

Anti-interleukin 5 antibody is effective for not only severe asthma and eosinophilic pneumonia but also eosinophilic bronchiolitis

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Abstract

A 60-year-old female with severe bronchial asthma developed persistent dyspnoea and an abnormal lung shadow. High-resolution computed tomography (HRCT) demonstrated patchy ground-glass opacities and diffuse, small nodular shadows. Elevated percentages of eosinophils were observed in the blood and bronchoalveolar lavage fluid. These results collectively indicated that her asthma was accompanied by eosinophilic pneumonia and eosinophilic bronchiolitis. Although previous, rare case reports suggest that systemic steroid therapy is necessary and effective for the control of eosinophilic bronchiolitis, we chose to treat her with an anti-interleukin 5 antibody, mepolizumab. Her asthma, eosinophilic pneumonia, and eosinophilic bronchiolitis each improved in response to mepolizumab as assessed from her symptoms, pulmonary function tests, and HRCT. Mepolizumab might be effective not only for asthma and eosinophilic pneumonia but also for eosinophilic bronchiolitis.

Introduction

There have been a few case reports of eosinophilic bronchiolitis that is characterized by radiographic findings showing diffuse bronchiolitis plus massive accumulation of eosinophils in the airways [1–4]. It has been suggested that systemic steroid therapy is effective for this disorder, although the precise pathogenesis is unknown. Here, we report a case of severe asthma complicated with eosinophilic pneumonia and eosinophilic bronchiolitis, all of which were alleviated by anti-interleukin 5 (IL-5) antibody.

Case Report

A 60-year-old female was referred to the outpatient clinic of Teikyo University Hospital for evaluation of persistent dyspnoea and an abnormal lung shadow.

She had been diagnosed with bronchial asthma 10 years earlier. Although she continued to use medium- or high-

dose inhaled corticosteroid (ICS) plus a long-acting β_2 agonist (LABA), leukotriene receptor antagonist (LTRA), and sustained-release theophylline, the asthma frequently flared up, and short-term oral corticosteroid bursts were needed. One year before referral, diffuse small nodular shadows were seen on chest X-rays, suggesting the possibility of bronchiolitis.

On the day of her first visit to our clinic, she complained of persistent dyspnoea both at rest and on exertion and presented expiratory wheezes. Her fractional exhaled nitric oxide (FeNO) was clearly elevated (72 ppb). Blood tests showed eosinophilia (790/ μ L), elevated serum total IgE (1280 IU/mL), and positivity for specific IgEs against house dust mites and aspergillus. Serum autoantibodies, including myeloperoxidase–anti-neutrophil cytoplasmic antibody (ANCA) and proteinase 3-ANCA, were negative. A chest X-ray showed diffuse small nodular shadows and irregular pulmonary infiltration shadows (Fig. 1A). High-resolution computed tomography (HRCT) images demonstrated a

tree-in-bud appearance and patchy ground-glass opacity (GGO) in both lung fields (Fig. 1B), suggesting the presence of bronchiolitis and pneumonia. Sinus computed tomography (CT) showed non-specific mild maxillary sinusitis but no ethmoid sinusitis.

After starting inhalation of tiotropium, a muscarinic antagonist, her asthma symptoms improved slightly, although a pulmonary function test clearly indicated airflow obstruction (Fig. 1C). Bronchoscopic examination found that the bronchial mucosa was oedematous, and the bronchoalveolar lavage (BAL) fluid showed an elevated percentage of eosinophils (28.5%) but not neutrophils. A biopsy specimen of the right B⁸ distal bronchial mucosa showed massive infiltration of eosinophils, detachment of airway epithelial cells, and thickening of subepithelial fibrosis, but no Charcot-Leyden crystals were observed (Fig. 1D). These findings resulted in a diagnosis of bronchial asthma, eosinophilic pneumonia, and eosinophilic bronchiolitis. As her symptoms persisted, we decided to start treatment with mepolizumab, an anti-IL-5 antibody, two months after her first visit to our hospital. Her dyspnoea gradually improved, and her blood eosinophil counts were controlled at low levels, although FeNO remained high (Fig. 2A). HRCT images indicated that GGO had disappeared, and the thickening of the bronchial mucosa observed in the initial HRCT images had become milder

(Fig. 2B, C). The tree-in-bud appearance and thickening of centrilobular shadows, suggesting bronchiolitis, were also alleviated. A spirogram showed improvement in both restrictive abnormality (percent vital capacity (%VC): 70.9% before mepolizumab; 94.8% after introduction of mepolizumab) and obstructive impairment (forced expiratory volume in 1 second (FEV1): 0.99 L before mepolizumab; 1.45 L after introduction of mepolizumab) (Fig. 2A). The residual volume/total lung capacity (RV/TLC), a useful index of air trapping in relation to small airway involvement, was initially as high as 46.9% (two months after mepolizumab was started), but it gradually improved with time to 44.4% (after four months on mepolizumab) and then 40.4% (after 10 months). Oral steroid bursts were not necessary during treatment with mepolizumab.

Discussion

Eosinophilic bronchiolitis is a relatively new disorder, first reported in 2001 [1]. So far, around 10 cases of this disorder have been reported; all of them displayed chronic progression of respiratory symptoms including cough, sputa, and dyspnoea at rest and exertion. This disorder is characterized by unique radiological findings, i.e. diffuse micronodular shadows and a tree-in-bud appearance, suggesting bronchiolitis and eosinophilia in both blood and

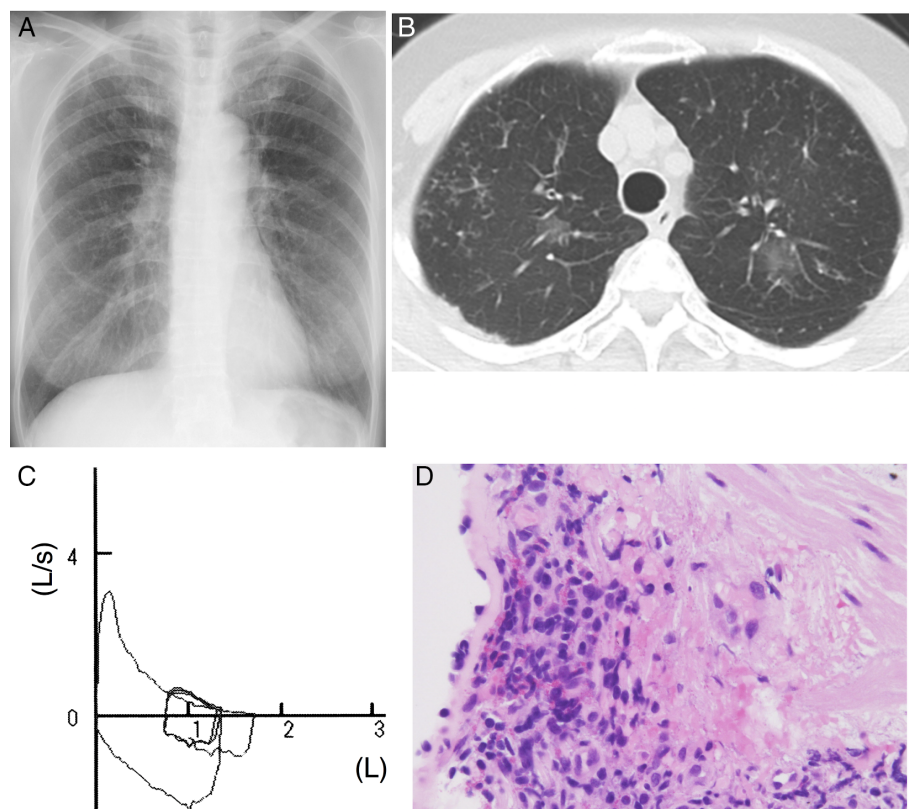


Figure 1. Chest X-ray (A) and computed tomography image (B) before administration of mepolizumab. A flow volume curve (C) showed airflow obstruction. (D) A transbronchial lung biopsy specimen showed massive infiltration of eosinophils and subepithelial fibrosis in the distal airway mucosa.

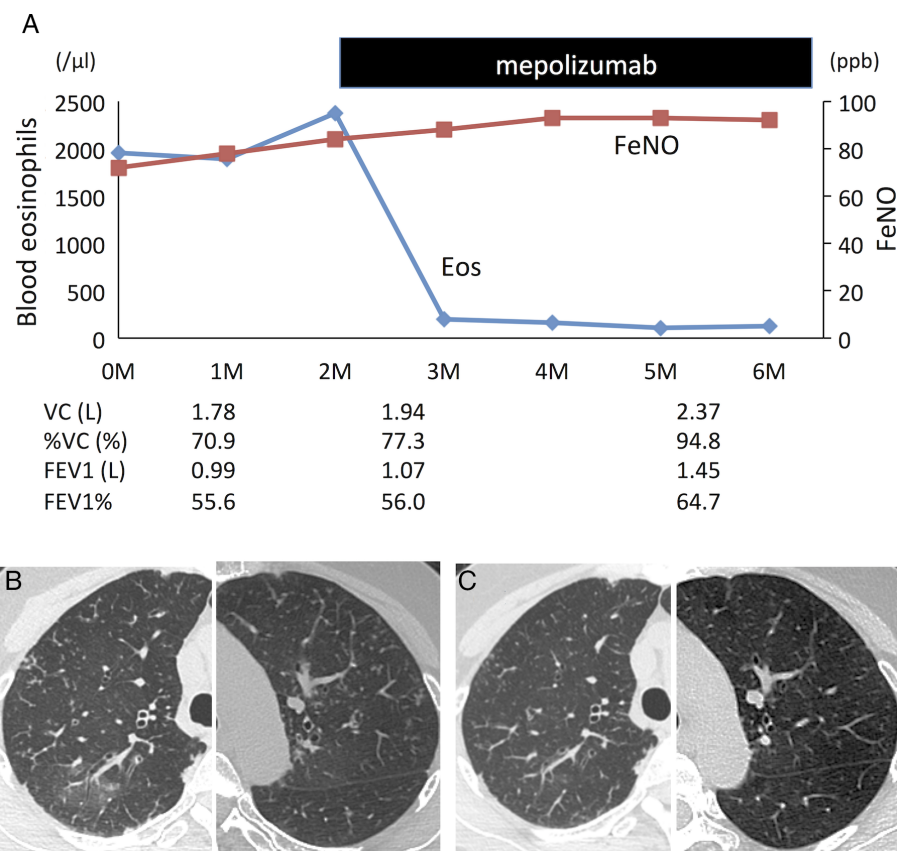


Figure 2. (A) Clinical course. Note that fractional exhaled nitric oxide failed to decrease. High-resolution computed tomography images show the status before (B) and 13 months after (C) mepolizumab was introduced.

pulmonary examinations [1–4]. The clinical features of our case are in line with those findings for eosinophilic bronchiolitis. Thus, we believe that the diagnosis of eosinophilic bronchiolitis is correct for the present case.

Accumulating evidence suggests that eosinophilic bronchiolitis is often accompanied by various other eosinophilic disorders [2,5]. Bronchial asthma is the most commonly reported disease accompanying eosinophilic bronchiolitis, as seen in our case, who also had eosinophilic pneumonia. In this patient, the findings of diffuse bronchiolitis on CT images were dominant and very striking, and we felt that they could not be regarded as features of bronchial asthma. The patient was thus diagnosed with a combination of asthma and eosinophilic bronchiolitis. We suppose that her asthma, eosinophilic pneumonia, and eosinophilic bronchiolitis might be mutually related, and these disorders collectively gave rise to cough, dyspnoea, and clear impairment of pulmonary function. It is important to note that BAL analysis may not be useful for distinguishing eosinophilic bronchiolitis as other disorders also demonstrate a similar increase in eosinophils.

The previous case reports on eosinophilic bronchiolitis suggested that oral corticosteroid was an effective and standard therapy, whereas ICS was not. Importantly,

discontinuation of oral corticosteroid was difficult, and long-term administration of systemic steroid was thus unavoidable [1,3,4]. For our patient, however, we chose a new anti-IL-5 antibody, mepolizumab, as her asthma was severe, and she strongly requested an additional effective anti-asthma drug other than systemic steroid. As a result, not only her asthma but also her eosinophilic pneumonia and eosinophilic bronchiolitis responded to mepolizumab: her symptoms improved, as did the findings of lung function and imaging studies. Her clinical course suggests that IL-5 may have been critically involved in the pathogenesis of all of her eosinophilic disorders, including eosinophilic bronchiolitis.

As there have not been many reports of eosinophilic bronchiolitis, we have limited evidence regarding the pathogenesis and standard therapy for this disorder. In view of recent robust progress in the field of allergology, further accumulation of basic and clinical information on eosinophilic bronchiolitis is anticipated. That information will contribute to the further confirmation of this clinical entity, e.g. whether eosinophilic bronchiolitis is a unique disorder or just a continuum of the pathological process of asthma and the therapeutic strategy for it, and to our overall understanding of eosinophilic lung diseases.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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