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REVIEW

Dupilumab-induced Eosinophilic Granulomatosis with Polyangiitis Complicated by Peripheral Neuropathic Pain: a Case Report and Literature Review

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Abstract

Purpose Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare vasculitis characterized by increased eosinophils in human tissues and peripheral blood. In this case, we present a 53-year-old female patient with EGPA. By this case and literature review, we want to explain the early manifestations, diagnosis, and management of EGPA, which will help clinicians to understand the disease and attach importance to the possibility of dupilumab-induced EGPA, to improve the early diagnosis rate of EGPA, and reduce misdiagnosis and missed diagnosis.

Methods The diagnostic criteria for EGPA established by the American Rheumatology Association (ACR) in 2022 were used; these criteria encompass clinical presentation, laboratory tests, and pathological biopsy. In addition, we conducted a comprehensive literature review on this case.

Result We present a 53-year-old female patient who developed severe peripheral neuropathic pain after the administration of dupilumab for the treatment of refractory asthma and sinusitis. The patient's symptoms, laboratory examination findings, and nasopharyngeal biopsy pathology results collectively support the diagnosis of EGPA. When dupilumab was converted to mepolizumab combined with glucocorticoid, her peripheral neuropathic pain and asthma symptoms were dramatically relieved. Our literature review also provides a detailed discussion on the relationship between Dupilumab and EGPA.

Conclusion We present a case of EGPA with peripheral neuropathic pain induced by Dupilumab, and mepolizumab has a good therapeutic effect on this patient. Our literature review shows that although dupilumab is effective in treating eosinophilic airway inflammatory diseases, clinicians must pay attention to the possibility of dupilumab inducing or aggravating EGPAs.

Keywords Eosinophilic Granulomatosis with Polyangiitis (EGPA) · Dupilumab · Mepolizumab · Asthma · Neuralgia · Sinusitis

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Introduction

EGPA is a type of systemic vasculitis histologically characterized by eosinophilic infiltration, necrotizing vasculitis, and granulomatous inflammation [1, 2]. The annual incidence of EGPA ranges from 0.9 to 2.4 cases per million, while the global prevalence is only 10.7 to 17.8 cases per million [3–10]. The EGPA is a subset of anti-neutrophil cytoplasmic antibody (ANCA) associated systemic vasculitis, which can be categorized into ANCA-positive and ANCA-negative subgroups [11]. Approximately 40% of EGPA is ANCA-positive subgroups that target myeloperoxidase (MPO) as their antigen, predominantly manifesting clinically as glomerulonephritis, purpura, and alveolar hemorrhage. Nevertheless, 60% of EGPA cases belong to the ANCA-negative subgroup, characterized pathologically by eosinophilic infiltration, frequently implicating the lung, heart, upper respiratory tract, and gastrointestinal system [12–14].

The current research tends to divide the development of EGPA into three stages: the prodromal phase, the eosinophilic infiltration phase, and the vasculitis phase [15]. The prodromal phase is commonly marked by asthma and allergic rhinitis as initial symptoms, which can persist for several years, and the level of eosinophils in the peripheral blood may remain within normal limits [16–18]. As the disease progresses to the eosinophilic infiltration phase, the eosinophils in the peripheral blood and tissues both start to increase, with multi-organ involvement including the lungs, heart, upper respiratory tract, and gastrointestinal system [19–23]. The vasculitis phase, primarily manifested as life-threatening granulomatous vasculitis, ultimately leads to systemic multi-organ dysfunction and endangers life [15].

The systemic use of glucocorticoids is the first-choice treatment for asthma and EGPA [24, 25]. However, in EGPA-associated asthma, most patients exhibit dependence on glucocorticoids. EGPA usually relapses or progresses after drug withdrawal. Dupilumab, a fully human monoclonal antibody, selectively inhibits the pivotal signaling pathways involving interleukin-4 (IL-4) and interleukin-13 (IL-13), blocking type II inflammatory pathways and alleviating the pathological responses of type II inflammation [26, 27]. Dupilumab is effective in treating atopic dermatitis, asthma, and chronic sinusitis with nasal polyps [28–31]. Dupilumab is often used for patients exhibiting asthma and chronic rhinosinusitis with nasal polyps rather than for those with EGPA, due to the challenges in early diagnosis of EGPA. Nevertheless, in the last few years, several articles have reported that dupilumab administration may cause a transient increase in peripheral blood eosinophils, thus carrying the potential risk of inducing or exacerbating EGPA [32–35].

In this case, we introduce a 53-year-old female patient who developed severe peripheral neuropathic pain after receiving dupilumab administration for refractory asthma and sinusitis. Her long-term use of glucocorticoids to control asthma symptoms was not effective. After she had switched to dupilumab treatment, the patient suffered severe peripheral neuropathic pain. According to the diagnostic criteria of the American Rheumatology Association (ACR) for EGPA in 2022, the cumulative score of patients is 11 points, which accords with the diagnosis of EGPA [36]. The symptoms of peripheral neuropathic pain and asthma were relieved when the patient stopped using dupilumab and started using mepolizumab combined with glucocorticoids. By this case, we want to explain the early manifestations, diagnosis, and management of EGPA, which will help clinicians to understand the disease and attach importance to the possibility of dupilumab-induced EGPA, to improve the early diagnosis rate of EGPA and reduce misdiagnosis and missed diagnosis.

Methods

Diagnostic Criteria

Using the diagnostic criteria established by the ACR in 2022. The seven criteria of ACR 2022 include: 1. maximum eosinophil count $\geq 1 \times 10^9$/L (+5);2. obstructive airway disease (+3); 3. nasal polyps (+3); 4. cytoplasmic antineutrophil cytoplasmic antibody (ANCA) or anti-proteinase 3-ANCA positivity (−3); 5. extravascular eosinophilic predominant inflammation (+2); 6. mononeuritis multiplex/motor neuropathy not due to radiculopathy (+1) and haematuria (−1). After excluding mimics of vasculitis, a patient with a diagnosis of small- or medium-vessel vasculitis could be classified as having EGPA if the cumulative score was ≥6 points.

Case Presentation

A 53-year-old female patient was admitted to the Pain Department of our hospital on September 2, 2024, due to persistent pain in the forehead, temporal, and maxilla for three months.

The patient was diagnosed with asthma in October 2017 and has since been effectively managing the condition through the long-term use of leukotriene receptor antagonists and inhaled corticosteroids.

On May 16, 2024, the patient went to another hospital for treatment because of asthma. At that time, the patient suffered from chest tightness, shortness of breath, cough and expectoration, thick breathing sounds in both lungs, and

wheezing sounds in the lungs. The chest CT showed bronchiectasis with infection in the middle lobe of the right lung and part of the lower lobes of both lungs, and emphysema in the lower lobes of both lungs.

Laboratory examinations are listed below. Blood routine: eosinophilia (0.91×10^9/L), basophil (0.09×10^9/L), lymphocyte ratio: 19.5%, eosinophil ratio: 10.6%, basophil ratio: 1.1%. There is no abnormality in the coagulation function. No obvious abnormalities were found in influenza A/B virus antigen, mycoplasma pneumonia/chlamydia pneumonia/adenovirus nucleic acid, and mycobacterium tuberculosis antibody. The attending physician diagnosed the patient with an asthma attack, and the patient started to use dupilumab (600 mg for the first time and 300 mg every two weeks thereafter), leukotriene receptor antagonists, and inhaled corticosteroids. After the second treatment with dupilumab, the patient's forehead, temporal region, and maxilla showed persistent swelling and pain. The sinus CT showed that the bilateral frontal sinus, maxillary sinus, ethmoid sinus, and sphenoid sinus were filled with density shadows. Considering the patient's facial pain was caused by sinusitis, the attending physician did not give special treatment, and the patient continued to receive dupilumab treatment. Over the past three months, six administrations of dupilumab have been administered to the patient. During the administration of dupilumab, the patient experienced significant worsening pain in the forehead, temporal, and maxillary areas.

The patient went to the Pain Management Department of our hospital on September 2, 2024. The blood test results showed that the C-reactive protein level increased (32.4 mg/L) and the erythrocyte sedimentation rate was 65 mm/h. Cranial Computed tomography angiography (CTA) showed that the anterior, middle, and posterior arteries of the double-layer brain were hardened, with sinusitis attached (Fig. 1A, B). Cervical vertebra computed tomography plain scan suggests: (1) Disc herniation at C3/4, C4/5, C5/6, and C6/7 levels, thickening and calcification of the posterior longitudinal ligament, and spinal canal stenosis. (2) Degenerative osteoarthritis of the cervical spine (Fig. 1C). The painologist used tramadol combined with celecoxib to control pain symptoms and performed an ultrasound-guided cervical 2 transverse process block and stellate ganglion block. The pain has not been significantly alleviated. The painologist suspected that sinusitis was the reason causing the patient's facial pain and recommended the patient be referred to the otolaryngology department.

After the patient was transferred to our department, based on past symptoms and lab results, we speculated that the neuropathic pain in the patient's head and face may be closely related to the patient's asthma. We found that the patient had a history of recurrent eosinophilia, with levels reaching as high as 4.42×10^9/L, while her myeloperoxidase and proteinase ANCA test results were negative. Chest CT: Slight thickening of the interlobular septa in both lungs, with multiple patchy areas of ground-glass opacity in a map-like pattern, most prominent in the apical segment of the right lung, with indistinct borders. Multiple small solid patches and nodules are adjacent to the bronchi in both lungs. Bilateral bronchial wall thickening and luminal narrowing, with some lumens filled with high-density shadows (Fig. 2A). Superficial ultrasound: localized increased echogenicity in the subcutaneous muscle layer of the left lower limb (Fig. 2B). Cranial CTA: mild sinusitis (Fig. 1B). Electromyography (EMG): Abnormal function of the right facial nerve conduction pathway (Fig. 2C). Laryngoscope: Mild redness and swelling of the bilateral nasal mucosa, with no obvious neoplasm observed (Fig. 2D). A small amount of tissue was taken from the posterior pharyngeal wall for pathological biopsy. Nasopharyngeal tissue pathology biopsy: Chronic mucosal inflammation with extensive lymphoplasmacytic infiltration and eosinophilic infiltration (approximately 40 per high-power field in hotspot areas), small vessel proliferation with no necrosis observed, or granuloma formation. Immunohistochemistry: CD68+, CD163+ (Fig. 2E). The above examinations indicate asthma, sinusitis, peripheral blood eosinophilia, pulmonary infiltrates, and eosinophilic infiltration in the nasopharynx, along with subsequent peripheral neuropathic pain and extravascular eosinophilic infiltration. Based on the evidence presented above, the patient's cumulative score reached 11 points, meeting the diagnostic criteria established by ACR in 2022.

As soon as the patient was diagnosed with EGPA, we told the patient to stop using dupilumab and switch to mepolizumab (300 mg once, every four weeks) combined with oral glucocorticoid (methylprednisolone 12 mg/day). One month later, the patient's neuropathic pain symptoms were significantly alleviated, and the glucocorticoid dosage was reduced to 8 mg/day. At first, the patient may have obvious head and face swelling and pain in the morning. This symptom disappeared when the glucocorticoid dosage was restored to 12 mg/day.

After 5 months, the patient's glucocorticoid dosage had been reduced to 4 mg/day, without any occurrence of neuropathic pain, asthma, or other clinical manifestations. By February 14, 2025, the patient had completed the sixth cycle of mepolizumab treatment and had already discontinued oral glucocorticoids, with no discomfort.

Literature Review

EGPA was first described in 1951 by Jacob Churg and Lotte Strauss through an analysis of autopsy cases of 13 patients, and they named it the "Churg-Strauss Syndrome" [1]. The

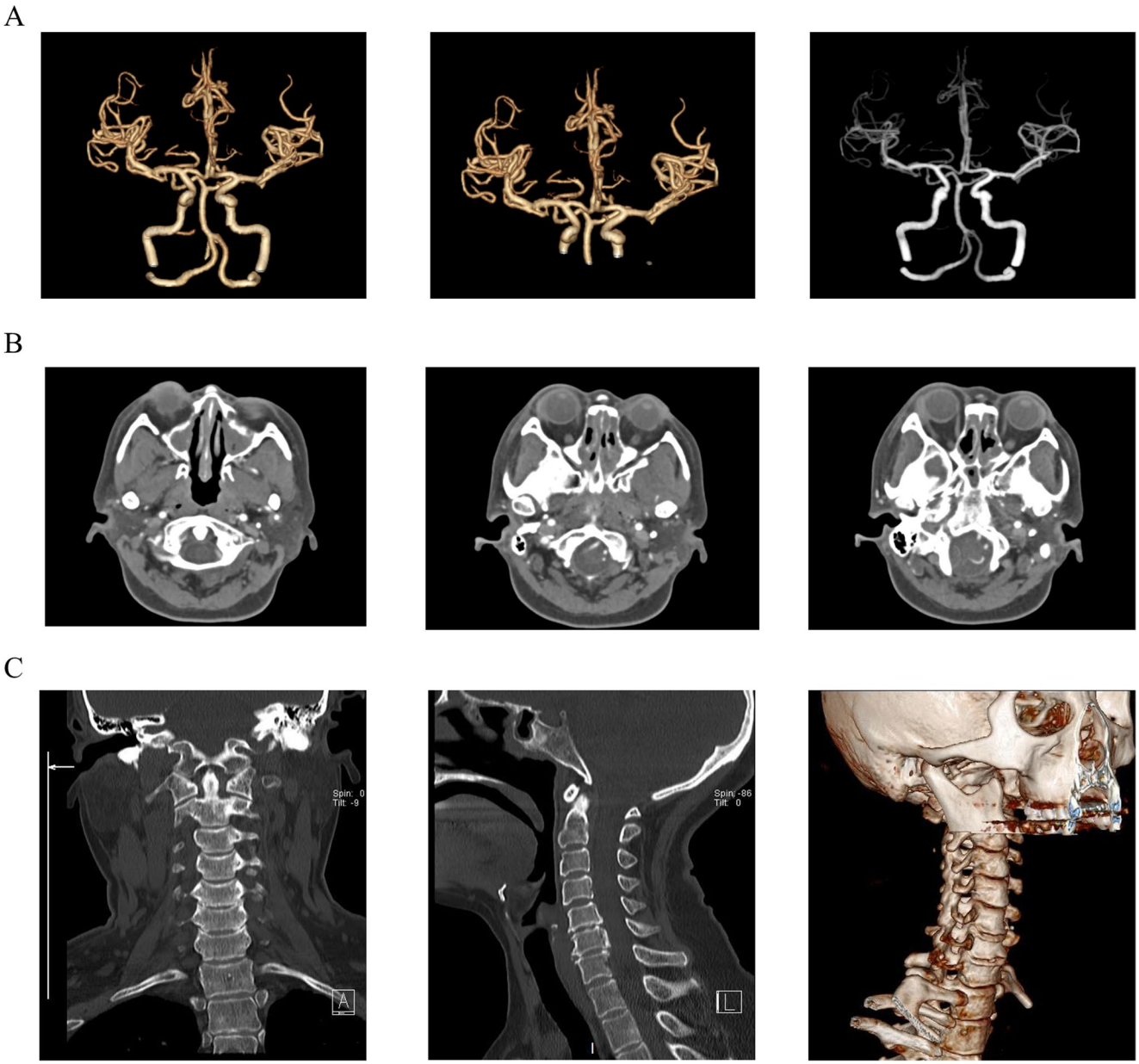
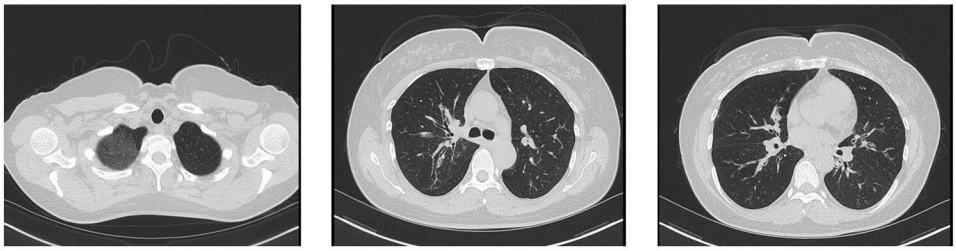


Fig. 1 Cranial computed tomography angiography (CTA) showed that the anterior, middle, and posterior arteries of the double-layer brain were hardened, with sinusitis attached (**A**, **B**). Cervical vertebra computed tomography plain scan suggests: 1. Disc herniation at C3/4, C4/5, C5/6, and C6/7 levels and spinal canal stenosis. 2. Degenerative osteoarthritis of the cervical spine (**C**).

pathological features of EGPA include asthma, fever, hypereosinophilia, and granulomatous necrotizing vasculitis [2]. Currently, the diagnosis of EGPA is primarily based on the criteria established by ACR in 2022. These criteria encompass clinical presentation, laboratory tests, and pathological biopsy. The seven criteria of ACR 2022 include: 1. maximum eosinophil count $\geq 1 \times 109/L$ (+5);2. obstructive airway disease (+3); 3. nasal polyps (+3); 4. cytoplasmic antineutrophil cytoplasmic antibody (ANCA) or anti-proteinase 3-ANCA positivity (−3); 5. extravascular eosinophilic predominant inflammation (+2);6. mononeuritis multiplex/motor neuropathy not due to radiculopathy (+1) and haematuria (−1). After excluding mimics of vasculitis, a patient with a diagnosis of small- or medium-vessel vasculitis could be classified as having EGPA if the cumulative score was ≥6 points. In addition, the consensus divides EGPA into localized type and systemic type. The localized EGPA only shows the involvement of the lung and respiratory system (including otorhinolaryngology). While systemic EGPA involves at least two organs. It is worth noting that localized EGPA may progress to systemic EGPA [36].

A



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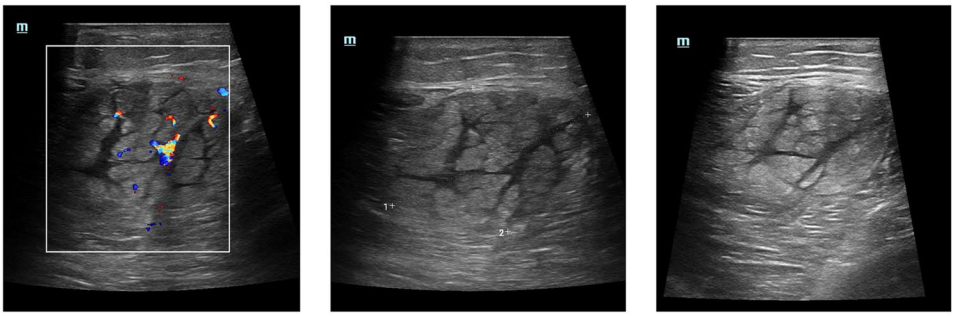

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	record	R1 incubation		R2 incubation	
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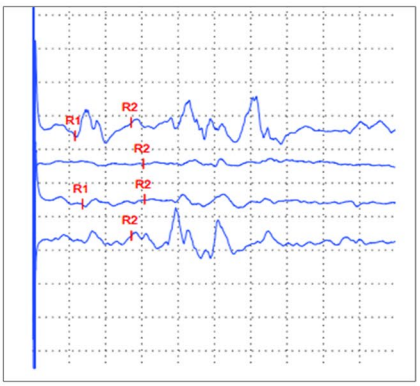

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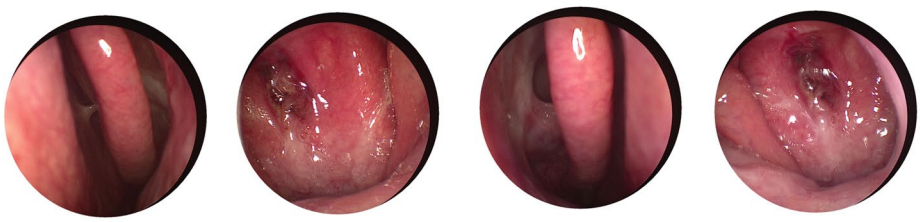

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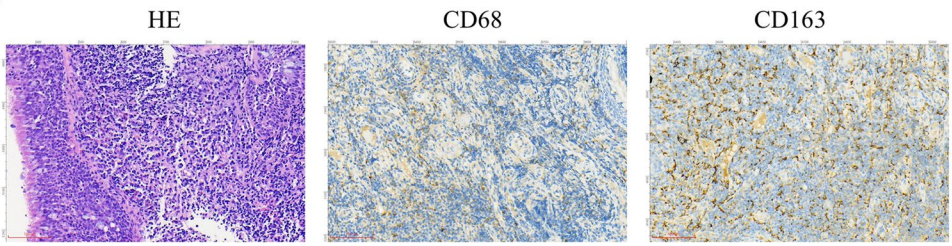

Fig. 2 Chest CT: Slight thickening of the interlobular septa in both lungs, with multiple patchy areas of ground-glass opacity in a map-like pattern, most prominent in the apical segment of the right lung, with indistinct borders. Multiple small solid patches and nodules are adjacent to the bronchi in both lungs. Bilateral bronchial wall thickening and luminal narrowing, with some lumens filled with high-density shadows (**A**). Superficial ultrasound: localized increased echogenicity in the subcutaneous muscle layer of the left lower limb (**B**). Electromyography (EMG): Abnormal function of the right facial nerve conduction pathway (**C**). Laryngoscope: Mild redness and swelling of the bilateral nasal mucosa, with no obvious neoplasm observed (**D**). Nasopharyngeal tissue pathology biopsy: Chronic mucosal inflammation with extensive lymphoplasmacytic infiltration and eosinophilic infiltration (approximately 40 per high-power field in hotspot areas), small vessel proliferation with no necrosis observed, or granuloma formation. Immunohistochemistry: CD68+, CD163+ (**E**).

So far, the etiology of EGPA is still not clear, and many scholars think that allergic reactions caused by eosinophilia may be one of its causes [37]. Eosinophilic cells originated from hematopoietic stem cells of bone marrow and matured under the synergistic effect of IL-3, interleukin-5 (IL-5), and granulocyte-macrophage colony-stimulating factor (GM-CSF) [38]. Eosinophils in blood vessels are closely combined with vascular endothelium through VLA-4 molecules (β1 integrin) and CD18 family (β2 integrin), and eosinophils are transferred out of blood vessels and further infiltrated into surrounding tissues and organs through the β1-VCAM-1 pathway and β2-ICAM-1 pathway [39]. The β2-ICAM-1 pathway can be activated by all kinds of leukocytes, while the β1-VCAM-1 pathway can only be activated by IL-4 and specifically binds to eosinophils and monocytes [40, 41].

EGPA can be divided into three developmental stages: the prodromal phase, the eosinophilic tissue infiltration phase, and the vasculitis phase [15]. In the prodromal phase, patients often have respiratory system involvement, with 95% exhibiting refractory asthma symptoms persisting for several years, which is hard to distinguish from simple asthma, which is the main factor leading to disease progression and delayed treatment [42]. Imaging abnormalities include migratory infiltrates, extensive bronchial wall thickening, patchy ground-glass opacities, and increased lung markings [14, 43, 44]. Other findings may include multiple centrilobular nodules, emphysema, bronchiectasis, thickened veins of pulmonary small vessels, pleural effusion, and pleural thickening [45, 46]. These pulmonary imaging manifestations are essential for distinguishing EGPA from refractory asthma. Lung biopsy pathology results indicating eosinophilic infiltration can strongly support the diagnosis of EGPA. During the eosinophilic tissue infiltration phase, the eosinophil count increases greatly in the blood, and eosinophils can invade various tissues and organs throughout the body. Patients may have purpura, nodules, and papules on their limbs if eosinophils infiltrate the skin [47–49]. If the gastrointestinal tract is involved, patients may suffer from diarrhea, abdominal pain, and gastrointestinal bleeding, which would lead to severe complications like gastrointestinal perforation [50–52]. During the vasculitis stage, EGPA mainly presents various pathological changes caused by progressive necrotizing vasculitis and granuloma formation. These changes may include eosinophilic endocarditis, eosinophilic myocarditis, congestive heart failure, and pericardial effusion due to cardiac dysfunction [53]; glomerulonephritis and chronic renal failure due to kidney damage [54]; and neurological damage leading to conditions like mononeuritis multiplex or sensory and motor mixed-type peripheral neuropathy. However, not all EGPA patients will go through all the stages of the disease completely, so there are no clear boundaries between these three phases.

Due to the diverse clinical manifestations of EGPA, patients often experience diagnostic delays, which in turn affect their prognosis. The most critical differential diagnosis for EGPA is hypereosinophilic syndrome (HES), a group of disorders characterized by persistent eosinophil proliferation (eosinophils $\geq 1.5 \times 10^9$/L) and multi-organ involvement. Based on clinical features and underlying etiology, HE can be divided into the following categories: familial (hereditary) HE (HEFA), HE of unknown significance (HEUS), secondary (reactive) HE (HER) and primary (clonal, neoplastic) HE [55]. Among them, HEUS is also called idiopathic HES, is typically ANCA-negative, with cardiac and pulmonary imaging and clinical features overlapping with EGPA. It is worth noting that the asthma or polyps and vasculitis complications (such as purpura, glomerulonephritis, neuropathy) rarely occur in idiopathic HES. The most important identification point is that the tissue biopsy of idiopathic HES does not show vasculitis [56]. In addition, Polzer et al. found that eotaxin-3 can distinguish EGPA from various forms of HES and other allergic or immune-mediated diseases associated with eosinophilia [57]. By the above-discussed differentiating points, HES and ANCA-negative EGPA can be effectively distinguished in clinical diagnosis.

The treatment methods for EGPA include hormone therapy, immunosuppressive therapy, and targeted therapy. Additionally, auxiliary treatments such as plasmapheresis and intravenous immunoglobulin are also available. Glucocorticoids are the foundational drugs for treating EGPA, and when patients experience life-threatening conditions or have severe organ involvement, glucocorticoids should be used in combination with immunosuppressive therapy [42]. In this report, we emphasize the efficacy and side effects of dupilumab and mepolizumab in targeted therapy for EGPA. Dupilumab is a fully human monoclonal antibody that selectively inhibits the IL-4 signaling pathway and prevents the activation of the β1-VCAM-1 pathway, thereby blocking the migration of eosinophils to the extravascular [34]. As a result, dupilumab cannot directly reduce eosinophils in the short term and may even lead to an increase eventually. In contrast, IL-5 is an important cytokine in the immune system that regulates immune response and inflammation. IL-5 is a major growth factor for eosinophils, promoting their proliferation, activation, and survival. Therefore, the IL-5 antagonist mepolizumab may have greater potential in treating EGPA [58]. Furthermore, in December 2017, mepolizumab became the first biologic agent approved by the FDA for the treatment of EGPA.

Currently, the relationship between dupilumab and EGPA is not clear. In a retrospective study involving 51 diagnosed

EGPA patients, 47 patients (92%) exhibited severe ENT symptoms, 29 patients (57%) showed high-dose glucocorticoid dependence, and 27 patients (53%) had refractory asthma symptoms. Of these patients, 21 patients (41%) achieved complete remission, 12 patients (24%) experienced partial remission, and 14 patients (27%) showed no significant improvement, with an additional 4 patients not adhering to the treatment. Among these, 16 patients (31%) experienced a relapse of EGPA after using dupilumab, including 10 patients who developed blood eosinophilia along with systemic symptoms. Two patients had normal blood eosinophil levels, but their asthma symptoms worsened further [59]. Additionally, in 2021, Roberto et al. conducted a prospective study involving 9 EGPA patients treated with dupilumab. After 3 months, 55.6% of the patients reported complete relief of nasal symptoms, which increased to 83.3% at 12 months [35].

The efficacy of dupilumab in improving EGPA symptoms has been reported in several cases. Sei et al. reported a 43-year-old patient who also suffered from acute respiratory failure, myocarditis, pericardial effusion, gastrointestinal symptoms, and peripheral neuropathy. The patient used rituximab and dupilumab to treat EGPA but did not respond significantly to mepolizumab. Upon switching to dupilumab, the patient's asthma, vasculitis, and heart failure symptoms showed considerable improvement [60]. Marco et al. reported on a 70-year-old male EGPA patient who had been using mepolizumab to control related symptoms. After three years without significant improvement, a multidisciplinary discussion led to a switch to dupilumab therapy, resulting in noticeable improvement after one year [61]. Additionally, there are reports of successfully treating EGPA with a combination of dupilumab and mepolizumab. Yosuke et al. also reported a case in which dupilumab combined with mepolizumab successfully improved the symptoms of an EGPA patient with atopic dermatitis [62].

Although dupilumab can improve some of EGPA's symptoms, its use in treating EGPA carries a significant risk of causing EGPA relapse and exacerbation. However, the specific mechanisms remain unclear. Kai Yamazaki et al. proposed two hypotheses. The first hypothesis suggests that dupilumab can inhibit the β1-VCAM-1 pathway by blocking IL-4, thus preventing eosinophils within the blood vessels from migrating and infiltrating surrounding tissues and organs. But dupilumab cannot stop already activated eosinophils in the periphery from functioning. The second hypothesis is that the patient was in the latent phase of EGPA, and treatment with dupilumab coincidentally triggered the corresponding symptoms [63]. In this case, the patient developed significant neuropathic pain symptoms after the second administration of dupilumab, which might accord with the second hypothesis.

Previous reports also suggest that dupilumab can induce or exacerbate EGPA. A 71-year-old male patient had been using dupilumab for two years to control asthma. After discontinuing dupilumab treatment for five months, his eosinophil counts in peripheral blood experienced a significant increase, along with leg pain and skin rash. This patient was eventually diagnosed with EGPA [64]. In addition, EGPA would happen not only after stopping the use of dupilumab but also during its usage. A 50-year-old male patient treated with dupilumab for asthma and eosinophilic rhinosinusitis with nasal polyps developed elevated eosinophil levels and significant pulmonary infiltrates after five months [65]. Isao et al. reported a 61-year-old female with MPO-ANCA positivity who undergoing her second cycle of dupilumab for treatment-resistant eosinophilic chronic rhinosinusitis, eosinophilic granulomatous otitis media, and severe asthma, developed symptoms including right-hand numbness, ear pain, hearing loss, cough, facial swelling, and headache. Following dupilumab administration, there was an increase in eosinophil count and MPO-ANCA levels. The authors suggested that dupilumab may directly trigger EGPA manifestations in MPO-ANCA-positive patients [66]. Additionally, Martine et al. reported a case of a 67-year-old female patient who was treated with dupilumab for asthma with eosinophilia. However, after 11 months, he developed symptoms of periarteritis and sinusitis and was ultimately diagnosed with EGPA [67]. Furthermore, the progression of EGPA induced by dupilumab can occur in a shorter period. A 58-year-old male experienced eosinophilia, acute kidney injury, and systemic symptoms just two weeks after starting dupilumab for chronic rhinosinusitis. It makes the author strongly suspect that the adverse drug reactions of dupilumab include EGPA [68]. Additionally, there is a significant connection between dupilumab treatment and EGPA progression. Federica reported a case of a 54-year-old female EGPA patient who did not respond significantly to omalizumab, mepolizumab, and bevacizumab. However, dupilumab led to a noticeable worsening of eosinophilia, asthma, and systemic symptoms in this patient [69]. It is very important to closely monitor the occurrence of adverse conditions and the changes of patients' condition when using dupilumab to treat patients suspected of EGPA.

Here, we report a patient with asthma-like symptoms, eosinophilia, and sinusitis who developed neuropathy and extravascular eosinophilic infiltration in the second treatment course of dupilumab. Her ANCA test was negative, and it took seven years from the onset of asthma symptoms to the diagnosis of EGPA. By reviewing pertinent literature, we found that the diverse symptoms of EGPA patients often lead them to seek medical treatment in different departments, making the diagnostic process very complex. Initially, patients commonly visit the respiratory department

and are often been misdiagnosed with refractory bronchial asthma. The average interval from disease onset to the correct diagnosis of EGPA is four years, which significantly affects the patient's prognosis. Dupilumab is commonly used in patients with refractory bronchial asthma and chronic rhinosinusitis. Although dupilumab can prevent eosinophils in blood vessels from migrating and infiltrating surrounding tissues and organs, it can't prevent activated eosinophils from playing their roles. Moreover, patients in the incubation period of EGPA may have symptoms of EGPA after receiving dupilumab treatment. Therefore, patients might experience symptoms of multiple organ involvement during or after withdrawing from dupilumab treatment. Under these circumstances, clinicians need to rule out the possibility of EGPA when prescribing dupilumab for uncontrolled asthma. Moreover, the peripheral blood eosinophil (PBE) count should be closely monitored during the use of dupilumab.

Discussion

In this case, we presented a patient with EGPA symptoms who had neuropathic pain and extravascular eosinophilic infiltration one month after dupilumab treatment. Her neuropathic pain was significantly alleviated after discontinuing dupilumab and switching to mepolizumab combined with glucocorticoid therapy. However, it remains unclear whether dupilumab directly triggers EGPA activation or accelerates the symptoms of EGPA. Therefore, during dupilumab treatment, regular monitoring of eosinophil levels is necessary regardless of ANCA status. Clinicians should pay more attention to any worsening of symptoms, such as asthma, sinusitis, or other systemic manifestations.

Author Contributions WM.H. and LZ.S. found this case. JJ.W. wrote the manuscript. WD.T and LL.L carried out investigation. YC.W and RQ.L collected data. BB.H, J.T and FL.D carried out supervision and project administration. KW.S. and HB.Z. were responsible for revision. All of the authors discussed the results, reviewed and approved the final manuscript.

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Data Availability No datasets were generated or analyzed during the current study.

Declarations

Author Disclosure Statement The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Informed Consent This manuscript has obtained the informed consent of the patient, and the patient agrees to publish all images, clinical data and other data contained in the manuscript.

Competing interests The authors declare no competing interests.

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