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Diagnostic Differences Between Allergic Bronchopulmonary Aspergillosis and Chronic Eosinophilic Pneumonia

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Abstract: In Uzbekistan, the differentiation between allergic bronchopulmonary aspergillosis (ABPA) and chronic eosinophilic pneumonia (CEP) is challenging due to limited data and similar clinical presentations. Both conditions show peripheral eosinophilia, leading to frequent misdiagnosis. This study aimed to investigate the clinical and radiographic differences between ABPA and CEP-like presentations to improve diagnosis in Uzbekistan. A retrospective analysis of 25 patients with ABPA from 2015 to 2019 was conducted. Patients were grouped based on high-resolution computed tomography (HRCT) findings: those with CEP-like features and those with typical ABPA. Clinical and immunologic data were compared. Results showed that while both groups had similar eosinophil counts and Aspergillus-specific immunoglobulin E (IgE) levels, only the non-CEP group showed a significant correlation between eosinophils and IgE. The non-CEP group also had higher levels of the fungal marker beta-D glucan. Recurrence rates were high, but no progression from CEP-like to typical ABPA was observed. These findings emphasize the importance of Aspergillus-specific IgE testing for accurate diagnosis and management of pulmonary eosinophilia in Uzbekistan, potentially preventing misdiagnosis and improving patient outcomes.

Keywords: Allergic bronchopulmonary aspergillosis (ABPA), Chronic eosinophilic pneumonia (CEP), Pulmonary eosinophilia, Diagnosis, Misdiagnosis, Uzbekistan, Resource-limited settings, High-resolution computed tomography (HRCT), Aspergillus fumigatus, Aspergillus-specific IgE, Beta-D glucan, Immunologic markers, Clinical features, Radiologic findings, Treatment.

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a complex lung disorder caused by an exaggerated immune response to Aspergillus fumigatus, particularly in individuals with underlying respiratory conditions such as asthma or cystic fibrosis. It is characterized by recurrent pulmonary infiltrates, bronchiectasis, and elevated levels of Aspergillus-specific immunoglobulin E (IgE). Chronic eosinophilic pneumonia (CEP), another condition involving pulmonary eosinophilia, presents with similar clinical and radiological signs, such as peripheral lung infiltrates and elevated blood eosinophil levels. This overlap can make differentiating between ABPA and CEP particularly challenging, especially in settings where diagnostic tools are limited.

In Uzbekistan, where data on ABPA and CEP are sparse, the lack of awareness and diagnostic clarity has led to frequent misdiagnosis, delaying appropriate treatment. While international guidelines for ABPA diagnosis emphasize the importance of Aspergillus-specific immunologic markers and high-resolution computed tomography (HRCT) findings, these diagnostic criteria are not consistently applied in many regions, including Uzbekistan. This creates a critical gap in knowledge regarding the clinical characteristics and appropriate diagnostic pathways for ABPA, particularly when it mimics CEP.

This study aims to explore the clinical and radiologic distinctions between ABPA and CEP-like conditions, focusing on improving diagnostic accuracy in Uzbekistan. By analyzing patient data and highlighting key differences between these two conditions, this research seeks to contribute to better diagnostic strategies and treatment approaches, ultimately improving patient outcomes in the region.

Literature Review

Allergic bronchopulmonary aspergillosis (ABPA) is a recognized pulmonary disorder caused by an exaggerated immune response to Aspergillus fumigatus and primarily affects patients with asthma or cystic fibrosis. The disorder is characterized by airway inflammation, recurrent pulmonary infiltrates, bronchiectasis, and elevated Aspergillus-specific immunoglobulin E (IgE) levels. First described by Hinson et al. in 1952, ABPA remains a diagnostic challenge due to its clinical and radiological overlap with other eosinophilic lung diseases such as chronic eosinophilic pneumonia (CEP)[1].

The prevalence of ABPA varies globally, with rates estimated at 1-2% in asthma patients and up to 15% in those with cystic fibrosis[2]. However, in resource-limited settings like Uzbekistan, epidemiological data on ABPA are scarce, which complicates early diagnosis and treatment. CEP, a separate pulmonary disorder marked by lung tissue infiltration of eosinophils, presents with non-specific symptoms like fever, cough, and dyspnea. Radiographically, both ABPA and CEP present with peripheral infiltrates, making radiologic differentiation difficult without specific testing for fungal markers or IgE[3].

The primary diagnostic criteria for ABPA, proposed by the International Society for Human and Animal Mycology (ISHAM), include elevated total IgE, Aspergillus-specific IgE, and characteristic high-resolution computed tomography (HRCT) findings. Several studies have demonstrated the importance of Aspergillus-specific IgE and immunologic markers in distinguishing ABPA from other eosinophilic lung diseases[4]. Furthermore, the detection of high-attenuation mucus on HRCT has been shown to have high specificity for ABPA[5]. Despite these advancements, limited use of these diagnostic tools in regions like Uzbekistan leads to misdiagnosis, particularly with CEP.

CEP, which is diagnosed based on eosinophilia in peripheral blood or bronchoalveolar lavage fluid, lacks the fungal association seen in ABPA. As a result, CEP can be treated effectively with corticosteroids alone, while ABPA often requires antifungal therapy in conjunction with corticosteroids[6]. Studies have highlighted the risk of misdiagnosis in ABPA, especially when fungal markers are not routinely tested[7]. This misdiagnosis can lead to improper treatment, resulting in disease progression and increased morbidity.

In Uzbekistan, there is a significant knowledge gap regarding ABPA and its differentiation from CEP, particularly because Aspergillus-specific diagnostic tools are not widely available. A study conducted in India, where diagnostic challenges are similar, demonstrated that routine testing for Aspergillus-specific IgE significantly improved diagnostic accuracy in suspected ABPA cases[8]. Such findings emphasize the need for improved diagnostic protocols in Uzbekistan and similar regions.

In summary, while ABPA and CEP share overlapping clinical and radiological features, key differences in immunologic markers and HRCT findings are crucial for accurate diagnosis. The absence of such

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diagnostic tools in Uzbekistan highlights the need for greater awareness and capacity building to prevent misdiagnosis and improve patient outcomes.

Methodology

The methodological framework of this study is grounded in a cross-sectional observational approach, aiming to achieve a diagnostic differentiation between allergic bronchopulmonary aspergillosis (ABPA) and chronic eosinophilic pneumonia (SEP) in pediatric asthma patients. This design allows for a systematic comparison of immunological and radiological markers, supporting evidence-based clinical practice in the context of respiratory disorders.

In studying chronic respiratory conditions in pediatric populations, it is critical to establish stringent inclusion and exclusion criteria to ensure the reliability of results. The selection of patients aged 6 to 18 with a history of atopic bronchial asthma allowed for the examination of ABPA and SEP within a demographically homogeneous group, where age-related immune responses and asthma management practices are likely consistent. Excluding other respiratory diseases, such as cystic fibrosis, minimized potential confounders, aligning the study with principles of diagnostic specificity.

ABPA and SEP, though clinically similar, are immunologically distinct. The theoretical foundation for categorizing patients into these two groups relies on immunological markers unique to fungal sensitization, particularly Aspergillus-specific IgE, and inflammatory responses indicated by eosinophil levels. This classification, based on immunological specificity and sensitivity, aids in refining differential diagnosis protocols, crucial for resource-limited settings where misdiagnosis can lead to inappropriate treatments and worsen patient outcomes.

Eosinophil Counts: Eosinophils are associated with allergic and parasitic responses, and elevated counts are characteristic of allergic asthma and ABPA. The rationale for measuring eosinophil levels stems from their role in hypersensitivity, which is theorized to be more pronounced in ABPA due to fungal exposure. By quantifying eosinophil levels, this study aimed to detect allergic inflammation patterns specific to ABPA.

Aspergillus-specific IgE: IgE antibodies respond specifically to allergens, such as Aspergillus fumigatus, and their presence at elevated levels indicates sensitization. Aspergillus-specific IgE serves as a targeted diagnostic tool for ABPA, based on immunological models of antigen-specific responses that differentiate ABPA from SEP. This marker is fundamental in distinguishing ABPA in cases where clinical symptoms overlap with SEP.

Beta-D Glucan: A polysaccharide component of fungal cell walls, beta-D glucan, signals fungal involvement in the respiratory system. Its measurement is theoretically linked to detecting fungal antigens, particularly relevant in ABPA where fungal allergens may exacerbate immune responses. Beta-D glucan, therefore, provides an additional layer of diagnostic specificity in differentiating ABPA from SEP.

High-resolution computed tomography (HRCT) imaging was chosen for its ability to provide detailed lung structures essential for identifying ABPA and SEP features. HRCT findings, such as central bronchiectasis in ABPA and peripheral consolidations in SEP, align with radiological theory that supports using imaging as a non-invasive diagnostic tool. These radiological markers are theoretically essential for visualizing disease-specific patterns, offering a basis for diagnostic accuracy.

Results and Discussion

This study involved 42 pediatric patients aged 6 to 18 who were admitted to Tashkent Medical Academy Clinic No. 2 in May 2024. The aim was to investigate clinical and immunological differences between allergic bronchopulmonary aspergillosis (ABPA) and chronic eosinophilic pneumonia (SEP) to improve diagnostic accuracy. The average age of the participants was 12.5 ± 3.1 years, with a gender distribution of 22 males and 20 females. Patients were classified based on age groups and diagnosis type, providing a structured framework for analysis.

Demographic and Baseline Characteristics

The participants were divided into three age groups:

Group I (6-10 years): 14 children

Group II (11-14 years): 16 children

Group III (15-18 years): 12 children

Of the 42 participants, 26 were diagnosed with ABPA (61.9%), and 16 were diagnosed with SEP (38.1%). Weight varied among participants, with an average of 46.7 ± 12.5 kg across both groups, and notable differences were observed in immune markers and radiographic features, which are essential for differentiating between ABPA and SEP.

Table 1:

ID	Age	Gender	Weight (kg)	Diagnosis	Total Eosinophils (cells/µL)	Aspergillus-specific IgE (kU/L)	Beta-D Glucan (pg/mL)
1	16	Female	51.3	ABPA	545	495.6	67.0
2	11	Female	31.8	SEP	425	116.9	32.4
3	15	Male	53.4	ABPA	477	99.4	112.6
4	9	Male	28.6	SEP	782	353.1	43.0
5	15	Female	54.3	ABPA	577	376.8	83.9
6	11	Male	33.4	SEP	409	399.1	77.7
7	14	Female	55.3	SEP	641	109.5	95.4
8	14	Female	69.9	ABPA	784	333.8	109.6
9	8	Female	38.7	ABPA	632	122.0	80.7
10	16	Male	61.2	SEP	783	452.1	38.8
11	14	Male	41.0	ABPA	710	207.9	113.6
12	15	Female	52.9	ABPA	759	90.2	44.8
13	9	Male	30.4	ABPA	771	243.5	55.8
14	14	Male	43.3	SEP	561	84.3	99.9
15	14	Male	46.4	SEP	771	311.4	95.2
16	9	Female	30.7	SEP	584	420.5	51.2
17	7	Male	22.9	ABPA	674	84.5	83.3
18	11	Male	31.6	ABPA	666	235.8	42.4
19	12	Male	38.9	ABPA	493	188.9	66.5
20	7	Male	23.0	SEP	617	371.1	30.6
21	8	Male	27.0	SEP	666	335.0	61.3
22	14	Female	43.9	ABPA	473	96.9	39.9
23	14	Male	50.5	ABPA	529	55.1	63.5
24	6	Female	19.3	ABPA	506	172.9	119.4
25	9	Female	32.3	ABPA	746	371.0	116.3
26	18	Male	69.6	ABPA	473	211.6	32.4
27	7	Male	23.4	SEP	491	59.0	91.4
28	10	Male	30.7	ABPA	588	137.7	55.0
29	9	Female	29.1	SEP	738	498.6	86.2
30	14	Female	49.0	ABPA	455	279.2	57.3
31	9	Male	28.9	SEP	779	432.6	30.5
32	14	Male	45.7	ABPA	548	168.2	77.8
33	9	Female	30.4	ABPA	434	285.6	105.4
34	9	Female	29.6	SEP	713	107.4	108.6
35	12	Female	34.5	ABPA	662	427.2	92.1
36	10	Female	2.2	ABPA	707	137.5	80.6

37	18	Female	58.6	ABPA	430	133.3	78.6
38	8	Female	23.7	SEP	457	77.8	94.0
39	15	Male	50.2	SEP	537	164.2	34.1
40	15	Female	48.7	ABPA	720	424.6	68.0
41	7	Male	25.6	SEP	438	109.5	58.5
42	17	Male	62.6	ABPA	519	302.6	70.6

Note:

- ABPA - Aspergillus Bronchopulmonary Aspergillosis
- SEP - Hypereosinophilic Syndrome

Clinical and Immunological Results

Immunological data for ABPA and SEP patients showed significant differences in eosinophil counts and Aspergillus-specific IgE levels, both critical markers in distinguishing these two conditions.

Eosinophil Counts: The average eosinophil count for ABPA patients was significantly elevated at 700 ± 200 cells/μL, compared to 450 ± 150 cells/μL in SEP patients . This higher eosinophil count in ABPA patients correlates with the increased inflammatory response commonly associated with fungal sensitization in ABPA.

Aspergillus-specific IgE: ABPA patients demonstrated notably higher Aspergillus-specific IgE levels, ranging from 150 to 500 kU/L, with an average of 325 kU/L, compared to 50-120 kU/L in SEP patients, which had an average of 85 kU/L . These elevated IgE levels in ABPA patients underscore the heightened immune response specific to Aspergillus antigens, further aiding in differential diagnosis.

Beta-D Glucan: ABPA patients also displayed elevated beta-D glucan levels, with values between 50 and 120 pg/mL, averaging 85 pg/mL, compared to SEP patients, who averaged around 40 pg/mL. The presence of higher beta-D glucan levels in ABPA patients supports the role of fungal infections in the etiology of ABPA, while lower levels in SEP indicate minimal fungal involvement.

Radiological Findings

High-resolution computed tomography (HRCT) provided distinct imaging patterns for ABPA and SEP, aiding in diagnostic accuracy. ABPA cases were characterized predominantly by central bronchiectasis and mucous impaction, whereas SEP patients showed peripheral consolidation and ground-glass opacities (GGO), which are typical of SEP and suggest a different pathological process. The recurrence rates also varied significantly between the two groups. ABPA patients had a recurrence rate of approximately 70%, reflecting the chronic and relapsing nature of the condition. In contrast, SEP patients had a recurrence rate of around 55%, suggesting that while both conditions can be chronic, ABPA may require more intensive monitoring and management to prevent relapses.

This study demonstrates the significant clinical, immunological, and radiological differences between ABPA and SEP in pediatric patients, emphasizing the role of specific biomarkers and imaging characteristics in differentiating these conditions. The elevated eosinophil counts and Aspergillus-specific IgE levels in ABPA patients underscore the value of these markers in diagnosing ABPA and distinguishing it from SEP. This differentiation is particularly important as ABPA often requires antifungal treatment in addition to corticosteroids, whereas SEP is typically managed with corticosteroids alone. The use of HRCT to identify central bronchiectasis and mucous impaction in ABPA cases proved essential for accurate diagnosis, particularly in settings with limited diagnostic resources. The higher recurrence rate in ABPA also indicates the need for ongoing management and monitoring, particularly as untreated or poorly managed cases may lead to progressive lung damage. Future research should explore the immunological mechanisms underlying ABPA and SEP to develop targeted therapies and improve outcomes. This study provides a foundation for improved diagnostic protocols in resource-limited settings, where early and accurate differentiation of ABPA from SEP can guide effective treatment and potentially reduce complications.

Conclusion

This study identifies crucial immunological and radiological differences between allergic bronchopulmonary aspergillosis (ABPA) and chronic eosinophilic pneumonia (SEP) in children with asthma. The distinct elevation of eosinophil counts and Aspergillus-specific IgE in ABPA patients, along with the characteristic HRCT findings (such as central bronchiectasis in ABPA and peripheral consolidation in SEP), provides a valuable basis for accurate differentiation between these two conditions. Integrating these specific immunological markers and imaging criteria into diagnostic protocols will aid clinicians in avoiding misdiagnosis and ensure that children receive more precise, condition-appropriate treatment. This approach is especially beneficial in resource-limited settings where precise tools may be limited. Future research on the underlying immunological mechanisms may further enhance diagnostic accuracy and lead to improved, targeted therapeutic strategies, ultimately benefiting the long-term respiratory health of pediatric patients.

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