

Clinical Communications

HIV-infected patient with severe asthma treated with mepolizumab: Case report

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Clinical Implication

- To date, this is the first reported case of HIV and severe asthma treated with anti-IL-5 monoclonal antibodies. Excellent clinical response was observed without adverse effects.

The relationship between respiratory disease and HIV has been widely studied, with more conclusive results regarding chronic obstructive pulmonary disease (COPD) than asthma. However, there is some evidence pointing out that asthma may be more frequent in patients with HIV, and establishing the relationship between HIV and T2 inflammation. We present the case of an HIV-infected patient 10 years ago who developed severe, poorly controlled eosinophilic asthma and who showed a good response to treatment with mepolizumab, without presenting any HIV-related complications or adverse effects. This is the first published case of these characteristics and opens up the possibility of administering anti-IL-5 drugs to this group of patients.

A 68-year-old man was referred to our clinic in October 2016. His personal history included tobacco exposure up to 1996 (15 packets per year), obesity with body mass index of 35.9 kg/m², and HIV diagnosed in 2011, on antiretroviral therapy (ART) since then, with undetectable viral load and stable CD4+ T lymphocytes. He had consulted his infectious disease specialist on several occasions complaining of dyspnea from exertion, coughing, and wheezing. He had been prescribed short-term bronchodilators with some improvement but persistence of symptoms, so he was referred to the Severe Asthma Clinics. Treatment with inhaled corticosteroid and long-acting β -agonist (ICS-LABA) was started, and spirometry was performed showing a fixed obstruction to airflow with a positive bronchodilator test (forced expiratory volume in 1 second [FEV₁] prebronchodilator 69% reference, 2300 mL, and FEV₁ postbronchodilator 80% reference, 2700 mL), a prick test that was negative, and a fractional exhaled nitric oxide (FeNO) of 66 ppb. The blood test showed high eosinophil count, mostly between 200 and 400 cell/mm³, but with some peaks over 800/mm³ (Figure 1, A). With these data, we confirmed the diagnosis of moderate persistent eosinophilic asthma. Treatment with medium-dose ICS-LABA was maintained and follow-up was started.

In the following year, the patient presented persistent symptoms, especially cough and dyspnea on exertion, 7 visits to the emergency department, and 12 bursts of systemic glucocorticoids. After the third follow-up visit at the Respiratory

Department (August 2018), he was on high-dose ICS-LABA, montelukast and tiotropium, and prednisone between 10 and 30 mg per day. To assess the phenotype of severe uncontrolled asthma, an induced sputum test was performed in which 69% of neutrophils and 11% of eosinophils were observed. To rule out allergic bronchopulmonary aspergillosis, a chest computed tomography scan was performed that showed slight signs of nonspecific bronchitis, and total IgE (415 IU/mL) and aspergillus-specific IgE quantification (negative) were measured. His FEV₁ postbronchodilator was 2400 mL and his FeNO 122 ppb.

After agreement with his infectologist, and taking into account that the patient had stable HIV with a normal CD4+ count (see Figure 1, B), we decided to start treatment with mepolizumab in November 2018. In January 2019, it was possible to completely withdraw the treatment with oral glucocorticoids. After 4 months of treatment, the eosinophil count was below 100/mm³ (Figure 1, A), asthma control test went from 14 to 24 points, FEV₁ postbronchodilator of 2870 mL, FeNO 38 ppb, and he did not have any exacerbation. This improvement remains to the present time, and medication has been tapered until medium-dose ICS-LABA and montelukast as maintenance therapy. No adverse events have been detected. CD4+ levels were monitored and initially showed a slight decrease without clinical impact, which subsequently returned to normal (Figure 1, B).

The association between HIV and respiratory disease is well studied,¹ especially in relation to COPD, but in asthma, the results have been less conclusive² and a lot of data come from the pediatric population. HIV-infected patients have a high incidence of respiratory symptoms, even without a confirmed respiratory disease, and this continues after the introduction of ART, theoretically due to the increase in CD4+ T lymphocytes after the immune reconstitution.

The T2 inflammatory pathway and eosinophil recruitment have been studied in patients with HIV because a shift between the T1- and T2-type inflammatory microenvironment was described at the onset of the disease that predicts the risk of developing more severe forms. Studies from the 1990s showed that high total IgE in blood is associated with a greater decrease in CD4+ T lymphocytes and a greater risk of developing AIDS.³ Greater eosinophilic inflammation has been described in HIV-infected patients than in healthy controls, and also indirectly at the bronchial level by measuring FeNO⁴ although the main conclusion for the moment is that eosinophilia in this population has a strong geographical component and is mainly related to exposure to helminths.⁵ Studies in children have shown that IL-5 correlates directly with the presence of neutralizing HIV antibodies⁶ and that children born to infected mothers have less risk of progression in category and to AIDS if they have high IL-5 values.

On the other hand, the availability of several drugs with anti-IL 5 activity has allowed us to broaden our knowledge regarding the role played by this interleukin in defense against viruses in general. In phase 2 and 3 clinical trials of mepolizumab, several cases of herpes simplex virus infection have been reported in the treatment branch, with an estimated incidence of 17 of 1000 patients per year.⁸ In the

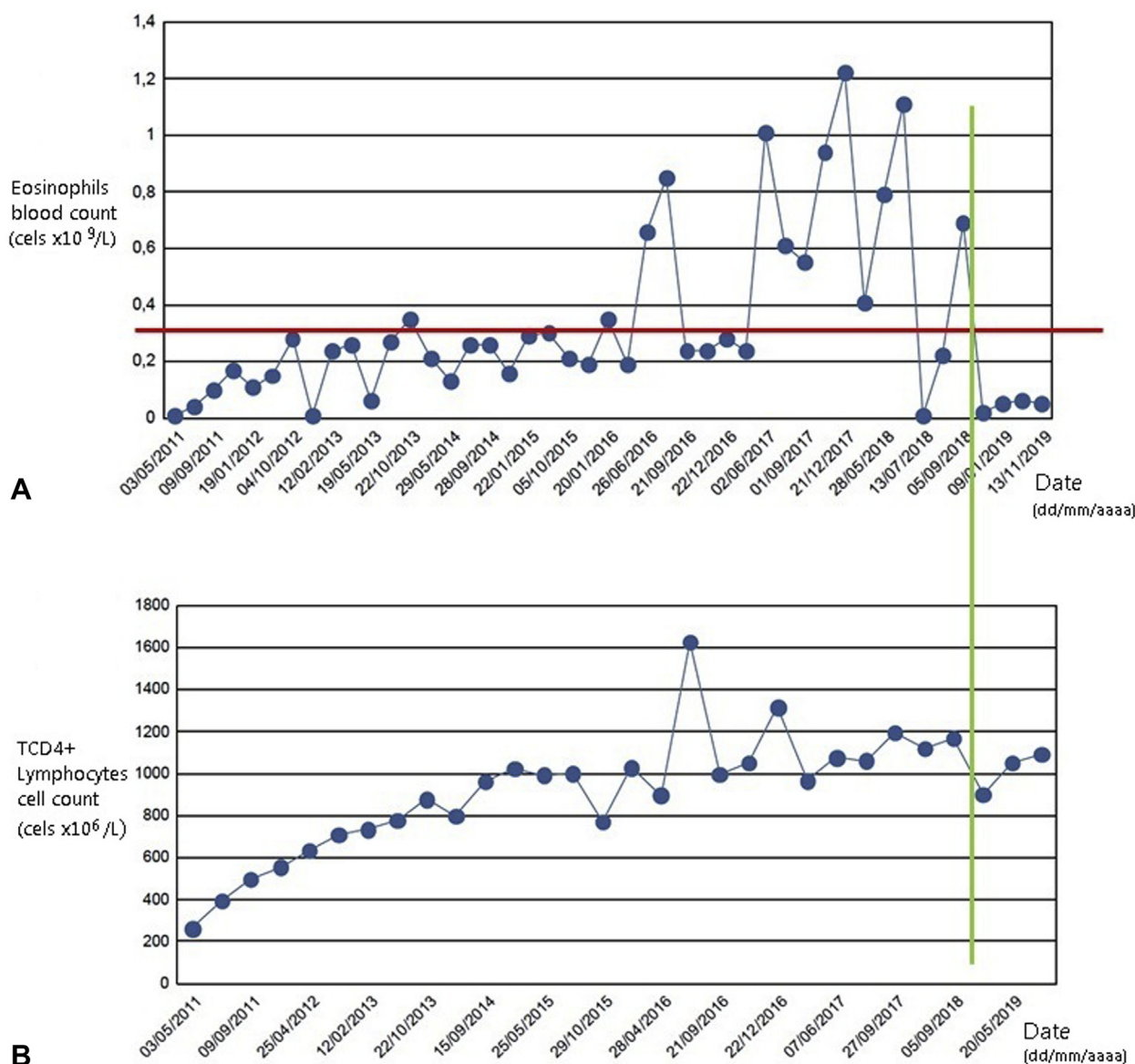


FIGURE 1. Evolutive levels of eosinophils (**A**) and CD4 count (**B**) in blood. The red line shows the cutoff point of 300 eosinophils/mm³, and the green line the time of introduction of mepolizumab, in November 2018.

MATERIAL study,⁹ mepolizumab was administered in a single dose to a cohort of mild asthmatics, and after 2 weeks, they were exposed to intranasal rhinovirus 16. The results showed activation of some antiviral mechanisms (natural killer, IgA, activation of the remaining eosinophils), but attenuation of others (neutrophilic response). There was no clear clinical effect on the response to rhinovirus, but more viral load was detected in patients treated with mepolizumab. With these results, it is possible to conclude that IL-5 plays a partial role in the antiviral response that requires further directed studies.

The available data are scarce on which to base the decision to treat or not with mepolizumab in our patient, but finally the stability of HIV and the severity, glucocorticoid dependence, and poor control of asthma motivated its indication. This case shows

the success of mepolizumab in a patient with highly eosinophilic asthma and the safety of administering it in patients with stable HIV.

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