

## **Is the Classical Classification of Aspergillosis of the Paranasal Sinuses to non invasive and invasive still valid or not ?**

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**Background:** Is the classical classification of Aspergellosis of the Paranasal Sinuses to non-invasive and invasive still valid or not?

**Aim:** To modify the classification system to non-invasive-semi-invasive and invasive.

**Method:** From 1998 to 2000, thirty two patients with the diagnosis of allergic chronic sinusitis were admitted for surgical treatment. Five have Allergic Aspergillus Sinusitis (AAS). They were treated by Surgery (FESS) combined with antiallergy and systemic antifungal chemotherapy (Itraconazol) regimen. Their follow up ranged from 6 to 23 months.

**Results:** All the five cases showed enough evidence to be diagnosed as AAS and all of them showed clinical, radiological and surgical evidence to be classified as semi-invasive. All responded very well to surgical and medical treatment.

**Conclusions:** Classification of fungal sinusitis should be made mainly based on clinical presentation radiological and surgical finding and not based on Histopathological findings only. Surgical debridement of the disease in combination with systemic antifungal treatment are the most effective treatment modality.

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Aspergillus species is the most common fungal infection of the Paranasal Sinuses. The causative organism is a spore-forming filamentous fungus which occurs as saprophyte in soil and decaying vegetable matter and is spread by airborne transmission<sup>1</sup>. Aspergillus is recognized histologically by its septate hyphae, which branches at 45<sup>0</sup> angle and produces asexual conidia. The three species which are most commonly implicated in human pathogenicity are Aspergillus Fumigatus, Aspergillus Flavus and Aspergillus niger<sup>2</sup>. The most common isolated organism is Aspergillus Fumigatus. Al Bhalal et al found that the most common organism in the

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Western and Eastern part of the Saudi Arabia was *Aspergillus Flavus*<sup>2</sup>. Another study from the Western part (Jeddah) showed isolation of *Aspergillus Fumigatus* in five cases<sup>3</sup>. Paranasal sinuses Aspergillosis is usually classified into four types; allergic, non-invasive (aspergilloma), invasive and fulminant<sup>2,4</sup>.

Through bacteriology, histopathology, CT-scanning and MRI imaging, it is possible nowadays to reach a reliable diagnosis, a proper classification and accordingly to start a proper treatment. The treatment regimen is usually a combination of surgical debridement and medically consist of antiallergy and/or antifungal<sup>1</sup>.

The following case reports discuss the presentation and management of AAS. The correlation of the different variables which may support our aim. The aim of our study is to modify the old traditional classification system to a more flexible and applicable one as follows: non-invasive, semi-invasive and invasive.

## **METHODS**

Between January 1998 and January 2000, thirty two patients with the preliminary diagnosis of chronic sinusitis have been admitted to the ENT- ward for surgical treatment. Five (15.6%) have been diagnosed as having “*Allergic Aspergillus Sinusitis*” (AAS). Patients history of allergy has been taken. ENT examination including endoscopy of nose and paranasal sinuses (PNS) have been performed. All patients have been screened for allergy including total IgE, nasal smear and blood eosinophilia. The patients had CT-scanning of their sinuses in axial and coronal projection pre-operative. MRI have been ordered selectively. All patients went through a regular endoscopic/ microscopic follow up. Follow up CT scanning was performed at the end of the 6 month follow up period.

Follow up ranged between 6-23 months. Liver, kidney function and CBC were monitored during the antifungal treatment. Report of 5 patients with AAS as follows:

### **Case 1**

A 10 year-old Teritrean male presented to the OPD complaining of right nasal obstruction, headache, postnasal discharge, occasional epistaxis, allergic symptoms and right proptosis of two years duration. No past-history of operations. On examination, there were multiple pale polyps in the right nasal fossa with intact mucosa. Posterior rhinoscopy showed fullness in the right posterior choana. Right proptosis was noticed with broadening of the nasal dorsum and fullness in the right cheek.

CT scan of the paranasal sinuses showed soft tissue mass filling the right nasal fossa, right ethmoid and sphenoid sinuses with hyperdense shadows, The right lamina papyracea was eroded and was pushed laterally causing his proptosis.

Laboratory tests showed normal CBC with mild eosinophilia (9.3%), normal liver function test and increased IgE (205 IU). This patient underwent right intranasal polypectomy followed by endoscopic sphenoidectomy. Both sinuses were filled

with cheesy material of necrotic tissue characteristic of fungal infection. The medial wall of the maxillary sinus was destroyed.

Histopathology revealed polypoidal masses covered by intact respiratory epithelium, edematous stroma filled with inflammatory cells and eosinophils, no fungal hyphae were seen.

Post-operatively, the patient received prednisolone in tapering dose and Itraconazole 200 mg daily for 6 months without side effect to liver. CT scan after 6 months showed well aerated sinuses. (Fig. 1)

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*Figure 1. Soft tissue occupying sinuses with hyperdense shadow, bony expansion and lateral push of lamina papyracea*

## **Case 2**

Sixteen years old Saudi female presented to OPD complaining of bilateral nasal obstruction, left proptosis, headache, loss of smell and allergic symptoms (rhinorrhea, itching and excessive sneezing). He had positive history of intranasal polypectomy one year ago. On examination, there were multiple bilateral pale nasal polypi, with left mild proptosis.

Laboratory test showed normal CBC with normal eosinophil count, normal liver function and moderately increased IgE. CT Scan of the paranasal sinuses showed absent frontal sinuses, soft tissue mass filling all the sinuses with hyperdense shadows. Medial wall of the maxillary antrum and the septae between the ethmoid air cells were eroded.

The patient underwent endoscopic sinus surgery of the sinuses with middle meatus antrostomy. During the procedure, the ethmoid and sphenoid sinuses were expanded and filled with polyps and chocolate brown necrotic tissue.

The histopathology revealed allergic polyps with eosinophils, inflammatory cells and fungal hyphae confirming the diagnosis of Allergic Aspergillus sinusitis. Post-operatively patient received Itraconazole 200 mg daily for 6 months and prednisolone in tapering dose. The first post-operative visit showed clear nose and sinuses by endoscopy. No polyps or adhesions could be seen. Liver function tests showed mild increased LDH up to 237 units at the beginning of the treatment. Four month post-operatively a small residual polyp was removed in the OPD. Post-operative CT at sixth month showed patent nose and well aerated sinuses (Fig.2).

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*Figure 2. Bone destruction of lateral nasal wall, cribriform plate and lamina papyracea.*

### **Case 3**

Thirty year old female patient was complaining of right nasal obstruction, headache, postnasal discharge and allergic symptoms. On examination, she had bilateral nasal polypi, more on the right side than the left. She had several operations of intranasal polypectomy, external fronto-ethmoidectomy and Caldwell-luc operation 5 years ago.

Laboratory test showed increased IgE (268 IU), hypochromic microcytic anemia and normal eosinophil count. Her liver function tests were within normal limits.

CT scan showed soft tissue with hyperdense shadows mainly in ethmoids and frontal sinuses pushing the lamina papyracea laterally and causing proptosis. There was bony destruction in the lamina with mild extension into the orbit. A destruction in the roof of the posterior ethmoid (Arrows) and in the antrum medial wall were seen. Patient underwent endoscopic ethmoidectomy with clearance of the frontal sinuses and middle meatus antrostomies. The cavities of the previous operation was filled with fungal sludges.

Histopathology showed allergic nasal polyps with edematous stroma, many eosinophils and septated fungal hyphae consistent with Allergic Aspergillous sinusitis. The patient was put on tapering dose of prednisolone and Itraconazole 200 mg daily for 4 months and was free of recurrence for 2 year. (Fig. 3)

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*Figure 3. Bony expansion and lateral push of lamina papyracea causing proptosis.*

#### Case 4

A 20 year old Saudi male patient presented to our clinic complaining of bilateral intermittent nasal obstruction of 6 months duration, nasal discharge, occasional Epistaxis and left proptosis. Examination showed bilateral multiple pale nasal polyps, with intact mucosa, post nasal thick discharge and left moderate proptosis.

Laboratory tests showed markedly increased IgE (2322) and eosinophilia with normal CBC. Liver function tests showed increased hepatic alkaline phosphatase. CT scan showed soft tissue filling and expanding the frontal, ethmoid and maxillary sinuses with hyperdense shadows. There was dehiscence of the left lamina papyracea with bulging of the soft tissue inside the left orbit pushing the globe anteriorly and laterally causing proptosis. There was bony destruction of the lateral wall of the nose.

The patient underwent endoscopic surgery of the sinuses. The left lamina papyracea was dehiscent mainly posteriorly but the orbital periostium was intact. Necrotic greenish muddy material were found in the sinuses.

Histopathology examination of the surgical specimens showed allergic polyps with edematous stroma and eosinophils infiltration and fungal hyphae consistent with allergic fungal sinusitis.

Post-operatively, the patient received prednisolone in tapering dose and itraconazole 200mg per day for one month. The liver function was not affected with the treatment. CT scan done six months post-operative showed clear well aerated sinuses (Fig. 4).

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*Figure 4. Histology of tissue showing normal respiratory epithelium, stroma invaded by eosinophils and fungal hyphae black stained and branching at 45<sup>0</sup>*

#### Case 5

Eighteen years old Saudi female presented to the clinic with bilateral nasal obstruction, headache, loss of smell, allergic symptoms and left proptosis.

On examination, she had bilateral multiple nasal polyps with intact mucosa and moderate nasal mucoid discharge. Laboratory test showed increased IgE (762 IU) and normal liver enzymes. Her CBC showed hypochromic anemia with normal eosinophilic count. CT scan of the paranasal sinuses showed soft tissue, with hyperdense areas filling the frontal, ethmoid and left sphenoid sinuses. The sinuses were expanded and the lamina papyrae was pushed laterally causing proptosis. There

were bony destruction of the ethmoid sinus septae and medial wall of the maxillary sinus.

She underwent bilateral endoscopic speno-ethmoidectomy with middle meatus antrostomy. The expanded sinuses were filled with muddy necrotic tissue.

Histopathology revealed allergic polyps covered with respiratory epithelium, stromal edema, eosinophil infiltration and septated fungal hyphae; a picture consistent with allergic aspergillus sinusitis.

Post-operative medications included prednisolone in tapering dose, and Itraconazole 200 mg per day for 6 months. Six months post-operative CT scan showed clear well aerated sinuses (Fig. 5).

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*Figure 5. Computed tomography scan of PNS show  
Hyperdense shadow, lamina papyracea pushed  
Laterally causing protosis, bony destruction of  
Ethmoid sinus septae and medial wall of maxillary  
Antrum.*

## **DISCUSSION**

Aspergillus infection of the paranasal sinuses have been classically divided into four types: the Allergic, non-invasive, invasive and fulminant<sup>5</sup>. Unfortunately, this traditional classification cannot accommodate and explain the different type of behavior of the disease<sup>6</sup>. Sarti and Lucente have noticed that invasive aspergillosis after a while may develop from non-invasive disease<sup>7</sup>.

Romelt and Newman and Von Haacke have demonstrated clearly that aspergillus infection may produce marked destruction and erosion of the sinuses without fungal tissue invasion<sup>8,9</sup>. Gefter et al illustrated clearly how the disease may progress from a long standing non-invasive form to the semi-invasive form<sup>10</sup>. Hartwick and Batsakis revealed 28% of patients with allergic aspergillosis sinusitis (AAS) to have bone expansion or erosion of the involved sinuses<sup>11</sup>. Nussenbaum et al reported bony erosion in 20% of his patients with allergic fungal sinusitis and he believed that bone erosion caused by AFS is not related to an invasive aspect of the disease<sup>12</sup>.

This problem was addressed in 1993 by Rowe-Jones, when he suggested that paranasal sinuses aspergillosis should be considered as a spectrum of disease with the following classification<sup>5</sup>:

1. Non-invasive, either aspergilloma or allergic in type (AAS).

2. Semi-invasive, being locally destructive without tissue invasion.
3. Invasive, representing true fungal invasion either non-fulminant or fulminant in course.

The five cases presented in this paper, showed an invasive character, clinically as proptosis and radiologically and surgically as bony destruction, erosion and expansion, but without a real tissue invasion. Hence they were classified as being semi-invasive. The diagnosis of the disease and its classification not necessarily being identical or in harmony with each other but they could be different or in disharmony with each other as in this study<sup>8,9,11</sup>. The diagnosis of the disease and its classification should not be made based only on the histopathological report and culture but also on the clinical presentation, behavior of the disease, the radiological and surgical findings<sup>5</sup>.

In general the diagnosis of paranasal Sinuses Aspergillosis should be based on high index of suspicion. Area of increased attenuation in paranasal soft tissue masses on unenhanced CT scan are strongly suggestive of fungal involvement. The histology and culture findings have the last word<sup>13</sup>.

Semi-invasive and invasive fungal sinusitis has to be treated with surgery and systemic antifungal chemotherapy with the aim to reach a complete eradication of the disease, to control wide spreading of the disease and to avoid recurrence<sup>5,6</sup>.

Triazoles (Itraconazole) in daily oral dose between 200-600 mg for 1-6 months have been proven to be very effective and with a minimal side effect. In fulminant fungal sinusitis, in life threatening cases and if the infection is wide spread, it is advised to use Amphotericin B or lipid-based amphotericin in IV form. During treatment, liver and kidney function has to be monitored<sup>5,14</sup>. The five cases presented have been treated with Itraconazole in a daily oral dose between 200-600 mg for 1- 6 months without any complications.

All were free of recurrence for at least 6 months post-operatively. Oyarzabal et al used Itraconazol, in addition to surgery, to treat a case with semi-invasive aspergillosis with intracranial invasion. The patient was free of recurrence for 5 year post-operatively<sup>6</sup>. Yagi et al treated 43 patients suffering from semi-invasive and invasive aspergillosis with short and long term Intraconazole, 92% of them were free of recurrence for one year post-operatively<sup>15</sup>.

## CONCLUSION

**Knowing the diagnosis and the type of fungal sinusitis is of great importance in order to arrange in advance the proper management of the case. This should be made through considering not only the histopathological finding and culture, but also the clinical presentation, the radiological and surgical finding. The suggested new classification will allow us to make use of the systemic anti fungal chemotherapy in addition to surgery to have a better control of the disease and better outcome.**

**The five cases presented in this paper showed invasive characters: proptosis, bony destruction, erosion and expansion, though, they are classified as semi-invasive.**

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