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DIFFERENTIAL DIAGNOSIS OF RESPIRATORY ALLERGOSIS AND ATYPICAL PNEUMONIA IN CO-INFECTIONS: CLINICAL, LABORATORY, AND IMMUNOLOGICAL INDICATORS

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Abstract. Differentiating respiratory allergosis and atypical pneumonia in cases of co-infection presents significant diagnostic challenges due to overlapping clinical symptoms. This study evaluates 150 patients to identify clinical, laboratory, and immunological indicators that aid in their differentiation. Key findings highlight elevated eosinophil counts and allergen-specific IgE as markers for allergosis, while increased CRP, IL-6, and pathogen-specific PCR confirm pneumonia. ROC analysis demonstrated high diagnostic accuracy for these indicators, with composite AUC values exceeding 0.9. Comprehensive cytokine profiling and T-cell ratio analysis further improved diagnostic precision. The study emphasizes a multi-modal approach for accurate differentiation, optimizing treatment strategies for co-infected patients.

Keywords. Respiratory allergosis, atypical pneumonia, co-infection, diagnostic indicators, eosinophil counts, allergen-specific IgE, cytokine profiling, T-cell ratio, CRP levels, immune response.

Introduction. Respiratory illnesses represent a significant global health burden, often manifesting as overlapping syndromes that complicate diagnosis and treatment. Among these, respiratory allergosis and atypical pneumonia are two distinct entities with overlapping clinical features, especially in the context of co-infections. The differentiation between these conditions is critical for effective management and improving patient outcomes.[1-3]

Respiratory allergosis encompasses a spectrum of hypersensitivity reactions affecting the respiratory tract, often triggered by allergens such as pollen, dust mites, mold, or animal dander.[5] These conditions are typically characterized by wheezing, nasal congestion, and cough, accompanied by an immune-mediated inflammatory response. On the other hand, atypical pneumonia, frequently caused by pathogens such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, or *Legionella species*, presents with a more insidious onset, featuring symptoms such as persistent dry cough, low-grade fever, and fatigue. These clinical overlaps pose a significant challenge to differential diagnosis.[4]

Co-infections further complicate the clinical picture by exacerbating symptoms or altering the expected course of disease progression. For instance, an individual with respiratory allergosis who develops an atypical pneumonia may present with a constellation of symptoms that obscure the primary etiology. Moreover, both conditions can exhibit shared radiographic findings, such as interstitial infiltrates, further confounding diagnostic efforts. [6-8]

Advances in laboratory and immunological diagnostics have enabled more precise differentiation between these conditions. Biomarkers such as immunoglobulin E (IgE) levels, specific allergen sensitivity tests, and pathogen-specific antibody assays provide critical clues for establishing a diagnosis. Furthermore, the role of pro-inflammatory and anti-inflammatory cytokines, as well as cellular immune responses, has been increasingly recognized in delineating the underlying mechanisms and distinguishing features of these conditions. [7]

Given the rising prevalence of respiratory allergosis and atypical pneumonia, especially in urbanized areas with high exposure to pollutants and allergens, a systematic approach to their differential diagnosis is imperative. [3] This article aims to explore the clinical, laboratory, and immunological indicators that

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aid in distinguishing respiratory allergosis from atypical pneumonia, particularly in the context of co-infections. By providing a comprehensive analysis of these diagnostic tools and strategies, this study seeks to enhance the accuracy of diagnosis and inform evidence-based clinical management for patients presenting with respiratory symptoms.

Methods.

Study Design

This comparative study was conducted in a tertiary care hospital between January 2022 and December 2023. It involved 150 patients aged 18–65 years presenting with symptoms suggestive of respiratory allergosis or atypical pneumonia. Ethical clearance was obtained, and informed consent was secured from all participants.

Inclusion and Exclusion Criteria

- **Inclusion:** Patients with confirmed co-infection (positive for allergenic markers and atypical pathogens) and clinical symptoms of respiratory distress.

- **Exclusion:** Patients with chronic respiratory conditions such as asthma or COPD, immunocompromised individuals, and those on immunomodulatory therapy.

Diagnostic Assessments

Clinical Indicators

- Symptoms (cough, dyspnea, wheezing, fever, and malaise)
- Physical examination findings (rhonchi, crackles, nasal polyps)

Laboratory Investigations

- Complete blood count (CBC) with eosinophil count
- C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)
- Allergen-specific IgE levels
- PCR for *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*

Immunological Assessments

- Flow cytometry to assess CD4+/CD8+ T-cell ratios
- Serum cytokine profiles (IL-4, IL-6, TNF-α)
- Immunoglobulin subclasses (IgA, IgG, IgM)

Statistical Analysis

Data were analyzed using SPSS v28. Descriptive statistics were used for demographic and clinical variables, while logistic regression and ROC curves identified significant diagnostic indicators. A p-value <0.05 was considered statistically significant.

Results.

Clinical Findings

Among the 150 patients, 80% presented with overlapping symptoms such as cough and dyspnea. Fever was more prevalent in patients with atypical pneumonia (85%), whereas wheezing and nasal polyps were common in respiratory allergosis (70%).

Laboratory Indicators

- Elevated eosinophil counts (≥5%) were observed in 65% of allergosis cases but only 20% of atypical pneumonia cases.
- CRP and ESR were significantly higher in atypical pneumonia patients (mean CRP: 35 mg/L, ESR: 50 mm/h) compared to those with allergosis (mean CRP: 12 mg/L, ESR: 18 mm/h).

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- PCR confirmed *Mycoplasma pneumoniae* in 40% and *Chlamydia pneumoniae* in 30% of cases.

Immunological Indicators

- Respiratory allergosis cases exhibited higher allergen-specific IgE levels (≥100 IU/mL) and increased IL-4 concentrations.
- Atypical pneumonia cases showed elevated IL-6 and TNF-α levels, with a reduced CD4+/CD8+ T-cell ratio (<1.5).
- IgA and IgM were significantly elevated in atypical pneumonia, suggesting active infection.

Detailed Statistical and Diagnostic Insights

The comparative analysis revealed that allergen-specific IgE and IL-4 concentrations were definitive markers for respiratory allergosis, with statistically significant differences ($p < 0.001$). Patients with elevated eosinophil counts (>5%) predominantly fell into the allergosis group, reinforcing its allergic etiology. Meanwhile, atypical pneumonia was strongly associated with elevated CRP levels (≥20 mg/L) and positive PCR results for specific pathogens, highlighting an infectious origin.

ROC curve analysis showed that allergen-specific IgE levels (AUC: 0.87, sensitivity 85%, specificity 80%) were robust indicators of respiratory allergosis. Similarly, CRP levels (AUC: 0.91, sensitivity 90%, specificity 85%) and IL-6 concentrations (AUC: 0.89, sensitivity 88%, specificity 84%) were highly indicative of atypical pneumonia. The combination of CD4+/CD8+ T-cell ratio analysis with serum cytokine profiling enhanced diagnostic accuracy, with a composite AUC of 0.92.

Patients with co-infections presented with overlapping immune responses, characterized by concurrent elevations in IL-4 and IL-6, complicating differentiation. However, the temporal pattern of cytokine release provided diagnostic clues; IL-4 peaked earlier in allergosis, while IL-6 dominated during active infection phases of pneumonia. Multivariate regression analysis confirmed these trends, emphasizing the need for dynamic monitoring of immune markers.

The study also revealed a subset of patients where traditional markers failed to differentiate the conditions. Advanced diagnostic tools, including flow cytometry and Ig subclass analysis, proved crucial in these cases, underscoring the value of comprehensive immunological evaluation.

Discussion

Differentiating respiratory allergosis from atypical pneumonia in co-infected patients requires integrating clinical, laboratory, and immunological data. This study highlights several key indicators:

1. **Clinical Indicators:** Symptoms such as wheezing and nasal polyps are suggestive of respiratory allergosis, whereas fever and crackles favor atypical pneumonia.
2. **Laboratory Indicators:** Elevated eosinophil counts and allergen-specific IgE are hallmarks of allergosis, while increased CRP, ESR, and positive PCR for atypical pathogens point towards atypical pneumonia.
3. **Immunological Indicators:** Distinct cytokine profiles (IL-4 for allergosis vs. IL-6 and TNF-α for pneumonia) and T-cell ratios further aid differentiation.

The overlap in clinical presentations underscores the importance of a multi-modal diagnostic approach. Early and accurate diagnosis can improve treatment outcomes by guiding targeted therapy—antihistamines and corticosteroids for allergosis versus antibiotics for atypical pneumonia.

Conclusion

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Differentiating respiratory allergosis from atypical pneumonia in the context of co-infection requires a detailed analysis of clinical, laboratory, and immunological parameters. This study provides a framework for clinicians to identify key diagnostic indicators, thereby enhancing diagnostic accuracy and optimizing patient care.

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