Anti-IL5/5R in the treatment of chronic eosinophilic pneumonia and severe asthma

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To the Editor,

Chronic eosinophilic pneumonia (CEP) is a rare disease among the diffuse parenchymal lung diseases characterized by significant eosinophil infiltrations in the pulmonary parenchyma and the alveolar spaces (1). Patients with CEP frequently have history of asthma and atopy, therefore it may occur predominantly in patients who are prone to develop a T-helper-2 response. Currently, it diagnosis is based on the presence of respiratory symptoms for at least two weeks, chest radiologic findings (diffuse pulmonary alveolar consolidation and/or ground glass opacities,especially with peripheral predominance), the presence of eosinophilia at bronchoalveolar lavage (BAL) and/or peripheral blood (a BAL cell count differential >25 % or blood eosinophils >1000/μL), and the absence of other known causes of eosinophilic lung diseases (2). Although oral corticosteroids (OCS) are the mainstay treatment with usually a good respond, relapses frequently occur while decreasing or stopping OCS, thus requiring prolonged treatment with the risk of long-term side effects (1,2).

In last years, the knowledge of eosinophil biology has led to the development of several biologics targeting eosinophils such as biologics targeting intelukin (IL)-5 (mepolizumab and reslizumab) and IL-5 receptor (benralizumab) (3). These therapies have revolutionized glucocorticoid sparing treatment of eosinophilic respiratory diseases (4). Due that eosinophils play a primary role in the pathophysiologic of CEP and the association with asthma (2), eosinophil-specific biologics may be alternative candidates for the treatment. Recent data in case series (5–7) and case reports (8–10) show their potential benefit effect in this disease.

Here, we present an additional case series of patients with diagnosis of CEP and concomitant severe eosinophilic asthma treated successfully with anti-IL-5/5R biologics.

We retrospectively analyzed the clinical records of patients with diagnosis of CEP and severe asthma treated with anti IL5/5R therapy in our department from to 2010 to 2023. We evaluated the effect of biologic therapy on the daily dose of OCS, number of annual asthma exacerbations, asthma control assessed by the Asthma Control Test (ACT) and peripheral blood eosinophil counts at baseline and after one year of treatment.

Six patients were included (five women and one man). The mean age at diagnosis of CEP was 39.6 years (from 21 to 49 years). Five had concomitant diagnosis of severe uncontrolled asthma and allergic rhinoconjunctivitis, and one asthma-chronic obstructive pulmonary disease overlap. Two were former smokers. CEP was diagnosed based on the criteria described before (2) and other causes of eosinophilic lung diseases were excluded. Five patients had compatible findings on the lung computed tomography (CT) (figure 1) with marked eosinophilia at BAL in three patients (mean of 38% of eosinophils, range 30-49%) and the other two patients presented peripheral blood eosinophilia (1730 and 4400/μL). One patient was diagnosed by transbronchial lung biopsy. In

this patient we could not collect the CT images nor the laboratory data at the moment of the diagnosis. In addition, all the patients underwent screening tests for eosinophilic granulomatosis with polyangiitis (EGPA) and had negative results for proteinase 3 antineutrophil cytoplasmic antibodies (PR-3 ANCA) and myeloperoxidase antineutrophil cytoplasmic antibodies (MPO-ANCA).

Anti-IL-5/IL5R were principally prescribed because of severe uncontrolled asthma and the prolonged glucocorticoid treatment. Prior the biologic therapy, all patients were treated with at least high-dose inhaled corticosteroids plus long-acting β-agonists with poor control of their asthma (mean of ACT 16.6, range from 16 to 18). Five patients were receiving OCS with a mean daily dose of prednisone of 12mg/day (from to 5-30mg). One patient presented avascular necrosis of the femoral head and shoulder and developed diabetes related to corticosteroid treatment.

Reslizumab was prescribed in two patients (200 and 337mg every 4 weeks according to the patient's weight), two received mepolizumab (100 mg every 4 weeks) and two benralizumab (30 mg every 8 weeks). One of them had received omalizumab previously. One patient reported headaches associated to mepolizumab. No other adverse effects of biologics were recorded.

After one year of treatment with anti IL5/IL5R, among the five patients with OCS, three could discontinued the corticosteroid treatment; in one patient the daily dose of prednisone was dropped from 30 to 10mg, and one continued with the same dose (5mg/day). All patients had reached asthma control according to the ACT (mean 23.3, range 21 to 25) and we found a decrease in the mean of asthma annual rate of exacerbations (from 2.5 to 0.6). Regarding the blood eosinophils count, we found a decrease from a mean 1316.6/μL (400-3970/μL) to 60/μL (0-150/μL). No

relapses of CEP have been observed since the introduction of anti IL-5/5R. No changes in the spirometry values had been observed. The summary of our findings is shown in table I.

Although there is clear evidence of the efficacy and safety of anti-IL-5/IL5R in severe asthma that led their approval for its treatment by the European Medicines Agency (EMA) and the Food and Drug Administration (FDA), there is still scarce data of their efficacy on CEP. In the present study, we found that anti-eosinophil biologics were effective in the treatment of both CEP and severe asthma, especially in terms of reducing or discontinuing the OCS therapy and controlling both diseases decreasing asthma exacerbations and CEP relapses. Recent published case series described similar findings: Quentin et al. (5) reported a case of series of 29 patients treated with mepolizumab and benrazilumab; after a median duration of 13 months, no CEP relapse was reported, the median annual rate of severe asthma exacerbations decreased from 0.15 to 0, and 72% of the patients were eventually weaned from oral corticosteroids. Moreover, Brenard et al. (6) reported a case series of 10 patients with CEP treated with mepolizumab, after a median follow-up of 9 months, the treatment was associated with a significant annual rate of relapse (from 0.8 to 0), a lower consumption of corticosteroids (tapered from 5 to 0 mg) and also a remission of lung lesions on follow-up high resolution CT.

In conclusion, based on our findings and the previous literature, anti-IL-5/5R can be a safe and effective treatment in steroid-dependent patients with CEP and severe asthma.

Fundings

None.

Contributions

MCB: conceptualization, data collection and interpretation, writing - original draft, writing-review & editing. DL: clinical management, data collection and interpretation, writing - review & editing. JDO, SQ, DR: clinical management, writing - review & editing.

Conflict of interests

The authors declare that they have no conflict of interests.

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	All patients (n=6)	Reslizumab (n=2)	Mepolizumab (n=2)	Benralizumab (n=2)
Blood eosinophil count (cells/µL)				
Prior treatment	1316.6 (400-3970)	1180 (520-1840)	585 (530-640)	2185 (400-3970)
After one year	60 (0-150)	65 (60-70)	105 (150-60)	10 (0-20)
ACT (mean, range)				
Prior treatment	16.6 (16-18)	(16-17)	(16-17)	(16-18)
After one year	23.3 (21-25)	(21-24)	(23-25)	(23-24)
Number of annual asthma exacerbations (mean, range)				
Prior treatment	2.5 (1-5)	(1-3)	(3-5)	(1-2)
After one year	0.6 (0-3)	0	(1-3)	0
Patients treated with OCS (*n*)				
Prior treatment	5	1	2	2
After one year	2	0	1	1
Daily dose of prednisone mg/día (mean, range)				
Prior treatment	12 (5-30)	5	(5-10)	30
After one year	7.5 (5-10)	0	5	10

Abbreviations: ACT, Asthma Control Test; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; OCS: oral corticosteroids

Figure 1. Chest computed tomography at the moment of diagnosis of chronic eosinophilic pneumonia