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Allergic Fungal Rhinosinusitis in Baquba

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Abstract

Background: Allergic fungal rhinosinusitis (AFRS) was a unique variant of chronic rhinosinusitis. It is one type of fungal rhinosinusitis which is divided into invasive and non invasive disease. It has variable modes of presentations and managements. It represents a challenge in diagnosis and management and have high rate of recurrence.

Objectives: To enhance the diagnostic ability for AFRS by clarifying its common presentations and to declare the role of local and systemic steroids in decreasing the rate of its recurrence.

Design: A prospective study.

Setting: Department of Otolaryngology Head and Neck Surgery. Baquba Teaching Hospital, Diyala, Iraq.

Patients: Forty patients with chronic rhinosinusitis with and without nasal polyps attending consultation unit of E.N.T from January 2019 to July 2020.

Methods: Patients were evaluated by thorough history and examination of nose and paranasal sinuses. Demographic and clinical

characteristics were gathered using a predesigned questionnaire form which include gender, age, residency, occupation and main symptoms as nasal obstruction(unilateral or bilateral), nasal discharge (anterior and posterior),facial pain and headache, sneezing, loss or decrease of smell, snoring and epistaxis. Past surgical history of nose as nasal polypectomy either endoscopic or conventional surgery. Past medical history of allergic rhinitis and asthma and other types of allergy recorded. Investigations that include plain sinus x- ray and computed tomography (CT) scan of nose and paranasal sinuses for all patients. Skin test for fungal antigen done for all patients. Histopathological and fungal study was also done for materials removed surgically. The patients received systemic steroid therapy as prednisolone tablet in high doses pre and post operatively and local steroid such as mometasone or fluticasone nasal spray with antifungal (fluconazole) for few months. All patients required surgical treatment by endoscopic surgery in E.N.T. department.

Results: Most patients were below the age of thirty (28=70%). There was an equal incidence in males and females 1:1.Most common symptom was nasal obstruction in all patients, unilateral nasal obstruction (24=60%) and bilateral in others, followed by nasal discharge(70%), sneezing (70%), anosmia and hyposmia (70%), facial pain (40%), and snoring. Nasal polyp was the most common sign (32=80%) with half of them in unilateral site and other half in both nasal cavities, post nasal drip(40%) and orbital proptosis (10%).Majority of patients had association with allergic history as allergic rhinitis and asthma (28=70%). All the patients required surgical debridement (100%) and prolonged systemic and local steroids to decrease recurrence.

Conclusion: Diagnosis and management of allergic fungal sinusitis represent a continuous clinical heath problem. CT scan is important for the diagnosis of AFRS. It is a disease of young immunocompetent patients with equal sex predominance and multiple recurrences. Prolonged local and systemic steroid therapy and adequate surgical debridement is crucial to decrease recurrences.

Keywords: Chronic Rhinosinusitis (CRS), Allergic Fungal Rhinosinusitis (AFRS), Allergic Mucin, Nasal polyp, Type 2 inflammation, type 1 hypersensitivity, Eosinophilic mucin

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Introduction

Allergic fungal rhinosinusitis (AFRS) is an increasingly recognized type of chronic rhinosinusitis (CRS).It was reported as distinct clinical entity in 1976 [1,2].The incidence of AFRS is estimated at 5-10% of patients with CRS who had surgical treatment [3-6]. It is possibly defined as non-invasive type of fungal rhinosinusitis; represent an allergic hypersensitivity response to the presence of fungi in sinuses, possibly similar to allergic bronchopulmonary aspergillosis (ABPA). [7-9] also defined as an immune competent patient with allergy to fungus. [10,11]. Patients usually have association with asthma, allergic rhinitis, eosinophilia, and increased total and fungus-specific IgE levels in blood.[12-15]The involved sinuses contain greenish black or brown muddy secretions known as (allergic mucin) and eosinophils, Charcot-Leyden crystals, debris and few fungal hyphae. For diagnosis of allergic fungal rhinosinusitis, presence of allergic mucin is important.[16-19]The most common fungi reported are dematiaceous species (Bipolaris, Curvuluria, Alternaria) and rarely aspergillosis.[20,21].

Bent and Kuhn described their diagnostic criteria (Table-1) based on histologic, radiographic and immunologic characteristics of the disease. [2,3,8,22]. Patients should meet major criteria for diagnosis which includes: presence of type 1 hypersensitivity by history, skin test or invitro test; nasal polyposis, characteristic CT scan finding, presence of eosinophilic mucin without invasion and the fungal stain of sinus contents removed by surgery.

Minor criteria used for enhancing the diagnosis of AFRS includes history of asthma, unilateral predominance, radiographic bony erosions, fungal culture, presence of Charcot-Leyden crystals in surgical specimen and serum eosinophilia.[2,3,8]

Clinically, most patients are in young age group (approximately 30 years of age), either male or female [23,24]. Usual presentation was bilateral, or unilateral nasal polyps with complete heterogeneous opacification of sinus cavities on CT scan associated frequently with bone expansion, although expanding inflammatory lesion are common

and highly suggestive of fungus, no direct invasion of dura or periorbit is seen. [9,10,13]The presence of hyphae in the mucin associated with eosinophilia is one of major criteria for diagnosis. Culture is necessary to identify the actual fungal agent but no growth is frequently observed. Type 1 hypersensitivity test or skin test appears to be minimal allergy test to perform for diagnosis. [4,5,7]

Table -1. Bent and Kuhn Criteria for diagnosis of AFRS

Major	Minor
Type 1 hypersensitivity	**Asthma**
Nasal polyposis	**Unilateral disease**
Characteristic CT finding	**Bone erosion**
Eosinophilic mucin without invasion	**Fungal cultures**
Positive fungal stain	**Charcot-Leyden crystals**
	Serum eosinophilia

Other investigations, such as total eosinophil count, total serum IgE, antigen specific IgE or IgG (if available), are suggested to reinforce the diagnosis. [18,25] IgE levels are frequently higher than in normal population. Allergic rhinitis is generally more frequently found in cases of AFRS. [13,26] Treatment is controversial but the removal of all mucin is crucial to decrease recurrence.[14-16] Prednisolone is the oral steroid most frequently given mainly postoperatively. Topical intranasal steroid given for long periods.[25,27] Topical and systemic antifungal therapy are not actually considered as sufficiently efficacious in this condition.[5,7,28] Immunotherapy trials after complete removal of allergic mucin by giving fungal antigen and positive non fungal antigen in weekly injections for 1 year was also used.[16,17,29,30]

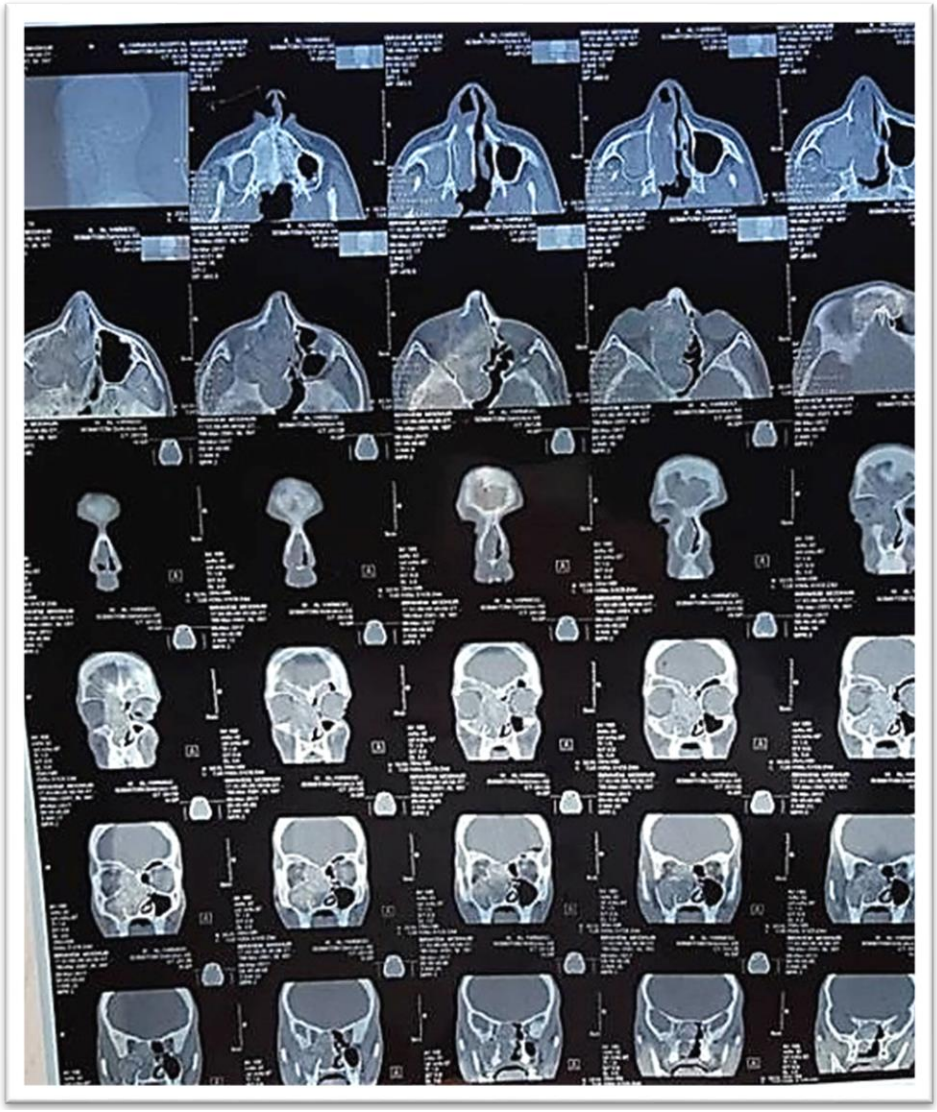

Figure- 1: CT-scan of nose and paranasal sinuses (axial and coronal views) of one of our patients showing unilateral heterogeneous expanding opacity with bone erosion (Characteristic for AFRS) involving all the right sinuses in previously operated patient.

Patients and methods

A Prospective study of 40 cases with AFRS was done in Otolaryngology Department in Baquba Teaching Hospital, Diyala Governorate, Iraq, from January 2019 to July 2020. All patients were subjected to thorough history, examination and investigations include CT scan of nose and paranasal sinuses and skin test. Questionnaire designed include age, sex, occupation, residence, chief complain and duration, other symptoms as nasal obstruction (unilateral or bilateral), nasal discharge (anterior, posterior), facial pain and headache, sneezing, loss of smell (partial or complete), epistaxis and snoring. Past medical history of bronchial asthma, allergic rhinitis, and other types of allergy as for drugs. Past surgical history of nasal surgery, nasal polypectomy endoscopically or by conventional approach. Social and family history of asthma or other type of allergy.

Otolaryngological examination in consultation department includes nasal patency, state of nasal mucosa and turbinate, nasal polyp probing looking for site of origin if possible and tenderness over sinuses, post nasal drip and examination by rigid endoscope. Investigations includes sinus x ray (Waters view), computerized tomography scan of nose and paranasal sinuses in axial and coronal view showing unilateral or bilateral heterogonous soft tissue opacity, expanding, with bone erosion but no invasion to surrounding tissues. It involves mainly maxillary and ethmoidal sinuses followed by frontal and sphenoid sinuses.

Skin test for allergy to fungus, fungal staining and histopathological study was done for specimens removed surgically. Diagnosis of AFRS for these patients depending on Bent and Kuhn criteria. All patients should meet the major criteria for diagnosis, while minor criteria used to support diagnosis. Medical treatment by topical and systemic steroids for all patients in the form of mometasone nasal spray twice daily for one month and maintenance dose once daily for 3-6 months postoperatively and prednisolone tablets 5 mg in scheduled dose for one month pre operatively and post operatively for 1-2 months depending on response of patients, oral antifungal as fluconazole capsule also used. Surgical treatment by functional endoscopic sinus surgery for most of the patients includes nasal polypectomy, good debridement of allergic fungal mud, uncinectomy, middle meatal antrostomy, anterior ethmoidectomy,

posterior ethmoidectomy, and in some patient's frontalrecess widening, and sphenoidotomy depending on extension of disease pathology. Patients were followed up post operatively for 6 months.

Results

In this study the male to female ratio was equal 1:1 20 males and 20 females. Age range from 9-60 year and majority of them was below thirty (70%). Residency of patients equally distributed between rural and urban areas. Presentations of allergic fungal sinusitis(AFRS) (Table-2): All patients had nasal obstruction, unilateral in(24=60%) and bilateral in(16=40%).All had nasal discharge either anteriorly in(28=70%) or posteriorly as post nasal drip in (16=40%).Alteration of smell was complete loss (anosmia) in (8=20%) and partial in (20=50%).Sneezing and history of atopy and allergic rhinitis was seen in(28=70%). Unilateral nasal polyp was seen in (16=40%), and bilateral in (16=40%) and no polyp in (8=20%). More than 70% had history of previous polypectomy or recurrence. Association of bronchial asthma in (8=20%), allergic rhinitis in (28=70%) and allergy to penicillin in (8=20%).

Characteristic Radiological finding in CT scan seen as heterogeneous soft tissue opacity with bone erosion and expansion was unilateral in (24=60%) and bilateral in (16=40%).All patients were treated with oral and systemic corticosteroids and antifungal orally. Surgical debridement done for all patients as functional endoscopic sinus surgery (FESS). Histopathological study done for surgical specimens grossly show clay-like mucinous material green, brown, or grayish color in all cases (100%). Microscopically showed fragments of edematous respiratory mucosa containing a mixture of acute and chronic inflammatory cell infiltrate , abundant basophilic mucin with laminated appearance of mixed infiltrate mainly eosinophils, necrotic debris, Charcot- Leyden crystals seen in all patients also(100%). Fungal staining of materials was positive in all (100%).

Discussion

This study revealed equal sex distribution in males and females, 20 males and 20 females 1:1 ratio. Torres – etal studied 16 cases of AFRS and found male predominance (10 male and 6 females) [21], while Sohail etal in a study of 32 cases recorded female predominance (11 males and 21 females). [22]Ponikau et al reviewed

200 consecutive cases of chronic rhinosinusitis requiring surgery and found 14 cases (7%) of them were AFRS with equal male to female ratio. [18]

Table- 2 Symptoms and Signs of Allergic Fungal Rhinosinusitis (AFRS)

Symptoms & Signs	Number	Percent %
Unilateral nasal obstruction	**24**	**60**
Bilateral nasal obstruction	**16**	**40**
Nasal discharge	**28**	**70**
Post nasal drip	**16**	**40**
Partial loss of smell	**20**	**50**
Anosmia	**8**	**20**
Snoring	**40**	**100**
Sneezing	**28**	**70**
Facial pain	**16**	**40**
Unilateral polyp	**16**	**40**
Bilateral polyp	**16**	**40**
Orbital proptosis	**4**	**10**
Previous surgery	**28**	**70**

Age range from 9 to 60 year, most of the patients is in second decade of life and 70% are below age of thirty. 20% was less than 10 years, 30% was between 20-29 years, 10% between 30-39 years and 20% was more than forty , so the peak incidence in age group 10-19 years. In Torres etal study (11 patients from16 =75%) were under the age of thirty. [21] Sohail etal noticed 21 of 32 (65%) were below the age of thirty [22], so it is a disease of young age. Residency of patients with AFRS was equally distributed between rural (50%) and urban (50%) areas. [28]

All patients have nasal obstruction; it was unilateral in (24 =60%) and bilateral in (16=40%). Most of studies revealed that AFRS was unilateral which is consistent with this study.[2,3,21,26] Rhinorrhoea seen in 70%,post nasal drip 40%, facial pain 40% and

loss of smell was complete in 20 % and partial (hyposmia) in 50 %. Sneezing present in 70% of cases. High number (28=70%) had multiple recurrences and previous polypectomy. Most frequent sign was nasal polyp (32=80%) either unilateral or bilateral involvement equally. Orbital proptosis was seen in 10 % of patients. Snoring occurred in almost all patients 100%. Bent and Kuhn described unilateral predominance in their minor criteria [2,3,8] while Bradly and Marble found (51%) of bilateral disease in 45 cases.[7,27]. Torres et al showed the same observation that the most frequent symptom was nasal obstruction and discharge which occurred in all cases with bilateral involvement more than unilateral one.[21,28] Sohail et al revealed also nasal obstruction as main symptom for prolonged periods of at least 6 months but with unilateral predominance(22 of 32=69%) [22,26], and this agree with our study. He also noticed the multiple recurrences which occurred in 8 of 32(25%) patients despite of medical and surgical treatment, this also agreed with this study which revealed past surgical history as polypectomy in 70 % of patients. Torres etal also found recurrences in 4 cases at 8, 11, 12, and 18 months after the initial surgical procedure. [21]

Majority (70%) of cases had allergic rhinitis and 20% had bronchial asthma and family history of atopy. Family history of asthma or allergic bronchitis seen in 30%, history of smoking in 20 %, also 20 % had allergy to drugs mainly for penicillin or aspirin. In Torres etal study 6patients had history of atopy seen in 3 as allergic rhinitis and 3 as asthma [21,29]. Sohail etal showed that most of patients had elevated IgE levels especially with those having recurrences.[22] All patients are immunocompetent and did not have diabetes mellitus as in other studies.[8,18,30] However ,significant association was seen with occurrence of type 1 hypersensitivity reaction ($p < 0.001$), Charcot- Leyden crystals ($p<0.001$), bony erosion ($p<0.05$-0.001) and heterogeneous opacity and sinus expansion ($p<0.05$-0.001) in this cases.[17,31]

Plain x ray of sinuses and computed tomography scan of nose and paranasal sinuses showed mainly unilateral or bilateral soft tissue heterogeneous mass involving mainly ethmoidal sinuses followed by maxillary and sphenoid. [2,3,8,13,32]. Hetrogeneousity may be attributed to Charcot-Leyden crystals in dead eosinophils or iron deposit in allergic mucin.[33,34] Variable degree of bony erosion but

without destruction or invasion also seen.[2,13,24,34] We found 70 % of cases had bone erosion in this study. CT scan is an important tool in diagnosis and is one of major diagnostic criteria in AFRS by characteristic heterogeneous opacity with bone erosion but without destruction [13,19,35] Torres et al mentioned that radiological study using CT scan and MRI showed soft tissue masses occupying the nasal cavity or multiple paranasal sinuses in all cases.[21] In 12 of 16 cases, bone erosion, including three cases with destruction of the clivus was reported. Sinus involvement was unilateral in 7 of 16 and bilateral in the remaining 9 cases. [21] This agreed with our study which found bony erosion in 70% of cases. It is also important in staging of the disease and need and type of surgical procedure required. [17, 23,32] It can detect early recurrences and response for medical therapy. [18,24,35]

In the form of local and systemic steroids mainly prednisolone in tapered dose for at least 1 month for all cases and some of them 60% offered ketoconazole (antifungal) tablet both pre and post operatively.[33,34,35] Sohail etal stated that corticosteroids , antifungal and immune therapy have been used as post operative medical treatment.[22] Most of studies prefer systemic steroid over nasal spray to decrease the recurrences.[14,17,25] Kinsella found a very high rate of recurrences when nasal steroid spray was used as the sole post operative therapy.[6,18] In Sohail et al study 32 cases 15 of them received nasal steroid spray and 17 received systemic steroid as post operative medication. [22] The incidence of recurrence was 4 in each group. Torres et al stated that recurrence is related to impacted allergic mucin and state of aeration of diseased sinuses .[21] Systemic steroid had been used successfully in cases of recurrent AFRS but their potential side effects limits their use.[25,32] Systemic antifungal are of no effect in non invasive fungal sinusitis.[19,33,35] However topical antifungal irrigation may play a role in eliminating residual fungal antigens, although no data available regarding efficiency of its clinical use.[15] Surgical treatment in the form of endoscopic sinus surgery by removing of nasal polyp and clearance of muddy tenacious material carefully and thoroughly with subsequent aeration of sinuses by widening of maxillary ostium was associated with good prognosis and low recurrences.[10,13,28] Bradly et al felt that inadequate initial surgery was an important contributory factor for recurrence in their

cases.[8,12] Recurrences are common in AFRS, although no large prospective study of long term results have been performed 5 of 8 patients of Torres et al with at least 6 months of follow up developed one or more recurrences from 8 months to 4 years after initial surgery.[20,21] This agree with this study which show multiple recurrences in 70% of cases. Sohail et al mentioned that surgery play an important role in the treatment of this disease.[22]This should include opening and if necessary widening of ostium of involved sinuses and complete removal of inciting fungal mucin, which should achieve long term postoperative drainage and ventilation of involved sinuses.[3,26]

Detection of fungal elements in allergic mucin is crucial factor in the diagnosis of AFRS in spite of the difficulty to demonstrate fungal hyphae because of small number. [8,19] Histopathology of materials removed from nose and sinuses was similar. In all cases 100% it consist of fragments of edematous respiratory mucosa containing a mixture of acute and chronic inflammatory cell, abundant basophilic mucin with laminated appearance that consist of densely packed bands of mixed inflammatory cell infiltrate predominantly eosinophils, necrotic debris, sloughed respiratory cell, and Charcoal-Leyden crystals. [3,7,31] Fungal study in all patients 100% showed scattered fungal hyphae within the mucin in all cases. They were identified by GMS stained sections in all cases and also by Fontana-Masson stains in 70 % of cases.[18,26] However, the Fontana-Masson stain showed a clearer background and identified fungal organisms better and more easily than GMS stain.[20,31] The fungal hyphae showed dichromate branching at 45- degree angles and moderately irregular contour.[5,27,29]

Conclusion and Recommendations

Allergic fungal sinusitis is a disease of young age which equally affects both sexes and associated with atopy in immunocompetent patients in most cases. CT scan is an important diagnostic tool. It needs prolonged steroid therapy as main treatment option in addition to good surgical debridement to decrease recurrence. We recommend doing more studies in this subject to enhance diagnostic ability and decreasing recurrences.

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