REVIEW ARTICLE

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS (ABPA) COMMONLY MISDIAGNOSED AS PULMONARY TUBERCULOSIS

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Abstract

BACKGROUND: Allergic bronchopulmonary aspergillosis (ABPA), a syndrome associated with asthma, manifests with transient pulmonary infiltrates and eosinophilia and can progress to severe proximal bronchiectasis, and pulmonary fibrosis. Early recognition and treatment should favorably influence these complications.

OBJECTIVES: To study the clinical and radiologic features of the patients of ABPA, with emphasis on their previous diagnosis and treatment especially of tuberculosis.

DESIGN AND SETTING: Prospective recruitment of all the patients of ABPA, diagnosed at the Pulmonology unit QAMC / Bahawal Victoria Hospital Bahawalpur during 2005-06.

PATIENTS AND METHODS: We studied the clinical and the radiological features of ABPA, with special emphasis on previous diagnosis and treatment of tuberculosis. Standardized data collection of symptoms, bacteriology, and review of radiology by two readers blind to the clinical data was done.

RESULTS: There were 672 patients of ABPA. Demographic analysis showed a preponderance of males, young patients (less than 35 years old), farming and rural communities. 90% patients were asthmatic with long history of wheezing. Most common symptoms were breathlessness (93 %), cough (96 %), expectoration (78 %), fever (92 %), chest pain (82 %) and hemoptysis (48 %). Forty five percent patients had associated nasal symptoms. More than 60 % patients were erroneously diagnosed and treated as pulmonary tuberculosis while about 30 % of them took two or more courses of anti-tuberculous treatment.
CONCLUSIONS: ABPA is more prevalent than previously appreciated. Its clinical presentation is similar to pulmonary tuberculosis hence most cases of ABPA are misdiagnosed as pulmonary tuberculosis; delay in diagnosis and treatment not only predisposes them to complications like bronchiectasis and fibrosis but also to potentially toxic anti–tuberculous therapy. For the clinician, it is imperative to consider the diagnosis in asthmatic patients with radiographic infiltrates and/or bronchiectasis.
INTRODUCTION:

Allergic bronchopulmonary aspergillosis (ABPA), a syndrome associated with asthma, manifests with transient pulmonary infiltrates and eosinophilia and can progress to severe proximal bronchiectasis, and pulmonary fibrosis. It was first described in 1952 [1].

The most common fungus implicated is Aspergillus fumigatus (AF) others include Aspergillus flavus and Candida, Penicillium, Curvularia, and Dreschleria organisms [2, 3, 4]. In the case of ABPA, aspergillus organisms are not invasive but rather colonize the respiratory tract of patients with asthma [2]. This induces an immune response to the numerous antigens that aspergillus elicits [3]. It is estimated that ABPA is present in 2% to 28% of all patients with chronic asthma [3, 5, 6].

The symptoms of ABPA occur most commonly during the third and fourth decades of life in atopic individuals and range from acute, recurrent asthma exacerbations with wheeze, cough, and chest x-ray infiltrates to generalized systemic features of fever, anorexia, headache, and malaise[3, 4]. Several radiographic patterns have been described; characteristically infiltrates involve the upper and middle lung fields and are accompanied by peripheral eosinophilia and elevated total serum Ig-E level [7-10]. Computed tomography (CT) is the most sensitive tool for the detection of bronchiectasis [13], which manifests as proximal bronchiectasis [9].
No single clinical or immunological feature is diagnostic of ABPA. Individuals meeting seven of the following eight criteria make the diagnosis of ABPA highly likely [11, 14].

Table 1.

<table>
<thead>
<tr>
<th>Diagnostic Criteria for ABPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Asthma or cystic fibrosis</td>
</tr>
<tr>
<td>2. Peripheral blood eosinophilia (&gt;1.0×10^9/L)</td>
</tr>
<tr>
<td>3. Immediate cutaneous reactivity to AF antigen</td>
</tr>
<tr>
<td>4. Precipitating antibodies against AF antigen</td>
</tr>
<tr>
<td>5. Elevated total serum Ig-E (&gt;1000 ng/ml)</td>
</tr>
<tr>
<td>6. Chest x-ray infiltrates (or history of), transient or fixed</td>
</tr>
<tr>
<td>7. Proximal bronchiectasis</td>
</tr>
<tr>
<td>8. Elevated serum Ig-E and Ig-G antibodies (specific to AF antigen)</td>
</tr>
</tbody>
</table>

Tuberculosis is also very common in this region. Exact data for tuberculosis incidence, prevalence and tuberculosis-related mortality is not available, however based on an estimated annual cumulative incidence of tuberculosis as 171 cases per 100,000, Pakistan has been ranked among the top 22 developing countries afflicted by the current tuberculosis epidemic [15, 16].
As can be expected ABPA is misdiagnosed as pulmonary tuberculosis in TB-endemic regions many of the clinical and radiological features are similar in both diseases.

The present study was conducted to see the clinical and radiological feature of allergic bronchopulmonary aspergillosis and to identify patients of ABPA who were erroneously labeled as pulmonary tuberculosis and took antituberculous therapy.
MATERIAL AND METHODS:

This was a prospective study conducted at the pulmonology ward QAMC/ Bahawal Victoria Hospital Bahawalpur, in 2005-06. All patients diagnosed as ABPA at pulmonology OPD or ward, were included in the study; information was collected from them with pre-tested questionnaire, with emphasis on previous diagnosis and treatment of tuberculosis.

ABPA was diagnosed according to the following criteria.

1. HISTORY (History of Asthma with productive cough, hemoptysis, systemic features like fever, malaise, fatigue), mostly with Rhonchi and/or crepitations on examination.

2. Peripheral blood eosinophilia, (Eosinophil count done in all patients)

3. Elevated total serum Ig-E (>1000 ng/ml), (serum Ig-E level done in all patients)

4. Chest x-ray infiltrates / proximal bronchiectasis, (CXR done in all patients)

5. CT Scan Chest for proximal bronchiectasis, (done only in patients where chest X-ray inconclusive i.e. no infiltrates but otherwise strong clinical suspicion of ABPA.

PLUS – strict follow up, and response to treatment.

Some of the investigations (precipitating antibodies against AF antigen and serum IgE and Ig-G antibodies-specific to AF antigen) are not available locally so we relied on clinical and radiological criteria and response to treatment.
Tuberculosis was diagnosed/ excluded according to standard sputum microscopy and/or culture in background of suggestive history and chest x-ray features.

Then results were analyzed on Microsoft Excel (version 2006).
RESULTS:

Out of total 672 patients, 437 (65%) were males.

Most cases (> 90 %) were less than 45 years of age. (The age distribution is shown in Table 2.)

490 patients (73%) belong to rural areas of Bahawalpur district.

After strong suspicion of ABPA from clinical history and physical examination and radiological evidence, we did Eosinophil count and serum IgE level in all patients.

- Eosinophilia (> 500/ cmm) was seen in 390 (58%) of patients.
- Serum Ig-E level (1000 ng/ml) was seen in all patients. In some patients.
- CT scan chest was done in 323 patients out of whom 258 patients (80 %) had confirmed proximal bronchiectasis.

Clinical and radiological data and details of previous anti-TB treatment is summarized in Tables 3, 4 & 5

Table No. 2

AGE DISTRIBUTION

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>81</td>
<td>12%</td>
</tr>
<tr>
<td>15-30</td>
<td>316</td>
<td>47%</td>
</tr>
<tr>
<td>30-45</td>
<td>222</td>
<td>33%</td>
</tr>
<tr>
<td>&gt;45</td>
<td>53</td>
<td>8%</td>
</tr>
<tr>
<td>Total</td>
<td>672</td>
<td>100%</td>
</tr>
<tr>
<td>Symptoms</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>Asthma</td>
<td>605</td>
<td>90%</td>
</tr>
<tr>
<td>General ill health</td>
<td>578</td>
<td>86%</td>
</tr>
<tr>
<td>Fever</td>
<td>618</td>
<td>92%</td>
</tr>
<tr>
<td>Cough</td>
<td>645</td>
<td>96%</td>
</tr>
<tr>
<td>Expectoration</td>
<td>524</td>
<td>78%</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>323</td>
<td>48%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>551</td>
<td>82%</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>625</td>
<td>93%</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>161</td>
<td>24%</td>
</tr>
<tr>
<td>Nasal Symptoms</td>
<td>302</td>
<td>45%</td>
</tr>
</tbody>
</table>
Table No 4

RADIOLOGICAL PATTERN

<table>
<thead>
<tr>
<th>Radiological Features</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolidation</td>
<td>470</td>
<td>70%</td>
</tr>
<tr>
<td>Glove &amp; Finger Shadows</td>
<td>370</td>
<td>55%</td>
</tr>
<tr>
<td>Non-homogenous Shadows</td>
<td>302</td>
<td>45%</td>
</tr>
<tr>
<td>Air- fluid level</td>
<td>101</td>
<td>15%</td>
</tr>
<tr>
<td>Fleeting Shadows</td>
<td>571</td>
<td>85%</td>
</tr>
<tr>
<td>Upper zone infiltrates</td>
<td>524</td>
<td>78%</td>
</tr>
<tr>
<td>Lower zone infiltrates</td>
<td>323</td>
<td>48%</td>
</tr>
<tr>
<td>Multiple shadows in both lung fields</td>
<td>437</td>
<td>65%</td>
</tr>
<tr>
<td>Central Bronchiactasis</td>
<td>423</td>
<td>63%</td>
</tr>
</tbody>
</table>

Table No. 5

DATA ABOUT PREVIOUS TB TREATMENT

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENTS CURRENTLY ON ATT</td>
<td>121</td>
<td>18.01%</td>
</tr>
<tr>
<td>PATIENTS WHO TAKEN ATT</td>
<td>291</td>
<td>43.30%</td>
</tr>
<tr>
<td>PATIENTS NOT ON ATT</td>
<td>260</td>
<td>38.69 %</td>
</tr>
<tr>
<td>TOTAL NO. OF PATIENTS</td>
<td>672</td>
<td>100 %</td>
</tr>
</tbody>
</table>

More than 60% of patients were misdiagnosed as Pulmonary Tuberculosis. 18% were currently on anti-tuberculous therapy (ATT) whereas 43% took ATT in recent
past; 72% once, 21% twice and another 7% more than two times. Neither was there any confirmation in these patients with AFB smear or TB culture, nor was there any clinical response to ATT; in addition the clinical picture was quite clearly that of asthma.
DISCUSSION

Allergic broncho pulmonary aspergillosis (ABPA), a syndrome associated with asthma, manifests with transient pulmonary infiltrates and eosinophilia and can progress to proximal bronchiectasis and pulmonary fibrosis. It was first diagnosed in 1952, when three patients of with recurrent episodes of wheezy bronchitis, peripheral blood eosinophilia, fever, sputum production and chest X-Ray shadowing were described (1). Since then ABPA has been described in many countries in a number of series of patients with similar syndrome (4-6).

Asthma is also a common disease in Pakistan; in ISAAC study conducted in Karachi, the prevalence of asthma in school going children was estimated to be around 10-15% [17].

Several features are common to both Allergic broncho pulmonary aspergillosis (ABPA) and Pulmonary Tuberculosis; clinical findings, raised ESR and even radiological appearance (upper lobe infiltrates).

The true prevalence of ABPA is not known in Pakistan, but individual cases are reported in literature. This, to our knowledge, is the largest case series of ABPA patients in Pakistan.

We studied the all cases of ABPA coming to pulmonology OPD BV Hospital Bahawalpur during the year 2005 & 2006. The demographic analysis of the study showed a preponderance of males and young age (similar to pulmonary tuberculosis). The disease seems to be common in farming and rural communities as
most of the patients in our cohort were from rural areas. We however, also accept that this may simply be a referral bias. The demographic data matches with literature (3).

Ninety percent patients were asthmatic with long history of wheezing. Most common clinical symptoms were breathlessness (93 %), cough (96 %), expectoration (78 %), fever (92 %), chest pain (82 %) and hemoptysis (48 %). 45 % patients have associated nasal symptoms. Cockrell BA described asthma in 90 % of patients, fever in 85 % and productive cough in 84 % patients [12].

Something worth noticing was their previous diagnosis and treatment. More than 60 % patients were erroneously diagnosed as having pulmonary tuberculosis and taking anti- tuberculous treatment and about 30 % of them took two or more courses of anti- tuberculous treatment. The late diagnosis of ABPA can result in permanent fibrosis and bronchiectasis of lungs. The reasons for this misdiagnosis may be:

- Pulmonary Tuberculosis is more common disease [15], and clinical symptoms (fever, cough, expectoration, chest pain and hemoptysis) are mostly similar in both diseases, so common diseases are commonly diagnosed.
- Our doctors (general practitioners as well as general physicians) are not properly trained in dealing with ABPA.
This study showing large number of ABPA patients from a single center, may indicate that ABPA is not a rare disease in Pakistan as is considered. The learning lessons are:

- The diagnosis of ABPA should be thought in those asthmatics with history of fever, expectoration, hemoptysis, or uncontrolled asthma or in asthmatic patients with radiographic infiltrates and/or bronchiectasis on CT scan chest and sputum production with or without growth of AF. In these patients, the physician should obtain total Eosinophil count and total serum IgE levels. Early diagnosis of ABPA is mandatory to prevent reversible airway obstruction to permanent fibrosis.

- Secondly our doctors should be properly trained and sensitized about the diagnosis and management of ABPA.

- Thirdly although in endemic areas tuberculosis treatment can be started empirically by trained physicians where sputum AFB is negative or unavailable in presence of suspicious history and CXR features, the diagnosis should be questioned if the clinical response is inadequate in 6 to 8 weeks. ABPA should be considered in cases with asthma and above mentioned clinical features.
CONCLUSIONS

In summary, ABPA is more prevalent than previously appreciated. The clinical and radiological features are similar to pulmonary tuberculosis, so the chances of misdiagnosis of ABPA as pulmonary tuberculosis are more but with the use of diagnostic criteria and especially with use of standardized immunologic testing, the diagnosis should be made more readily. Moreover, our doctors should be properly trained about the disease.
REFERENCES:


14. Rosenberg M, Patterson R, Mintzer R, Cooper BJ, Roberts M, Harris KE.

