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An Uncommon Case of Severe Asthma - Eosinophilic granulomatosis with polyangiitis (EGPA)

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Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA) previously known as Churg-strauss syndrome is a multisystem disorder most commonly involving the lungs. It is a form of vasculitis that targets small to medium-sized blood vessels. It is a necrotizing granulomatous inflammation that is eosinophil-rich and frequently affects the respiratory system. It is also associated with difficult-to-treat asthma and eosinophilia. We describe a case of a 49-year-old man with documented severe asthma who presented with proximal myopathy and asthma exacerbation. Blood investigations showed that he had eosinophilia. Mononeuritis multiplex was confirmed by NCV (Nerve conduction velocity). Transbronchial lung biopsy and nerve biopsy proved vasculitis with eosinophils confirming the diagnosis of EGPA.This case highlights the diagnostic challenges with the manifestations of EGPA in a case of difficult-to-treat asthma.

Key words: Eosinophilic granulomatosis with polyangiitis (EGPA), Difficult-to-treat asthma, Severe asthma, Mononeuritis multiplex, Transbronchial lung biopsy (TBLB), Antineutrophil cytoplasmic antibodies (ANCA).

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is a type of vasculitis that commonly affects the lung predominantly involving small to medium sized vessels. It is an eosinophil-rich granulomatous inflammation of lungs with necrotizing vasculitis and is commonly associated with asthma and peripheral eosinophilia. [1] Most patients with EGPA have antineutrophil cytoplasmic antibodies (ANCA) detected in the blood at the time of the initial presentation. It usually affects people between the ages of 40 and 50, and both men and women are affected equally. The prevalence of EGPA is grossly about 10–18 cases per million population.[2] A strong index of suspicion is required to correctly diagnose the rare disease like EGPA, which presents with a wide spectrum of multisystemic symptoms, especially in cases with severe asthma.. It does, however, respond well to treatment, therefore early suspicion and precise diagnosis are critical for better outcomes.

Case Report

49-year-old male, non-smoker who was a known case of bronchial asthma since past ten years, presented with acute asthma exacerbation. He was on treatment with high dose ICS-LABA (budesonide 320mcg+formoterol 9mcg- B.I.D) and leukotriene receptor antagonist. His inhaler technique was acceptable and was using it with suboptimal adherence. He also complained of numbness and tingling sensation in both his legs and palms for one year and loss of power of his right foot. He gave history of bronchial asthma with frequent exacerbations in the past. On auscultation bilateral polyphonic rhonchi was heard. On neurological examination wasting of muscles was noted in bilateral palms and both the feet. Dorsiflexion of the left lower limb was 2/5 and right limb was 4/5. In the upper limbs hand grip was weak and weakness in all the small muscles was present. Bilateral ankle reflex was absent. The findings were suggestive of asymmetrical axonal motor-sensory neuropathy.

Hemogram showed 30% eosinophils, and serum ACE level was 960. Chest x-ray, 2-D echo and HRCT thorax were normal. There were no ENT manifestations and computed tomography paranasal sinuses (CT PNS) was

normal.The patient was subjected to a spirometry which showed severe obstruction with no post-bronchodilator reversibility. (Forced expiratory volume in 1 second [FEV_1] 0.86 L (44% predicted); forced vital capacity [FVC] 1.54L (60% predicted); FEV_1/FVC, 56.1%). ANCA studies were done as vasculitis was suspected, ANCA-PR3 also known as cytoplasmic-ANCA (c-ANCA) was positive (20.32RU/ml) and ANCA-MPO also known as perinuclear-ANCA (p-ANCA) was negative.

As EGPA was suspected bronchoscopy with transbronchial lung biopsy was performed as histopathology confirmation is a mainstay of diagnosis BAL reports were normal and the TBLB revealed alveolated lung parenchyma with small vessel vasculitis and bronchial mucosa with prominent increase in eosinophils which was suggestive of EGPA (Figure1 and 2). NCVwas suggestive of asymmetrical axonal motor sensory neuropathy, involving bilateral ulnar, left peroneal nerve and bilateral sural nerves confirmed mononeuritis multiplex. Nerve biopsy of right sural nerve was done which showed vasculitis. Patient was diagnosed as a case of EGPA.Patient was treated with prednisolone 40mg daily for two months and responded well and is now on maintenance dose of steroids [1].

Discussion

Severe Asthma is a subset of Difficult-to-treat asthma which is uncontrolled despite adherence with maximal optimal dose ICS-LABA treatment and management of contributory factors or that worsens when high dose treatment is decreased. [3]EGPA is a type of vasculitis that commonly affects the lung and should be suspected in a case of severe asthma.

Differentials considered in our case for eosinophilia included chronic eosinophilic pneumonia (CEP), hypereosinophilic syndromes (HES), parasitic infections and other vasculitis. CEP primarily involves the lungs without involvement of other organs and bronchial asthma is not seen in HES patients. The final diagnosis of EGPA was challenging to establish and it was only after all the patient's investigations were completed that the diagnosis was made.

EGPA manifests in three phases that follow one another: the prodromal phase, which is marked by asthma, aller gic rhinitis, and atopic illness.

The second phase is known as the eosinophilic phase, and it is characterised by the presence of eosinophilia in p eripheral blood smears as well as eosinophilic infiltration of several organs, including the lung and the digestive system. The third stage, known as the vasculitic stage, is characterised by systemic vasculitis of the medium and small vessels and is linked to a potentially fatal vascular and extravascular granulomatosis. [4, 5] Our patient presented in the vasculitic phase of the disease.

The most popular classification of EGPA was developed by the American College of Rheumatology (ACR) and consists of six criteria. For the diagnosis of EGPA, the presence of four or more of these criteria has an 85% sensitivity and a 99.7% specificity. The criteria include bronchial asthma, presence of eosinophils (>10%), mononeuritis multiplex, presence of lung infiltrates, paranasal sinus abnormality and presence of eosinophils in extravascular areas. [6] The ACR criteria were met by our patient and the diagnosis of EGPA was made.

ANCA is detected in approximately 40% of all EGPA patients, with p-ANCA being the most common type. Roughly 5% of EGPA cases have c-ANCA, while about 40% of cases have p-ANCA[2]. Our patient was c-ANCA positive which made it a challenging diagnosis.

Peripheral neuropathy, usually affecting at least two separate nerve areas (mononeuritis multiplex), is seen in up to 75 percent of patients with EGPA and presents with pain, numbness, and/or weakness. Patients with mononeuritis multiplex are more likely to have a positive ANCA[1]. Our patient presented with similar neurological complaints and was diagnosed with mononeuritis multiplex by NCV.

Based on the severity of the disease, the patients are started on corticosteroids and cyclophosphamide for three months. Our patients responded well to corticosteroids and was continued on maintenance regimen of corticosteroid taperingand the EGPA is currently in remission. In individuals with systemic vasculitis, corticosteroids and immunosuppressants, particularly cyclophosphamide, have significantly improved prognosis and overall survival rates.

Conclusion

Eosinophilic granulomatosis with polyangiitis is a rare multisystem disease and needs high index of suspicion. Severe asthma with eosinophilia and neurological symptoms prompted us to evaluate the patient for EGPA. EGPA diagnosis is difficult and is often missed in the absence of diagnostic criteria.Clinical and imaging features could assist in the diagnosis of EGPA, but biopsy remains the confirmatory test for the diagnosis.

Patient consent for publication: Obtained.

FIGURES

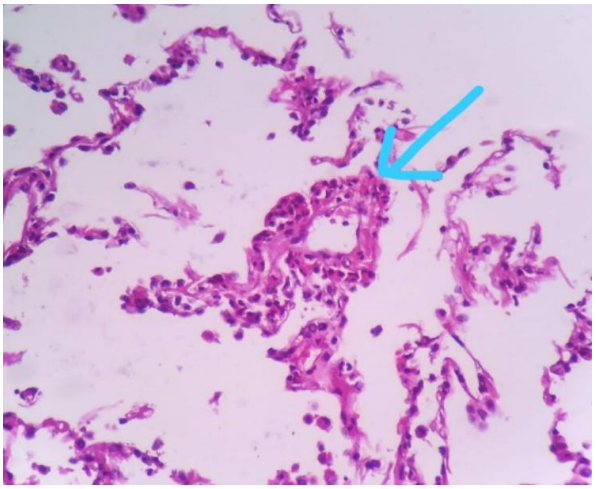

Figure 1: Specimen of TBLB showing vessel in the interstitium with eosinophilic vasculitis

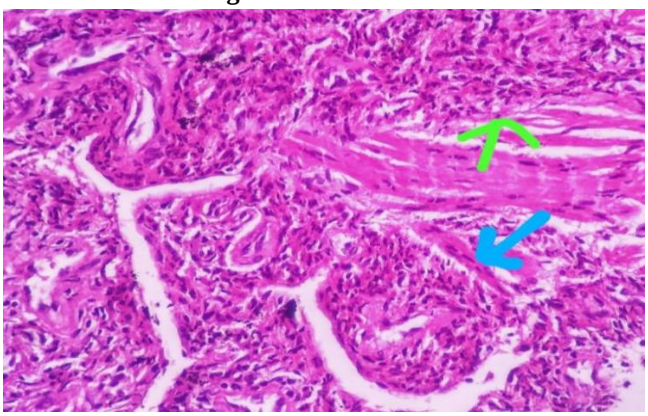

Figure 2: Specimen of TBLB, Blue arrow depicting vasculitis and yellow arrow depicting aggregation of eosinophils in bronchial wall.

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