FB group.

In conclusion, Both AFS and FB are two categories of fungal sinusitis affect immunocompetant patients but each has different aetiopathology and accordingly different management.

Through bacteriology, immunology and CT-scanning it is possible to reach a proper diagnosis and accordingly to start a suitable treatment. A combination of surgical debridement and medical treatment consist of antiallergic drugs is the treatment of choice in AFS while surgery remains the mainstay of treatment for FB without need for medical treatment.

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