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CASE REPORT

Hypereosinophilic Syndrome in a 15-Year-Old Girl with Persistent Eosinophilia and Asthma-like Symptoms

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Abstract

This case report highlights a 15-year-old girl diagnosed with Hypereosinophilic Syndrome (HES) following a history of childhood eczema, asthma-like symptoms, and persistent eosinophilia. Despite standard asthma treatment, including inhaled steroids and oral prednisolone, the patient experienced recurrent eosinophilia and respiratory exacerbations. After ruling out secondary causes and diagnosing HES, the patient was successfully treated with benralizumab, resulting in complete resolution of her respiratory and gastrointestinal symptoms.

Keywords:
- Eosinophilia
- Hypereosinophilic Syndrome
- Asthma
- Steroids

Introduction

Hypereosinophilic Syndrome (HES) is a rare hematologic disorder characterized by persistent eosinophilia, often resulting in organ damage due to eosinophil infiltration [1]. It is frequently misdiagnosed as asthma or other allergic conditions, particularly when eosinophilia is present. In this case, a 15-year-old girl with a history of asthma-like symptoms, recurrent eosinophilia, and

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eczema was ultimately diagnosed with HES following an extensive work-up. The patient's favorable response to biologic therapy further confirmed the diagnosis.

Case Presentation:

A 15-year-old girl with a history of eczema since childhood was diagnosed with asthma a year ago due to recurrent respiratory symptoms and persistent eosinophilia. Despite treatment with long-acting β-2 agonists, inhaled steroids, and oral prednisolone (40 mg daily, tapered to 5 mg), the patient experienced recurrent eosinophilia and exacerbations of respiratory symptoms. The patient was then started on Omalizumab. She is a non-smoker and has no family history of asthma.

The patient's medical history includes eczema affecting her hands, legs, and thighs, associated with urticaria. She also experienced migratory arthralgia, episodes of lower limb edema, eye puffiness, and hand swelling, which responded well to corticosteroids. Additionally, the patient had recurrent admissions for pneumonia over the past year and developed episodes of non-projectile vomiting, nausea, and abdominal pain.

Clinical Course:

On January 9, 2024, the patient was admitted with worsening shortness of breath that developed two weeks after a flu-like illness. Her respiratory symptoms progressively worsened, particularly with exertion. She experienced a productive cough, yellowish in color, mild in amount, but without hemoptysis. Associated with these symptoms were non-typical chest pain, migratory arthralgia, and recurrent episodes of bilateral lower limb non-pitting edema, eye puffiness, and hand swelling. These episodes resolved with oral steroids. The patient also reported easy fatigability.

Clinical Examination:

- Fully conscious, alert, and oriented.
- Right upper eyelid swelling.

Chest Examination: Bronchial breathing noted (Figure 1).

- No lower limb edema.

Laboratory Findings:

Item	Result	Normal Value
WBCs	58.85 X10^9/L	4.5 - 10
Eosinophil percent	66.7%	1 - 6
Eosinophil count	39.23	0.04 - 0.4
Total IgE level	534 IU/ml	10-15 Years <200
RAST test	Positive for banana: 0.69 KU/I, barely: 0.59 KU/I	
ANCA profile	Negative	
RA, Anti-CCP, Anti-SCL-70, Anti-Centromere, ANA, Anti-Ro, Anti-La	Negative	
Thyroid Function Test	Normal	
Urine examination	Normal	
Liver/Renal function tests	Normal	
LDH/CRP/ESR	Normal	

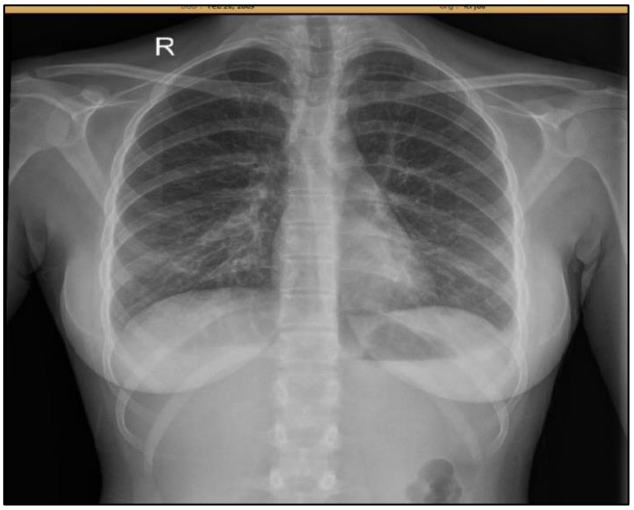

Figure 1: Chest X-ray: Right lower zone patchy ground-glass opacity

Further Investigations:

- **Bronchoscopy (08-02-2024):** Airways and segments patent, no significant findings.
- **Bronchoalveolar lavage (BAL) and pleural fluid analysis (19/2/2024):** Turbid appearance with high WBC counts, predominantly polymorphonuclear cells and eosinophils (42%).
- **Histopathology (Bronchial Biopsy):** Eosinophil-rich inflammation with mixed chronic inflammatory infiltrates. No granulomas or vasculitis.
- **BAL Culture:** Negative for infections; fungal and AFB/MTB PCR: Negative.
- **HRCT (8/23):** Mild bilateral pleural effusion, ground-glass attenuation, and interstitial thickening.

Peripheral Blood Smear Examination:

- **WBCs**: Marked leukocytosis with predominant eosinophils. No blasts nor significant dysplasia.
- **RBCs**: Mild anisopoikilocytosis.
- **Platelets**: Mild thrombocytosis with few large platelet forms.

Bone Marrow Aspirate:

- **Quality**: Particulated with cellular particles and trails.
- **Megakaryocytes**: Mild increased with unremarkable morphology.
- **Erythropoiesis**: Relatively reduced.
- **Myelopoiesis**: Present.
- **Eosinophils**: Markedly increased with few showing atypia.
- **Blasts**: Not increased.

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- **Others**: Plasma cells are slightly prominent with no significant atypia.

Bone Marrow Trephine Biopsy:

- **Quality:** Adequate.
- **Cellularity**: Hyper cellular ~80%.
- **Megakaryocytes**: Mildly increased.
- **Erythropoiesis**: Present.
- **Myelopoiesis**: Present.
- **Eosinophils**: Markedly increased.
- **Infiltrates**: No clear immature cellular collection.
- **Others**: Plasma cells are slightly prominent with no clear abnormal collection.

Immunohistochemistry:

The following immunohistochemical stains were performed on bone marrow biopsy with appropriate positive controls:

- **CD138**: Highlight plasma cells.
- **Kappa/Lambda**: Polyclonal plasma cells.
- **CD3:** Highlight some reactive T-cells in the background.
- **CD20:** Highlight some reactive B-cells in the background.
- **CD34:** No excess blasts.
- **Karyotype**: 46, XX [20]

Interpretation:

No clonal chromosome abnormality was apparent. Absence of a microscopically visible clonal abnormality does not rule out the presence of neoplasia.

FISH using probers for PDGFR b(5q32-q33) break apart control probe (Vysis, Abbott Molecular, Inc.). 100 nuclei scored manually from a 24 hours unstimulated cultured bone marrow sample.

1. **FISH Interpretation:** PDGFR b gene rearrangement was not detected by interphase FISH using probers for FIP1L1, CHIC2, PDGFR a (4q12) break apart probe (Vysis, Abbott Molecular, Inc.). 100 nuclei scored manually from a 24 hours unstimulated cultured bone marrow sample.

2. **FISH Interpretation:** FIP1L1, CHIC2, PDGFR a rearrangement/deletion was not detected by interphase FISH.

The above Cytogenetics results will rule out all hematological malignancies

Diagnosis and Management:

After extensive investigations, the patient was diagnosed with Hypereosinophilic Syndrome (HES) after ruling out secondary causes of eosinophilia (e.g., Infections, Allergies, and Malignancies [2]). The patient was started on benralizumab 30 mg subcutaneously every 4 weeks, alongside a step-down steroid regimen.

Outcome/Results:

Following the second dose of benralizumab, the patient showed complete resolution of her respiratory symptoms, including cough, dyspnea, and wheezing. Gastrointestinal symptoms (Nausea and Vomiting) resolved, and the angioedema and lower limb edema also subsided. Laboratory results showed significant improvement in total leukocytic counts and eosinophilia. The patient remains clinically stable (Figure 2).

- **WBCs normalized**: 5.66 X10^9/L
- **Eosinophil count**: 0.9%, 10.6%

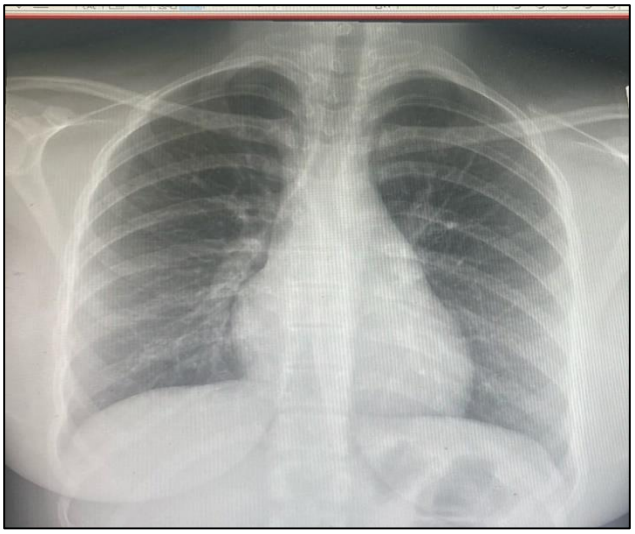

Figure 2: Chest X-ray: Regression of right lower zone opacity

Discussion:

This case emphasizes the importance of considering Hypereosinophilic Syndrome (HES) in patients with persistent eosinophilia and unexplained respiratory symptoms, particularly when standard asthma therapy fails. The use of benralizumab, an IL-5 antagonist, proved to be an effective treatment option, highlighting the role of biologic therapies in managing eosinophilic disorders. Early identification and tailored treatment can lead to significant improvement in both symptoms and laboratory findings.

Conclusion:

This case highlights the challenges in diagnosing Hypereosinophilic Syndrome in a patient initially thought to have asthma. A thorough diagnostic work-up, including imaging, blood tests, and bone marrow biopsy, ultimately led to the correct diagnosis. The patient's positive response to benralizumab demonstrates the efficacy of targeted biologic therapy in managing HES.

This case report presents an important learning opportunity in recognizing HES and effectively managing it with biologic

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therapies, potentially improving outcomes for patients with this rare condition.

Conflict of interest: None

Ethical Consideration: None

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