

Aspergillus Rhino sinusitis and Associated Risk Factors

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ABSTRACT

Objective: To identify the predisposing factors for both invasive and non-invasive Aspergillus rhinosinusitis and to understand the relationship of these factors with Aspergillus infection of the paranasal sinuses.

Study Design: Retrospective analytic study

Place and Duration of Study: This study was carried out in Department of ENT Unit 1; Mayo Hospital affiliated with King Edward Medical University, Lahore. It spanned over a period of 18 months from January 2008 to June 2009.

Material and Method: A total of 29 patients diagnosed to have Aspergillus rhinosinusitis were included in the study. A properly designed, structured, validated and tested questionnaire was used for data collection. Categorical variables included were gender, diabetes mellitus, tuberculosis, asthma, contact with birds and animals. Chi-square test was used to see the association between final diagnosis and the variables tested.

Results: In our study the average age of patients with non-invasive disease was 28.22 ± 11.875 years and with invasive disease was 29.18 ± 18.132 years. The ratio of male patients was almost twice that of females. 11 (37.93 %) patients had indolent invasive Aspergillus rhinosinusitis and 18 (62.7 %) had non-invasive Aspergillus rhinosinusitis.

Final diagnosis was independent of gender ($p=0.149$), Diabetes ($p=0.379$), Asthma ($p=0.864$), contacts with birds ($p=1.00$) and animals ($p=0.466$). Interestingly, 5 (45.45 %) out of 11 patients with invasive disease had tuberculosis and only 1 (5.55 %) out of 18 patients with non-invasive disease had tuberculosis ($p=0.018$).

Conclusion: Aspergillus rhinosinusitis is a disease of the young adults. No specific predisposing factor could be identified in the causation of non-invasive Aspergillus rhinosinusitis. Tuberculosis was the only positive factor identified in invasive indolent Aspergillus infection of the paranasal sinuses.

Key Words: Aspergillus, Paranasal Sinuses, Predisposing factors

INTRODUCTION

Patients with chronic rhinosinusitis have high probability to develop Aspergillus rhinosinusitis. Exact pathophysiology of the disease remains unclear but blockage of the sinus ostium favors the environment for the proliferation of the fungus.^{1, 2}

In immunocompetent patients Aspergillus rhinosinusitis typically presents with nasal congestion and periorbital discomfort. Disease is generally limited to its four varieties namely fungus balls, chronic erosive (non-invasive sinusitis), allergic Aspergillus rhinosinusitis and indolent invasive variety. Aspergilloma or fungus balls may manifest as an asymptomatic radiographic abnormality, in a patient with preexisting cavitary lung disease due to the tuberculosis. Allergic Aspergillus rhinosinusitis is driven by hypersensitivity response to the presence of small numbers of extra mucosal fungi found growing

within the airway-impacting allergic mucin. Sinus CT shows central areas of increased contrast ('hyper attenuation') within abnormal paranasal sinuses that represent the presence of fungal-containing allergic mucin. Sinus surgery remains the mainstay of the treatment. Adjunctive anti-mycotic therapy is not required usually. Allergic mucin is typically cultures positive for either dematiaceous fungi such as *Bipolaris Spicifera* or *Curvularia Lunata* in the West and Aspergillus species in South Asia.^{3, 4}

Local factors that may predispose healthy patients to fungal infection of the paranasal sinuses may include recurrent bouts of sinusitis, massive exposure to air and food contaminated with mycotic spores and domestic pets. Environmental factors could also play a role, especially in Sudan and Saudi Arabia, where incidence of Aspergillus sinusitis is so high that it is

sometimes described as endemic. Sandstorms are believed to help disseminate fungal spores, exposing people to large inoculate. The sociodemographic factors appear to have a significant impact on the incidence and frequency of the disease. In sub-continent, living in open houses with poor socioeconomic status leads to more exposure of fungal spores than in Europe where closed houses are mostly used for the living. Moreover etiological agents involved in different forms of the disease here are different from Western countries.^{5, 6, 7}

Chronic invasive (indolent) sinonasal Aspergillosis usually found in patients living in dry-air climates, similar to the weather found in Egypt, Sudan, Saudi Arabia, India and Pakistan. It presents as a slow growing disease with involvement of the orbit and brain. Prompt use of imaging, surgical debridement and initiation of antifungal therapy are potentially life-preserving tactics to avoid invasive cerebral aspergillosis.^{8, 9}

Local tissue hypoxia or injury with impaired T-cell immune response, leading to increased inflammatory response due to local production of gliotoxin (a mycotoxin produced by *Aspergillus fumigatus*) are highly associated with increased morbidity and mortality in cases of invasive aspergillosis.^{10, 11}

Multiple predisposing factors have been implicated in fungal infection in immunocompromised patients including diabetes mellitus, tuberculosis, alcoholism, hepatic failure, drug addiction, hematopoietic stem cell transplant and solid organ transplant, hematological malignancies, long term corticosteroid therapy and HIV infection^{12, 13, 14, 15, 16}

OBJECTIVE

To identify the predisposing factors for both invasive and non-invasive *Aspergillus* sinusitis and to understand the relationship of these factors with *Aspergillus* infection of paranasal sinuses.

MATERIAL AND METHOD

This study was carried out in Department of ENT Unit 1; Mayo Hospital affiliated with King Edward Medical University, Lahore. It spanned over a period of 18 months from January 2008 to June 2009. A total of 29 patients diagnosed to have *Aspergillus* rhinosinusitis were included in the study from different areas of the country irrespective of age, gender, socioeconomic status and geographical origin. All 29 patients were

admitted through the outpatient department of ENT Unit 1. They were evaluated by CT scan after obtaining detailed history and performing clinical examination. Plane and contrast enhanced CT sequences of nose, paranasal sinuses, orbit and brain with 3-5 mm thin slices of axial and coronal views were obtained on soft tissue and bone window settings. All patients underwent external ethmoidectomy and the specimen obtained at surgery was submitted for histopathology and fungal staining by Gomori Methenamine Silver, PAS and Sabourad with chloramphenicol. A properly designed and structured, validated and tested questionnaire was used for data collection. Data was entered in SPSS version 11, a computer based software programme. Mean and standard deviation were computed for qualitative variables like age. Categorical variables included were gender, diabetes, tuberculosis, asthma and contact with birds and animals. Chi-square was used to see the association between final diagnosis and variables tested. P value < 0.05 was taken as significant.

RESULTS

In our study the average age of patients with non-invasive disease was 28.22 ± 11.875 years and in patients with invasive disease was 29.18 ± 18.132 years (Table 1). The ratio of male patients was almost twice. 11(37.93 %) patients had indolent invasive *Aspergillus* rhinosinusitis and 18 (62.7 %) had non-invasive *Aspergillus* rhinosinusitis (Table 2).

Final diagnosis was independent of gender ($p=0.149$), Diabetes ($p=0.379$), Asthma ($p=0.864$), contacts with birds ($p=1.00$) and animals ($p=0.466$). Interestingly, 5 (45.45 %) out of 11 patients with invasive disease had tuberculosis and only 1 (5.55 %) out of 18 patient with non-invasive disease had tuberculosis ($p=0.018$). (Table 3)

Age distribution of the patients table 1(n=29)

Type of disease	Age + SD
Non-invasive disease	28.22+11.875
Invasive disease	29.18+18.132

SD= Standard Deviation

Table 2 (n=29) Incidence of tuberculosis and % age of disease types

Type of disease	(n)	% age	Tuberculosis	
			(n)	% age
Non-invasive disease	18	62.7%	1	5.55 %
Invasive disease	11	37.93 %	5	45.45 %

Table 3 (n=29) Statistical analysis of predisposing factors

Predisposing factors	Chi square test	P value
Gender	0.149	> 0.05
Diabetes	0.379	> 0.05
Asthma	0.864	> 0.05
Contact with birds	1.00	> 0.05
Contact with animals	0.466	> 0.05
Tuberculosis	0.018	< 0.05

DISCUSSION

In this retrospective analytic study, 29 patients treated for suspected *Aspergillus* rhinosinusitis. 5 (45.45 %) out of 11 patients with invasive disease had history of tuberculosis. On the other hand, Only 1 (5.55 %) of 18 patients with non-invasive disease had tuberculosis. So the overall incidence of tuberculosis with *Aspergillus* rhinosinusitis in our study remained 20.68 %.

Our results were in accordance with a foreign study by Dubev A et al in this regard, where 18 % of the patients with extensive fungal disease had associated tuberculosis. On the other hand our results regarding type of the disease were also close to a study in India by Micheal RC et al, where non-invasive disease was found in 63 % and invasive in 34 % of a total 211 culture positive fungal sinusitis samples. According to the results of their study, significant proportion of these patients did not have any known predisposing factors. All other predisposing factors remained statistically insignificant among invasive and non-invasive disease in our study.^{2,7}

The Delayed Type Hypersensitivity response seen in invasive *Aspergillus* infection and Tuberculosis needs further studies to evaluate a positive correlation.

CONCLUSION

Aspergillus sinusitis is a disease of the young. No specific predisposing factor could be identified in the causation of non-invasive *Aspergillus* sinusitis. Tuberculosis was the only positive factor identified in invasive indolent *Aspergillus* infection of the paranasal sinuses.

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