The Egyptian Journal of Hospital Medicine (June 2010) Vol., 39: 275 - 280

Allergic bronchopulmonary aspergillosis among patients with bronchial asthma

Al-Najada M, Al-Nadi K, Sharara AM
Department of chest disease, King Hussein Medical Centre, amman -jordan

Abstract

Objective
To determine the different presentations encountered upon diagnosis of ABPA among patients with bronchial asthma and the two-year-follow-up results.

Patients and method
All patients with bronchial asthma and ABPA were included in the study .Specially formulated sheet was done include age, gender, duration of bronchial asthma ,new clinical,radiological,and laboratory findings suggestive of ABPA and two year follow up of them. Diagnosis of ABPA was based on Rosenberg-Patterson criteria.

Result
Fifteen patients with ABPA 3.9% out of 385 patients with bronchial asthma were included in our study, (5males)and (10 females) there mean age was 28.8 years , and mean duration of asthma was 8.9 years, and they represent all stages of asthma severity. Fleeting shadows mainly in the upper lobes were the most common radiological findings observed in nine patients (60%), five patients (33.3%) had proximal bronchiectasis detected by high resolution chest ct-scan, one of our patients had collapsed consolidation. All patients had moderate to severe eosinophilia and positive immediate skin test for aspergillus.

Conclusion
As the prevalence of ABPA is not uncommon among patients with bronchial asthma regardless the severity and the level control of asthma, high index of suspicious for ABPA should be maintained when followed up any patient with bronchial asthma.

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is an immunologically mediated lung disease characterized by a complex hypersensisitivity reaction in patients with asthma which occurs when bronchi become colonized by Aspergillus.Repeated episodes of bronchial obstruction inflammation and mucoid impaction can lead to bronchiectasis, fibrosis, and chronic lung disease.
The clinical manifestation of pulmonary aspergillosis is variable and range from saprophytic aspergillosis in the form of aspergilloma to chronic necrotizing pulmonary aspergillosis, and invasive aspergillosis(Soubani AO, Chandrasekar PII ,2000).

The prevalence of ABPA in patients with bronchial asthma ranged from 3.7 to 11% in western countries (Henderson AII *et al*,1968;Agbayani BF *et al*,1967).And in India the prevalence reached 16% (Kumar and Gaur ,2000).

Material and Methods:

Specially formulated data sheet was done to all patients with ABPA and bronchial asthma, who are on regular follow up in the chest department at King Hussein Medical Centre (KHMC).
The sheet included age ,gender, duration of bronchial asthma, clinical presentation, radiological and laboratory findings and skin testing .The diagnosis of ABPA was made using Rosenberg-Patterson

criteria(Rosenberg M *et al* ,1977; Patterson R *et al* ,1986) which include major and minor criteria.
major criteria include (1)history of bronchial asthma,(2)fleeting or fixed pulmonary shadows,(3)positive immediate skin test for aspergillus,(4)serum IgE level >1000 IU/ml,(5)eosinophilia,(6)proximal bonchiectasis,(7)raised specific serum IgE and IgG against aspergillus fumigates,(8)precipitating antibody against aspergillus fumigatus ,and minor criteria include (1) sputum culture positive for aspergillus fumigates,(2)type III cutaneous reactivity to aspergillus fumigates,(3)expectoration of mucus plugs.
In our study at least six criteria had to be present for diagnosis of allergic bronchopulmonary aspergillosis.

Results

Fifteen patients with ABPA (3.9%) were found out of 384 patients with bronchial asthma included in our study (table 1), (5males)and (10 females) there mean age was 28.8 years and mean duration of asthma was 8.9 years, and they represent all stages of asthma ,three of them(20%) were smoker.
Eight patients (53%) described other allergic disorders like allergic rhinitis and eczema, and eight patients (53%) gave a history of family atopy.All patients presented with exacerbation of cough, dyspnoea and wheezes, five patients (33.3%) described expectoration of mucus plugs, and two patients (13.3%) had haemoptysis.
Fleeting shadows mainly in the upper lobes were the most common radiological findings observed in nine patients (60%), five patients (33.3%) had proximal bronchiectasis detected by high resolution chest ct-scan, one of our patients had collapsed consolidation.
Nine patients (60%) had absolute eosinophils counts above 1000 cells/µL, and sex patients (40%) had eosinophils counts between 500-1000 cells/ µL.
Immediate skin test showed type I reactivity in all patients, and serum precipitins (IgG) against aspergillus fumigate was positive in all patients.
Serum total IgE concentration was greater than 1000IU/mL in all patients.
All patients were followed up for two years, those with fleeting shadows had smooth coarse without any new radiological findings, and those with bronchiectasis had frequent exacerbations ,but none of them developed any new radiological finding.

Table 1

Clinical profile	**Number(absolute)**	**percentage**
Male	5/15	33.3
Female	10/15	66.6
Mean age	28.8	
Smoking history	3/15	20
History of Bronchial asthma	15/15	100
Mean duration of asthma	8.9	
Other allergic disorders	8/15	53.3

Family history of atopy	8/15	53.3
Symptoms Cough Mucus plug Dyspnea Wheezes haemoptysis	 15/15 5/15 15/15 15/15 2/15	 100 33.3 100 100 13.3
Radiological findings Normal Fleeting shadows Proximal bronchectasis Collapse consolidation	 None 9/15 5/15 1/15	 60 33.3 6
Absolute eosinophils count 500 500-1000 1000	 None 6/15 9/15	 40 60
Immediate skin test reactivity to aspergillus antigen	15/15	100
Serum total IgE concentration greater than 1000 IU /mL	15/15	100
Serum precipitin against aspergillus	15/15	100
Aspergillus specific IgE/IgG	Not done	

Discussion:

The pathogenesis of ABPA is still not fully understood. Repeated inhalation of aspergillus spores especially aspergillus fumigates leads to airway colonization in sputum plugs in the bronchi of asthmatic patients with little or no tissue invasion (Raj Kumar *et al* ,2003).

The clinical classification of ABPA set by Patterson *et al*(1982) includes five stages, *(see table 2);* stage I (acute), stage II (remission), stageIII (exacerbation), stage IV (steroid dependent ABPA), stage V (fibrosis-end stage). The classification proposed by Kumar (2003) was based on radiological findings and includes three stages 1) ABPA-S (serological positive without bronchiectasis), 2) ABPA-CB (with central bronchiectasis), 3)ABPA-CB-ORF (with central bronchiectasis and other radiological findings).

ABPA is quite not uncommon in patients with bronchial asthma, it was found in (3.9%) of our patients with bronchial asthma. The prevalence of ABPA range from 3.7 to 11% in western countries (Henderson AII *et al*,1968;Agbayani BF *et al*,1967). In the study done by Kumar and Gaur (2000) from India the incidence of ABPA in asthmatics reached up to 16% . The most common radiological finding of ABPA in our study was the fleeting shadows, It is found in 60% of our patients which nearly similar to that (69%) in Kumar and Gaur study (2000). All of our

patients had high absolute eosinophilic count a finding that should always alert the clinician to the possibility of ABPA in patient with asthma ,the same findings were seen in Kumar and Gaur study (2000) , and Chakrbarti *et al* . study (2002). During the 2 years follow up ,the nine patients who presented with fleeting shadows had smooth course ,none of them reached stage IV (steroid dependent ABPA),but unfortunately two of them lost follow up for one year ,and they return back with severe symptoms ,ended with steroid dependent ABPA without any new radiological findings. This outcome was similar to that reported in Kumar R study (2003) and Greenberger PA *et al* study (1993).

All patients who primarily presented with proximal bronchiectasis (ABPA-CB) had recurrent exacerbation, but none of them developed other radiological findings.

None of our patients included in the study, developed new radiological findings during the 2 year follow up, but many of them had frequent exacerbation and needed oral corticosteroid therapy.

The natural history of ABPA is poorly characterized and is difficult to predict [17,8,15] (Wang JL *et al* 1979; Lee TM *et al* 1987; Rosenberg M *et al* 1978).An early diagnosis and initiation of systemic corticosteroid is essential to prevent irreversible damage (Patterson R 1998).

The course of patients who presented primarily with (ABPA-S) looks to be less severe than those who presented with (ABPA-CB), and this also was observed in the study done on 18 patients with ABPA by Raj Kumar (2003), and in another study done by Kumar and Chopra (2002).

In a multivariate analysis of 155 patients with ABPA done by Agawal and colleagues (2007) they demonstrated that the severity of bronchiectasis and presence of hyperattenuating mucoid impaction on HRCT-predicted relapses of ABPA and the severity of bronchiectasis was an independent predictor of failure to achieve long-term remission.

Conclusion

As the prevalence of ABPA is not uncommon among patients with bronchial asthma regardless the severity and the level control of asthma, high index of suspicious for ABPA should be maintained when followed up any patient with bronchial asthma .An immediate skin test for aspergillus fumigates should be done for every patient with bronchial asthma ,and if positive other immunological studies should be requested for diagnosis or exclusion of ABPA ,this is because early diagnosis and treatment of ABPA will prevent irreversible damage.

Table 2

stages	Clinical picture	Biology	Radiological findings
I)Acute	fever,coygh,haemoptysis,weight loss, sputum	↑ total serum IgE level>1000IU/mL ∓ blood eosinophilia	Normal or pulmonary infiltrates(upper/middle lobes
II)Remission	asymptomatic	Normal or ↑total serum IgE level	Normal or significant resolution of radiological infiltrates from the acute stage
III)Exacerbation	**allergic bronchopulmonary aspergillosis**	Doubling of IgE level from the baseline	Transient or fixed pulmonary infiltrates
IV)Glucocorticoid –dependent	Sever persistent asthma	Normal or	Transient or fixed

ABPA		elevated serum IgE level	pulmonary infiltrates
V) End- stage (fibrotic) ABPA	Sever pulmonary dysfunction, fixed airway obstruction, type II respiratory failure, cor pulmonale	Normal or elevated serum IgE level	Extensive Bronchiectasis, pulmonary fibrosis, pulmonary hypertension

References

1 Agarwal R ,Gupta D, Aggarwal AN,*et al.* (2007):clinical significance ofhyperattenuation mucoid impaction in allergic bronchopulmonary aspergillosis :an analysis of 155 patients.Chest;132:1183-1190

2 Agbayani BF, Normal PS,Wekenwerden W,*et al*.(1967):The evidence of allergic aspergillosis in chronic asthma.J Allergy,40:319-326

3 Chakrabarti A,Senthi S , Raman DSV ,Behera D. (2002): Eight-year study of allergic bronchopulmonary aspergillosis in an Indian teaching hospitals.Mycoses,45:295-299

4 Greenberger PA ,Miller TP ,Roberts M, *et al*. (1993):Allergic bronchopulmonary aspergillosis in patients with and without bronchiectasis .Ann Allergy,70:333-338

5 Henderson AII,English MP,Vecht RJ. (1968):Pulmonary aspergillosis:a survey of its occurrence in patients with chronic lung disease and a discussion of significance of diagnostic test.thorax,25:513-553

6 Kumar R. (2003): Mild, moderate, and severe forms of allergic bronchopulmonary aspergillosis: a clinical and serologic evaluation. Chest, 124:890-892

7 Kumar R ,Gaur SN . (2000): prevalence of allergic bronchopulmonary aspergillosis in patients with bronchial asthma.Asian Pac J Allergy Immunol , 18:181-185

8 Lee TM, Greenberger PA, Patterson R, *et al*.(1987):Stage V(fibrotic) allergic bronchopulmonary aspergillosis: a review or 17 cases followed from diagnosis. Arch Intern Med , 147:319-323

9 Patterson R.(1998):Allergic bronchopulmonary aspergillosis and hypersensitivity reactions to fungi. In: Fishman AP , Elias JA, Fishman JA, *et al*, eds. Fishman's pulmonary diseases and disorders. New York, NY: McGraw-Hill,; 777-782

10 Patterson R, Greenberger PA, Halwig JM, *et al.* (1986):Allergic bronchopulmonary aspergillosis: natural history and classification of early disease by serologic and roentgenographic studies. Arch Intern Med, 146:916-918

11 Patterson R, Greenberger PA, Radian RC, *et al*. (1982): Allergic bronchopulmonary aspergillosis: staging as an aid to management. Ann Intern Med, 96:286-291

12 Raj Kumar, Deepti Chopra.(2002):Evaluation of allergic bronchopulmonary aspergillosis in patients with and without central bronchiectasis. *Journal of asthma*, 39(6) : 473-477.

13 Raj Kumar, tarun chugh,S. N. Gaur . (2003): allergic bronchopulmonary aspergillosis – a review. Indian J allergy asthma immunol,17(2) :55-66

14 Rosenberg M, Patterson R, Mintzer R, *et al.* (1977): Clinical and immunologic criteria for the diagnosis of allergic bronchpulmonary aspergillosis. Ann Intern Med, 86:405-414

15 Rosenberg M, Patterson R, Roberts M, *et al*. (1978):The assessment of immunologic and clinical changes occurring during corticosteroid therapy for allergic bronchopulmonary aspergillosis. Am J Med, 64:599-606

16 Soubani AO, Chandrasekar PII.(2002): The clinical spectrum of pulmonary aspergillosis. Chest, 121:1988-1999

17 Wang JL, Patterson R, Roberts M, *et al.* (1979):The management of allergic bronchopulmonary aspergillosis. Am Rev Respir Dis,120:87-92

داء الرئة والقصبات الفطري التحسسي بالاسبيرجلس

د.محمد النجادا د.خالد النادى د.عبدالمنعم شرارة
قسم الامراض الصدرية- مدينة الحسين الطبية – عمان-الاردن

الهدف:- لتحديد الصور المختلفة التي تواجه عند تشخيص داء الرئة والقصبات الفطري التحسسي بالاسبيرجلس عند مرضى الربو القصبي خلال سنتين ومتابعة النتائج.

المرضى والطريقة:- جميع المرضى اللدين يعانون من الربو القصبي و داء الرئة والقصبات الفطري التحسسي بالاسبيرجلس ادخلوا في الدراسة. ولقد تم صياغة نشرة خاصة اشتملت على العمر,االجنس,مدة الاصابة بالربو القصبي,بالاضافة الى الموجودات السريرية والشعاعية والمخبرية الجديدةالتي ترجح الاصابة بداء الرئة والقصبات الفطري التحسسي ومتابعة هؤلاء المرظى لمدة سنتين.
المعايير التي اعتمدت في تشخيص المرض هي معايير روزنبيرغ باترسون.

النتائج:- خمسة عشر مريضا مصابا ب داء الرئة والقصبات الفطري التحسسي بالاسبيرجلس من اصل 385 مريض بالربو القصبي ادخلوا في الدراسة وبنسبة 3,9% خمسة مرضى ذكورا والبقية كانوا اناثا متوسط العمر كان 28,8 سنة اما متوسط مدة الاصابة بالربو القصبي كانت 8,9 سنة و جميعهم شوهدوا بكافة مراحل الربو القصبي الشديدة.
اكثر المظاهر الشعاعية شيوعا كانت الارتشاحات سريعة الزوال في الفصوص الرئوية العلوية وظهر ذالك عند تسعة مرضى وبنسبة 60%.التصوير الطبقي المحوري عالى التصميم اظهر توسع القصبات الهوائية المركزي عند خمسة مرضى وبنسبة 33,3%. مريض واحد كان عنده كثافة انخماصيه .
جميع المرضى كان عندهم ارتفاع متوسط الى شديد في نسبة الخلايا الحامضية بالاضافة الى ايجابية الفحص الجلدى الفوري الخاص بالاسبرجيلس.

الخلاصة:- بما ان انتشار داء الرئة والقصبات الفطري التحسسي بالاسبيرجلس ليس من غير المعروف بين مرضى الربو القصبي بغض النظر عن شدة المرض ومستوى السيطرة على الربو القصبي.ارتفاع مؤشر الاشتباة بالمرض يجب ان يتابع عند أي مريض مصاب ب الربو القصبي.