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Resolution of Chronic Eosinophilic Pneumonia during Treatment with Benralizumab in Patient with Peripheric Blood Eosinophilia

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Abstract Chronic eosinophilic pneumonia is a rare idiopathic form of pneumonia. A differential diagnosis is crucial to distinguish idiopathic from secondary forms and it requires clinical, laboratory and imaging investigations. In this case report we present a case of Chronic eosinophilic pneumonia and discuss differential diagnosis in a patient with a history of uncontrolled chronic asthma and moderate peripheral eosinophilia. Benralizumab, an anti-Interleukin-5 receptor drug, was administered to our patient, who remained asymptomatic throughout a ten-month follow-up. Further studies are essential to confirm the favorable effect of this novel therapy for Chronic eosinophilic pneumonia.

Keywords: *eosinophilia, benralizumab, chronic eosinophilic pneumonia, asthma, fever*

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1. Introduction

Eosinophilic lung diseases are a group of pathologies characterized by the presence of a lung tissue eosinophilic infiltration, with or without peripheral eosinophilia. Here we present a case of chronic eosinophilic pneumonia, focusing on the differential diagnosis and the use of anti-interleukin-5 receptor (IL-5R) therapy.

2. Clinical Case

A fifty-year-old man was hospitalized in our department, presenting fever and a productive cough for several days.

He had a history of atopy, multiple episodes of asthma exacerbations and pneumonia, which responded to treatment with empiric antibiotic and systemic corticosteroid treatments.

From 2014 peripheral blood eosinophilia and elevated serum IgE levels had been recorded.

The patient had severe uncontrolled persistent asthma despite treatment with medium-to-high-dose inhaled corticosteroids, long-acting beta2-agonists and leukotriene antagonists.

At the admission, the patient did not present with respiratory failure. Blood tests showed an elevated eosinophil count (WBC 12300/µL, EOS 4182/µL).

Computed tomography (CT) scan showed bilateral peripheral ground-glass opacities, mostly in the upper lobes (Figure 1 A). Bronchoalveolar lavage eosinophil percentage (BEP) was 80%. The diagnosis of chronic eosinophilic pneumonia (CEP) was made. Oral steroid therapy with prednisone 0.5 mg/kg per day was prescribed, resulting in clinical response, normalization of the eosinophilic count (Table 1) and CT scan opacities completely resolution after a week of steroid therapy (Figure 1 B).

Table 1. Laboratory results of the patient at the time of the admission, after the different treatments and at the time of the present report

	WBC (cell/µL)	EOS (cell/µL)	CRP (mg/dL)
Admission	11700	4900	9.13
After 72h of steroid therapy	12600	230	1.71
After a single dose of benralizumab	9410	0	0.5
At the time of the present report (after 10 months of follow-up)	8000	0	0.3

Abbreviations: WBC: white blood count, EOS: eosinophil, CRP: C-reactive protein.

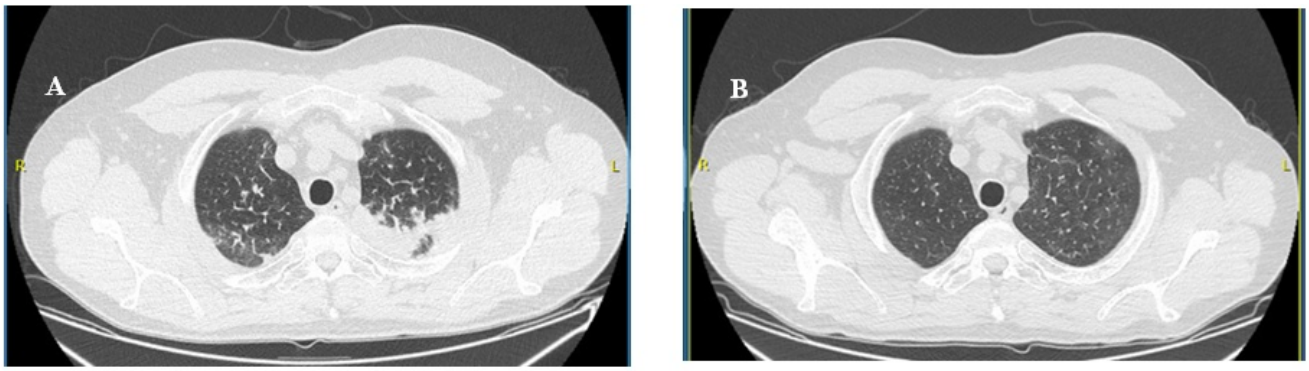

Figure 1. CT scan before corticosteroid therapy (A). CT scan one week after commencement of corticosteroid treatment (B)

In view of his clinical history, the patient started therapy with benralizumab. The treatment was administered by subcutaneous injection with an accessorized prefilled syringe, containing 30 mg/mL in 1mL, every 4 weeks for the first 3 doses and then every 8 weeks. The patient did not experience CEP relapse after commencing benralizumab and remained asymptomatic throughout the ten-month follow-up.

3. Discussion

We reported a case of CEP. Table 2 summarizes the possible differential diagnoses in patients with pulmonary eosinophilia.

First of all, a pharmacological etiology was excluded; indeed, drugs are one of the most common causes of induced eosinophilic pneumonia [1].

Allergic bronchopulmonary aspergillosis (ABPA) is characterized by asthma exacerbation, the presence of Aspergillus IgE and IgG, generally recurrent unilateral opacity in the upper lobe [2], high serum levels of IgE, high peripheral eosinophilia and BEP. Tasting for specific mutations such as Jak-2 mutation, FiP1L1-PDGFRA and PDGFRB is useful to exclude neoplastic causes.

In our patient, blood cultures and microbiology tests on fecal samples ruled out an infectious etiology, which is epidemiologically more frequent than an idiopathic one [1]. Neither Aspergillus serology nor galactomannan were positive. The absence of systemic involvement ruled out an autoimmune etiology.

The history of asthma and the absence of respiratory failure directed to a diagnosis of CEP.

Laboratory tests and imaging play a crucial role in the differential diagnosis of the idiopathic forms. Peripheral eosinophilia and elevated total serum IgE levels are common in CEP [3] than in AEP. In both AEP and CEP, a high BEP generally greater than 40% is present [4].

In CEP the most frequent are unilateral or bilateral areas of consolidation and ground-glass opacities with a peripheral distribution. In AEP the periphery is involved in only 30% of cases [5].

Table 2. Differential diagnosis of eosinophilic pneumonia

DIAGNOSIS		Secondary forms			Idiopathic forms			
		DIEP	IP	ABPA	CEP	AEP	EGPA	HES
INVESTIGATION	History of Asthma	–	-	+ (also cystic fibrosis)	+	+/-	+	+/-
	Use of Drugs	+	–	-	-	-	-	-
	Total IgE	+	+	+	+	+	+	+/-
	BEP	+/-	+	+	+	+	+	+
	Culture[A]	-	+	-	-	-	-	-
	Serology	-	+ (Parasitic form)	+ (Aspergillus)	-	-	-	-
	Genetic Mutation	-	–	-	-	-	-	+ (FIP1L1-PDGFRA, PDFRB)
	Typical Imaging	Peripheral and upper consolidation/ ground-glass opacity	No specific features	Central bronchiectasis and large unilateral upper nodule	Peripheral upper consolidation/ground-glass opacity	Craniocaudal and central ground-glass opacity	Bilateral peripheral ground-glass opacity (upper or lower lobes)	No specific features
	Systemic involvement[B]	+/-	+/-	-	-	-	+	+
	Autoimmunity	-	–	-	-	-	+	-

Abbreviations: ABPA: Allergic Bronchopulmonary Aspergillosis. AEP: Acute Eosinophilic Pneumonia. BAL: Bronchoalveolar Lavage. BEP: Bronchoalveolar Lavage Eosinophil Percentage. CEP: Chronic Eosinophilic Pneumonia. DIEP: Drug Induced Eosinophilic Pneumonia. EGPA: Eosinophilic Granulomatosis with polyangiitis. HES: HyperEosinophilic Syndrome. IP: Infectious Pneumonia.
Notes: A. Culture of BAL, faecal and blood samples. B. Systemic involvement: proteinuria, renal/hepatic injury, heart infiltrate.

CEP diagnosis is based on the following working criteria: 1) clinical symptoms (for more than two weeks); 2) imaging anomalies; 3) BEP> 25%, peripheral eosinophilia and/or eosinophilic infiltrate on lung biopsy; 4) exclusion of other types of eosinophilic pneumonia such as those secondary to drugs, parasitic infections, ABPA and EGP; 5) a dramatic response to steroid therapy [6].

Accordingly, a diagnosis of CEP was made.

The cornerstone of the therapy for CEP is steroid treatment. The prognosis is often good, although the use of long-term steroid therapy can cause numerous side effects. Little is known about the pathogenesis of CEP; anyway several studies have shown the presence of elevated levels of IL-5 in BAL and in the peripheral blood of patients with CEP [7]. Our patient has been treated with benralizumab which is a humanized, afucosylated, monoclonal antibody directed against the alpha subunit of the IL-5R. It induces a rapid and complete depletion of peripheral blood eosinophils [8], and has been approved in the treatment for refractory hypereosinophilic asthma. Only few case reports to date have evaluated the use of benralizumab in patients with CEP and uncontrolled chronic asthma. Reference [9] reported a case of a young woman treated with a single dose of benralizumab, leading to the resolution of symptoms and consolidation at CT scan, without any evidence of relapse until 8 weeks after the administration. Reference [10] also observed in their case report the rapid effectiveness of a single dose of benralizumab, which continued during a six-month follow-up.

In our patient the peripheral eosinophil count fell to zero after a single administration of benralizumab and no CEP relapse was observed throughout the following ten-month period.

4. Conclusion

Chronic eosinophilic pneumonia is a rare clinical entity, characterized by severe disease flare-ups and frequent hospitalization.

Benralizumab may represent the future for the treatment of this pathology. Further prospective studies, however, need to better evaluate the effectiveness of benralizumab in CEP.

Declaration of Competing Interest

None of the authors have conflicts of interest to declare.

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Conflicts of Interest

Guarantors of the article: A. C., A.G., F.M.

Writing: original draft: A.G., F.M.

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Abbreviations

AEP: acute eosinophilic pneumonia*;* **ABPA:** allergic bronchopulmonary aspergillosis; **BAL:** bronchoalveolar lavage; **BEP:** bronchoalveolar lavage eosinophil percentage; **MTB:** mycobacterium tuberculosis; **CEP:** chronic eosinophilic pneumonia; **CT:** computed tomography; **CRP:** c-reactive protein; **DIEP**: drug-induced eosinophilic pneumonia; **EGPA**: eosinophilic granulomatosis with polyangiitis; **EOS**: eosinophils; **HES:** hyper-eosinophilic syndrome; **IL**: interleukin; **IL-5R**: interleukin 5 receptor; **IP:** infectious pneumonia; **WBC:** white blood count

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