Case Report

The diagnosis of eosinophilic granulomatosis with polyangiitis has been 'masked' by asthma: a case report

Hua Xie[1], Xiaojun Zhang[2], Junli Zhang[1], Meicen Liu[1], Xiangqian Che[1]

[1]The PLA Center of Respiratory and Allergic Disease Diagnosing Management, General Hospital of Northern Theater Command, Shenyang, China; [2]Department of Respiratory and Critical Care Medicine, The 2nd Medical Centre, Chinese PLA General Hospital, Beijing, China

Contributions: (I) Conception and design: H Xie, X Zhang; (II) Administrative support: None; (III) Provision of study materials or patients: J Zhang, M Liu; (IV) Collection and assembly of data: X Che; (V) Data analysis and interpretation: H Xie; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Hua Xie, PhD. Chief Doctor, The PLA Center of Respiratory and Allergic Disease Diagnosing Management, General Hospital of Northern Theater Command, No. 83 Wenhua Road, Shenyang 110016, China. Email: huaxie823@hotmail.com; Xiaojun Zhang, Master of Medicine. Chief Physician, Department of Respiratory and Critical Care Medicine, The 2nd Medical Centre, Chinese PLA General Hospital, No. 28 Fuxing Road, Haidian District, Beijing 100853, China. Email: 13801151778@163.com.

Background: Patients with asthma exhibit a significantly heightened susceptibility to eosinophilic granulomatosis with polyangiitis (EGPA) when compared to the general population. Vigilance for EGPA manifestations is crucial, especially in cases where asthma remains poorly controlled despite high-dose corticosteroid therapy or when eosinophil counts exceed 5%. The diagnosis of EGPA can be complex due to the absence of definitive biomarkers, as indicated by the American College of Rheumatology (ACR)'s 1990 classification criteria. EGPA is categorized as an antineutrophil cytoplasmic antibody (ANCA) associated vasculitis, with updated classification criteria released in 2022, which require a cumulative score of 6 or more for the diagnosis of small and medium vessel vasculitis. Enhancing knowledge of EGPA facilitates its early detection and effective management.

Case Description: The patient was initially diagnosed with allergic rhinitis in 2006 and developed cough and wheezing in 2016. In 2017, EGPA was diagnosed based on ACR criteria, with a cumulative score of 14 according to the 2022 ACR and the European League Against Rheumatism (ACR/EULAR) criteria, indicating small and medium vessel vasculitis. The patient showed myocardial, gastric, and neurological involvement, reflecting generalized EGPA. Prognostic assessments should use the five-factor score (FFS), which indicates a 46% 5-year mortality rate for those with an FFS of 2 or higher. This patient had an FFS of 3, tested negative for ANCA, and cardiac emission computed tomography (ECT) confirmed myocardial involvement. However, as EGPA was diagnosed only 13 months after the onset of wheezing, the patient had been undergoing glucocorticoid therapy, as of today (7 years later), has effectively managed the symptoms and facilitated normal daily activities.

Conclusions: If asthma symptoms persist despite intensive corticosteroid treatment or the eosinophil count exceeds 5%, consider the possibility of EGPA. The presence of ANCA exerts a substantial impact on the prognostic outcomes in EGPA. ANCA-negative patients typically exhibit reduced survival rates, primarily attributed to a higher incidence of cardiac involvement. Nevertheless, advancements in early diagnosis and therapeutic interventions have led to improved survival rates, even in cases complicated by cardiac and pulmonary manifestations.

Keywords: Eosinophilic granulomatosis with polyangiitis (EGPA); asthma; eosinophil levels; antineutrophil cytoplasmic antibody (ANCA); case report

Received: 09 April 2024; Accepted: 17 October 2024; Published online: 20 December 2024.

doi: 10.21037/acr-24-79

View this article at: https://dx.doi.org/10.21037/acr-24-79

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), an uncommon systemic disorder, is defined by elevated levels of eosinophil granulocytes and their infiltration into various tissues. This condition has the potential to impact numerous bodily systems or organs (1-3). The understanding and management of EGPA vary among medical specialists across different disciplines, due in part to a scarcity of comprehensive clinical studies and data on the disease, which often leads to its underdiagnosis. The probability of incorrectly diagnosing or completely overlooking EGPA remains high, and this is associated with the absence of definitive diagnostic criteria. EGPA, along with granulomatous polyangiitis (GPA) and microscopic polyangiitis (MPA), are conditions in which patients' blood may reveal the presence of neutrophil cytoplasmic antibodies (ANCAs), grouping them under ANCA-associated vasculitis (AAV) (4,5). In 2022, the American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR) introduced new classification criteria for AAV (6), with MPA showing the highest classification agreement at 96.6%, followed by EGPA at 86.3%, and GPA at 73.8%. When applying AAV classification criteria to patients suspected of having AAV, it is advisable to integrate the new 2022 ACR/EULAR standards with existing criteria. The confirmation of an EGPA diagnosis becomes challenging if ANCA is not detected in blood tests, despite clinical presentations that align with EGPA, contributing to its high rate of undiagnosed cases.

The incidence of EGPA in asthma patients was markedly elevated compared to the general population. Notably, EGPA should be considered regardless of the administration of high-dose inhaled corticosteroids (ICS) or systemic corticosteroids, or if peripheral blood eosinophil granulocyte counts exceed 5%. Cough variant asthma has been identified as a potential initial manifestation of EGPA (7). Cardiac involvement complicates the diagnosis and management of EGPA, as EGPA-associated endocarditis can be detected through cardiac imaging (8). A 16-year-old male presented with peripheral gangrene and atypical vegetation on the tricuspid valve's support apparatus, initially thought to have infective endocarditis but later diagnosed with EGPA. Therefore, a comprehensive cardiovascular evaluation is essential in the initial diagnostic assessment of patients with EGPA (9). Nevertheless, it is frequently overlooked in clinical practice, and the level of attention it receives is insufficient.

The clinical evaluation of a 35-year-old male diagnosed with EGPA highlights the critical need to include EGPA in the differential diagnosis for asthma patients presenting with rhinitis and marked eosinophilia. Asthma patients whose symptoms persist or worsen despite the administration of higher doses of inhaled or systemic glucocorticoids should be meticulously assessed for the potential presence of EGPA. The multi-organ involvement, particularly the cardiac system, correlates with poor prognosis and increased mortality in EGPA; however, early diagnosis and timely therapeutic intervention can decelerate disease progression and improve patient outcomes. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-24-79/rc).

Highlight box

Key findings

- The diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) has been 'masked' by asthma.

What is known and what is new?

- EGPA is an uncommon disorder that often goes unrecognized in patients with asthma. Especially if their asthma remains poorly controlled despite high-dose inhaled or systemic corticosteroids, or if their peripheral blood eosinophil count exceeds 5%. Diagnosing antineutrophil cytoplasmic antibody (ANCA)-negative EGPA presents significant challenges, and the 2022 American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR) revised classification criteria for ANCA-associated vasculitis provide valuable assistance in the accurate identification of EGPA.
- Individuals diagnosed with ANCA-negative EGPA presenting a five-factor score exceeding 2, coupled with myocardial involvement confirmed by cardiac emission computed tomography, exhibit diminished survival rates. However, prompt diagnosis and therapeutic intervention enhance prognostic outcomes.

What is the implication, and what should change now?

- Elevated eosinophil counts in individuals with asthma may indicate a potential risk for EGPA, particularly if conventional therapeutic approaches prove ineffective.
- EGPA is classified under ANCA-associated vasculitides. For cases that are ANCA-negative, it is imperative to compute cumulative scores in accordance with the 2022 ACR/EULAR criteria, with a cumulative score of 6 or higher being requisite for the diagnosis of small and medium vessel vasculitis.
- Cardiac involvement is the predominant cause of mortality in EGPA patients. Therapeutic approaches for EGPA are customized based on disease severity and prognostic indicators.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent for publication of this case report and accompanying images was not obtained from the patient or the relatives after all possible attempts were made.

Chief complaints

A 35-year-old male has been experiencing chronic rhinorrhea and sneezing for over a decade, accompanied by recurrent bouts of coughing and asthmatic episodes for the last 13 months.

History of present illness

In 2006, an individual presented with clinical manifestations including chronic cough and morning-predominant rhinorrhea with serous nasal discharge. The differential diagnosis initially included "allergic rhinitis", for which the patient was managed with intranasal corticosteroids and systemic antihistamines. Despite therapeutic interventions including turbinate reduction surgery and administration of leukotriene receptor antagonist montelukast, the patient's condition persisted. A decade later, in 2016, exacerbation of cough and adventitious breath sounds necessitated a reevaluation, culminating in a diagnosis of "bronchial asthma". Treatment with the ICS and long-acting beta-agonist (LABA) combination budesonide/formoterol resulted in clinical improvement. Subsequently, exercise-induced bronchospasm warranted hospitalization, indicating the need for further diagnostic workup and refinement of the therapeutic approach.

History of past illness

The subject has been managing essential hypertension for half a decade, with a recorded blood pressure of 190/110 mmHg, yet has not commenced any antihypertensive pharmacotherapy. The patient's surgical history reveals bilateral inferior turbinectomies performed in May 2012 and November 2016. A diagnosis of left facial neuritis in 2015 resulting in left facial paralysis post systemic treatment. Currently, the individual is hospitalized due to lobular pneumonia compounded by right middle lobe bronchiectasis. The patient's medical record is devoid of any antecedents such as diabetes mellitus, ischemic heart disease, viral hepatitis, tuberculosis, plasmodium infections, significant physical injuries, hemotransfusions, substance dependence, or hypersensitivity to foodstuffs. Immunizations have been executed in strict adherence to regional healthcare guidelines.

Personal and family history

Originating from Tongliao in the Inner Mongolia Autonomous Region and having resided there for a considerable duration. The individual has no prior domicile history in any endemic areas, nor exposure to pathogens, ionizing radiation, hazardous chemicals, or pharmacological agents. Practices abstinence from tobacco and engages in moderate alcohol consumption on social occasions. In a conjugal union for a triennium with a partner of sound health and progenitor of one offspring. Familial medical records reveal no trace of hereditary illnesses, with progenitors and siblings extant and devoid of any genetic susceptibility to conditions such as arterial hypertension.

Physical examination

The patient's core temperature is 36.2 ℃, pulse rate is 85 beats per minute, respiratory rate is 20 breaths per minute, and blood pressure is 145/94 mmHg. The individual shows normal physical development and adequate nutritional status but presents with left-sided facial nerve palsy. They walked into the ward independently, exhibiting a normal gait, alertness, clear speech, and appropriate social interaction. Skin examination shows no abnormalities, jaundice, rashes, or bleeding signs. Lymphatic examination reveals no swollen lymph nodes. The cranial assessment indicates no facial deformities or tumors, with preserved facial symmetry and no swelling. Eye examination is normal, with intact eyelids, sclera, and pupils, all reacting appropriately to light. Ear examination shows no unusual discharge. The oral cavity is odorless, with a normal tongue coating, intact mucosa, and no gum bleeding or cavities. The oropharynx and tonsils appear normal. Neck examination reveals no structural issues or thyroid enlargement. Chest assessment shows a symmetrical wall with clear lung sounds and no pleural friction. Cardiovascular check confirms a pulse of 85, with no murmurs heard. Abdominal palpation reveals a soft abdomen with no liver or spleen enlargement and no swelling in the extremities.

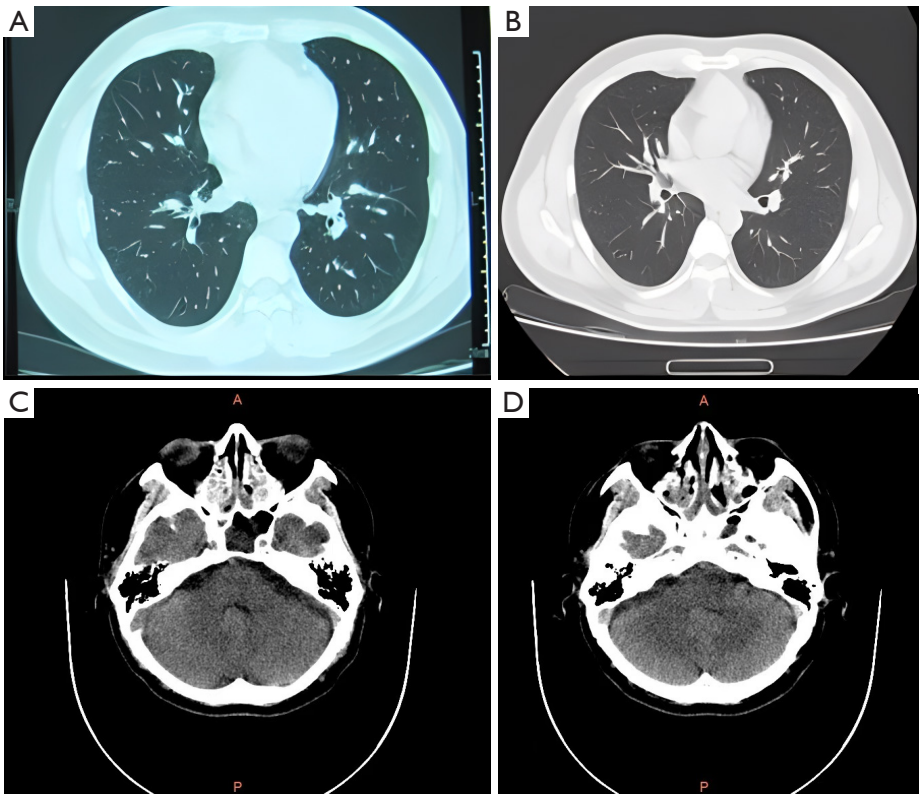

Figure 1 Radiological findings. (A) Prior to admission, CT revealed a few scattered shadows in the right middle lobe. (B) Post-admission. No evident abnormalities were detected on the CT scan. (C) Bilateral sinusitis. (D) Hypertrophy of the bilateral inferior turbinates. A, anterior; P, posterior; CT, computed tomography.

Further diagnostic work-up

On November 2, 2017, the patient's blood test showed a leukocyte count of 8.7×10^9/L, with eosinophils making up 18.8% (1.6×10^9/L). Spirometry results indicated a forced vital capacity (FVC) of 3.94 L (79.7% of predicted) and a forced expiratory volume in one second (FEV1) of 2.89 L (70.4% of predicted), with a post-bronchodilator FEV1/FVC ratio of 0.79. After administering 400 µg of salbutamol, the patient experienced a 580-mL increase in FEV1, reflecting a 19.89% improvement. The fractional exhaled nitric oxide (FeNO) level was 165 parts per billion (ppb). Skin allergy tests were negative, but total serum immunoglobulin E (IgE) was significantly elevated at 772.25 IU/mL, exceeding the normal range of 0–100 IU/mL.

Following hospitalization, lab tests showed:

- Hematology: white blood cell count of 7.4×10^9/L, eosinophils at 18.7% (1.4×10^9/L).
- Urinalysis: pH 5.0, specific gravity 1.025, bile present, other parameters normal.
- Arterial blood gas: pH 7.415, PaO_2 82.0 mmHg, $PaCO_2$ 38.7 mmHg.
- Autoantibody tests: negative for myeloperoxidase (MPO), proteinase 3 (PR3), cytoplasmic-anti-neutrophil cytoplasmic antibodies (cANCA), and perinuclear-anti-neutrophil cytoplasmic antibodies (P-ANCA); thyroid peroxidase antibody (TPOAb) at 18.9 IU/mL, thyroglobulin antibodies at 51.4 IU/mL.
- Serum biomarkers: procalcitonin <0.02 ng/mL, beta-D-glucan 37.5 pg/mL, Aspergillus galactomannan antigen 0.45 µg/L.

Imaging studies showed patchy opacities in the right middle lobe on chest computed tomography (CT) (*Figure 1A*), while no significant pulmonary issues were detected at admission (*Figure 1B*). The CT of the paranasal sinuses revealed bilateral sinusitis (*Figure 1C*) and enlarged inferior turbinates (*Figure 1D*).

Bronchoscopy: the examination showed a smooth epiglottis, fully mobile vocal cords, clear tracheal rings, and a distinct carina. All lobar segments in both lungs had open

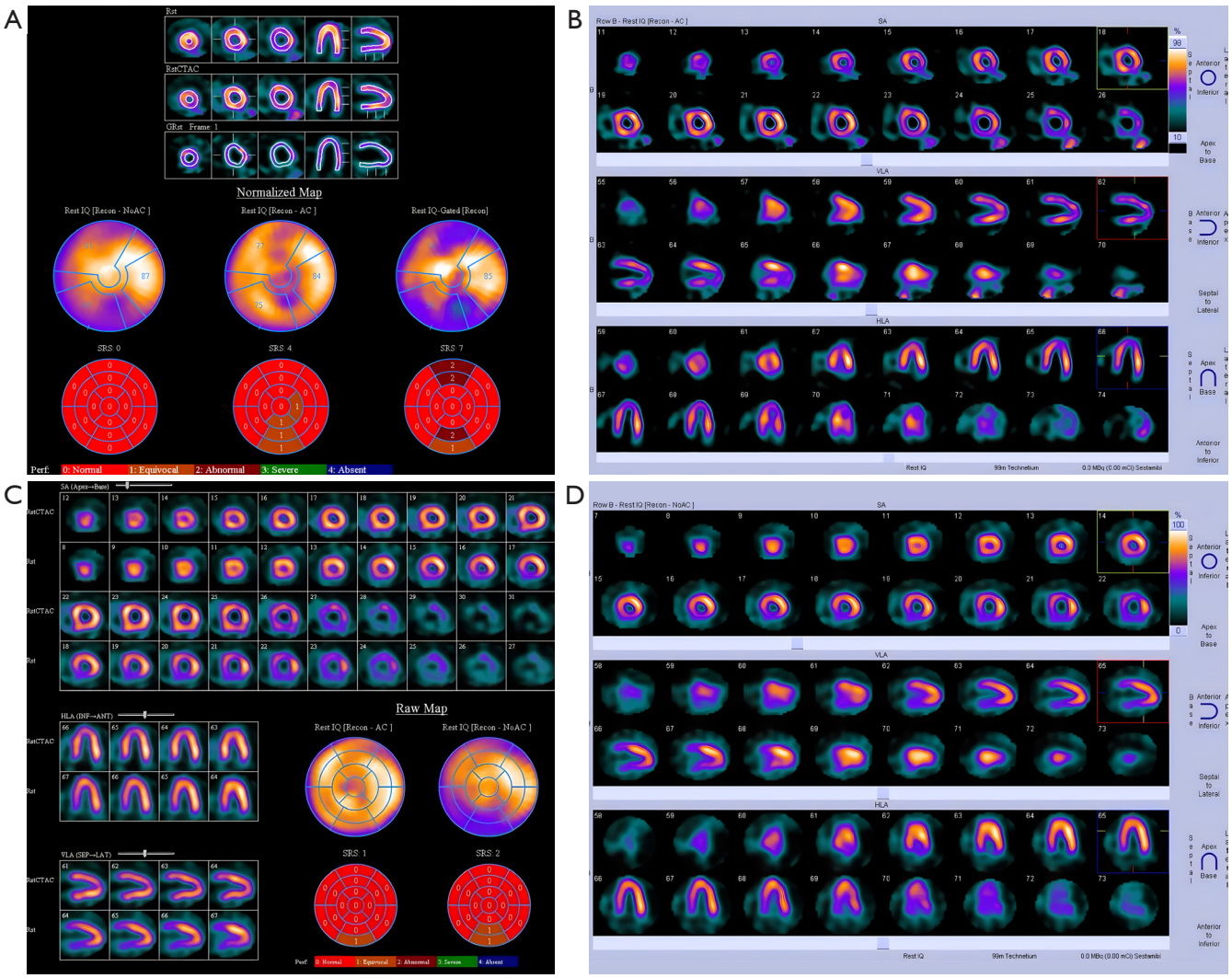

Figure 2 The cardiac ECT. (A,B) Limited radionuclide defects in the apical, anterior, and inferior regions of the left ventricle, indicating the presence of myocarditis. (C,D) A year later, the ECT images revealed a distinct reduction in the size of sparse areas with radioactive distribution in the left ventricle, left ventricular apex, anterior wall, and lower wall compared to previous scans, with some areas showing signs of filling up. Rst, rest; CTAC, computed tomography atlenuation correction; GRst, gate rest; IQ, intelligence quotient; Recon, reconstruction; AC, atlenuation correction; SRS, summed rest score; Perf, perfusion; SA, short axis; VLA, vertical long axis; HLA, horizontal long axis; INF, inferior; ANT, anterior; SEP, septum; LAT, lateral; ECT, emission computed tomography.

bronchial lumens with smooth mucosal surfaces, and no new organisms were found. The biopsy samples, preserved in the mucosa, revealed chronic mucosal inflammation with minor eosinophilic infiltration upon hematoxylin-eosin (HE) staining.

Emission computed tomography (ECT) revealed localized perfusion deficits in the apical, anterior, and inferior regions of the left ventricular myocardium, indicating inflammation (see *Figure 2A*,*2B*). The left ventricular ejection fraction (LVEF) was 61%, with an end-diastolic volume (EDV) of 113 mL, an end-systolic volume (ESV) of 44 mL, and a stroke volume (SV) of 69 mL, all within normal ranges.

Gastroscopy showed a normal esophageal mucosa, with an intact gastroesophageal junction. The gastric area was partially obscured by excessive secretions, but the fundus showed intact rugae. Some erosive changes were noted in the angular incisure's mucosa, while the antral mucosa

appeared erythematous but retained peristalsis. The pylorus was a patent, rounded opening with a normal mucosal surface. Both the duodenal bulb and sweeps exhibited smooth mucosal surfaces without ulcers.

Final diagnosis

(I) EGPA;
(II) Allergic rhinitis;
(III) Hypertension grade 3 (very high risk).

Treatment

Upon admission, patients received the following medications: methylprednisolone sodium succinate 40 mg intravenously twice daily for anti-inflammatory purposes, azelastine hydrochloride nasal spray 0.14 mg once daily for nasal inhalation, budesonide nasal spray 32 μg twice daily, esomeprazole 40 mg intravenously twice daily for gastric mucosa protection, ramipril 5 mg orally once daily for blood pressure control, and bisoprolol 1.25 mg orally once daily for reducing ventricular rate. The clinical symptoms were effectively managed, and an oral hormone replacement therapy regimen was initiated.

Post-discharge instructions: take methylprednisolone 60 mg orally once daily and attend follow-up appointments. Take esomeprazole 40 mg daily and watch for hormone-related side effects. Monitor blood pressure and take bisoprolol 1.25 mg, ramipril 5 mg, and nifedipine 30 mg orally.

A timeline chart as follows:

- In 2006, the patient received a combination of nasal steroids and antihistamines for allergic rhinitis.
- In 2012, high blood pressure was found, the highest was 190/110 mmHg; turbinectomy in May 2012 and November 2016.
- In 2015, left facial neuritis was diagnosed and left facial paralysis was still left after systemic treatment.
- In September 2016, asthma was diagnosed and given anti-asthma medication.
- In November 2017, RGPA was diagnosed and given intravenous steroid therapy.
- The five-factor score (FFS) was 3 and the prognosis was poor. But the patient was diagnosed early and treated in time.
- In 2018, the area of sparse distribution of radioactivity in left ventricular apex, anterior wall and inferior wall was smaller than before, and partial filling was seen in the area of sparse distribution of radioactivity.
- The 2024 was followed up by telephone in June. The patient remained under management with hormone therapy and cyclophosphamide administration. Self-reported symptoms were effectively managed, allowing for unrestricted physical activities.

Discussion

At the age of 24 years, the male subject started showing signs of allergic rhinitis, and 10 years later, he was diagnosed with bronchial asthma. Despite a year of treatment with ICS and LABAs, the treatment was ineffective, leading to four hospital admissions in the last 3 months. Bronchodilator tests during outpatient visits were positive, but later inpatient evaluations revealed acute asthma attacks along with other issues such as nasal problems, skin rashes, facial nerve weakness, stomach pain, and high blood pressure. Blood tests showed increased eosinophil counts, and an endobronchial biopsy indicated chronic inflammation with eosinophilic infiltration. Previous hospital admissions for respiratory issues showed no significant abnormalities on CT scans, suggesting a possible unusual lung condition rather than typical asthma. The differential diagnosis plays a critical role in the assessment of this patient.

Allergic rhinitis is often concomitant with asthma, as outlined in the allergic rhinitis and its impact on asthma (ARIA) guidelines (10-12). It is crucial to consider aspirin-exacerbated respiratory disease (AERD), previously termed aspirin-induced asthma, which impacts 2% to 25% of patients with asthma, chronic rhinosinusitis, or aspirin-associated nasal polyps (13). In this scenario, the initial exclusion of AERD as a differential diagnosis was due to the lack of a documented history of drug hypersensitivity.

Hypereosinophilic syndrome in peripheral blood is characterized by an eosinophil count exceeding 0.5×10^9/L, caused by various factors, including hypersensitivity reactions, infections, inflammation, and cancer (14). Conditions like allergic bronchopulmonary aspergillosis (ABPA) and EGPA can occur alongside asthma. Although the patient exhibited asthma symptoms and elevated eosinophil levels, their total serum IgE was 772.25 IU/mL, which does not meet the ABPA diagnostic threshold of over 1,000 IU/mL. Additionally, the Aspergillus-specific galactomannan level was 0.45 μg/L, falling within the normal range (0–0.5 μg/L). These results are not sufficient for diagnosing ABPA (15,16).

The patient presented with (I) asthma-like symptoms, (II)

a significant eosinophil count of 18.7% in the bloodstream, (III) a diagnosis of left-sided facial nerve inflammation resulting in residual hemifacial weakness after systemic treatment, (IV) thoracic CT scans prior to hospitalization showing scattered opacities in the right middle lobe, with follow-up scans showing no abnormalities, (V) paranasal CT scans revealing bilateral sinusitis and enlarged inferior nasal conchae, and (VI) bronchoscopic findings of chronic inflammation with mild eosinophilic infiltration in the basal segment of the right inferior lobe. These clinical and imaging findings met six criteria for EGPA (4,6,17).

The process of diagnosing EGPA is complex, typically necessitating a team of specialists from various disciplines. The current diagnostic standard adheres to the AAV-backed 1990 ACR criteria, with the revised 2023 protocols (18) stratifying EGPA into localized, confined to the pulmonary and respiratory structures, or systemic, encompassing multiple organ systems. Diagnosis of localized EGPA necessitates fulfillment of a minimum of four 1990 criteria, while systemic EGPA is confirmed with additional organ involvement. The case at hand pertains to systemic EGPA with cardiac, gastric, and neurologic engagement.

A scoring system for classification indicates that a total score of 6 or higher, reflecting 85% sensitivity and 99% specificity, suggests the presence of EGPA. The scoring criteria are as follows:

- Clinical criteria: obstructive pulmonary disease—3 points.
- Laboratory tests and histopathology:
  - Nasal polyposis—3 points;
  - Polyneuritis—1 point;
  - Blood eosinophilia ($>1\times10^9$/L)—5 points;
  - Eosinophilic infiltration on biopsy—2 points;
  - cANCA or PR-3 antigen positivity—3 points;
  - Hematuria—1 point.

The total score in this case is 14, calculated from the following: airway obstruction (3 points), nasal polyposis (3 points), neuritis (1 point), hyper-eosinophilia (5 points), and a pulmonary biopsy showing minor eosinophilic infiltration (2 points). There are no deductions for the absence of cANCA and urinary blood.

Distinguishing between small vessel vasculitis and eosinophilic diseases is important in EGPA diagnosis. ANCA testing is crucial, with around 30–40% of EGPA patients testing positive, mainly for myeloperoxidase-anti-neutrophil cytoplasmic antibodies (MPO-ANCA). MPO-ANCA positivity often indicates vasculitis symptoms such as glomerulonephritis, neuropathy, and purpura. Patients without ANCA positivity may show signs of cardiomyopathy and lung problems. In this case, ANCA was negative.

In EGPA treatment, the regimen varies based on the patient's condition. Despite incomplete phone follow-up, this patient was deemed to be in remission.

FFS comprising renal dysfunction, proteinuria, heart muscle disease, gastrointestinal and brain involvement, is currently utilized for predicting outcomes. The scoring system, introduced in 2011, assigns one point to each element with a total of 5 points. The higher the score, the graver the prognosis. With FFS scores of 0, 1, and ≥2, the 5-year mortality rates were 12%, 26%, and 46%, respectively (3,19).

The patient initially had an FFS score of 3 and a poor prognosis, but showed improvement in cardiac function after follow-up at another tertiary hospital. A cardiac ECT reexamination performed a year later revealed reduced cardiac radioactivity distribution and clear visualization of the left ventricle (*Figure 2C,2D*). Currently, the patient is working in Beijing, receiving treatment at Union Hospital's Rheumatology and Immunology Department, with well-controlled symptoms and good living conditions.

The present advancements in EGPA treatment are as follows.

Induction therapy: remission in EGPA is defined as the absence of active disease symptoms, such as asthma and otolaryngology manifestations. Remission criteria include a daily prednisone dose not exceeding 7.5 mg. Treatment for newly diagnosed EGPA involves glucocorticoids initially. For uncomplicated cases, glucocorticoids alone suffice, while cyclophosphamide (1) and rituximab (20) may be added for patients with serious complications.

In severe EGPA, rituximab, mepolizumab (21), and glucocorticoid can be used for maintenance remission. For non-severe EGPA (22,23) glucocorticoid alone or with mepolizumab (24) may be used.

In severe systemic relapse of EGPA, treat with rituximab, cyclophosphamide, and glucocorticoids. For non-severe relapses with respiratory symptoms, consider increasing glucocorticoid dose or adding mepolizumab (25).

Management of refractory EGPA involves using mepolizumab alongside glucocorticoids to induce remission in patients with relapsed, treatment-resistant EGPA (21,24).

Lessons learnt from this case

- Importance of comprehensive evaluation: a 24-year-old male was diagnosed with allergic rhinitis, later developing

asthma 10 years later. After one year of ICS/LABA treatment, his symptoms remained poorly controlled. A bronchodilator test showed significant improvement (FEV1 increased by 580 mL, a 19.89% increase after 400 µg salbutamol), yet he was still admitted due to an acute asthma exacerbation. His medical history included nasal issues (rhinitis, sinusitis, nasal polyps), prior nasal surgeries, recurrent rashes, facial neuritis, gastric discomfort, and hypertension upon admission. During hospitalization, his eosinophil count was elevated (18.8%, 1.6×10^9/L), and bronchoscopy revealed chronic mucosal inflammation with eosinophilic infiltration. He had a previous admission for left pneumonia and right middle lobe bronchiectasis, but a CT scan at our facility showed no significant lung abnormalities, indicating a likely complex pulmonary condition rather than simple asthma.

❖ Prompt identification and treatment of critical illnesses can significantly enhance outcomes. EGPA is a rare systemic disease characterized by elevated eosinophils and tissue infiltration, impacting multiple organ systems. Diagnosing EGPA is often difficult and typically necessitates a multidisciplinary approach due to the absence of specific diagnostic markers, resulting in frequent misdiagnoses. Nonetheless, early detection and intervention can greatly improve patient outcomes, highlighting the need for greater awareness of EGPA among healthcare professionals. Patients with ANCA-negative EGPA, an FFS score over 2, and confirmed myocardial involvement via cardiac ECT tend to have poorer survival rates. However, early diagnosis and treatment can enhance prognosis.

Conclusions

Asthmatic individuals demonstrate an increased predisposition to EGPA compared to the general population. When corticosteroid treatment proves ineffective and peripheral eosinophilia surpasses 5%, EGPA should be suspected. Key clinical features of EGPA include asthmatic symptoms and elevated eosinophil counts, with neuropathy being a common and potentially severe manifestation requiring immediate medical intervention. Cardiac involvement is the primary cause of mortality in EGPA. Diagnosing ANCA-negative EGPA is notably challenging, and the 2022 ACR/EULAR revised classification criteria for AAV provide substantial aid in the precise identification of EGPA. Patients with ANCA-negative EGPA, who present an FFS score above 2 and have myocardial involvement, exhibit reduced survival rates; however, early diagnosis and treatment improve prognostic outcomes. Therapeutic strategies are customized based on the severity of the condition and the specific organs affected, often incorporating pharmacological agents such as glucocorticoids, cyclophosphamide, rituximab, methotrexate, or mycophenolate mofetil.

Acknowledgments

Funding: This work was supported by the Liaoning Province Science and Technology Planning Project (No. 2021JH2/10300022).

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-24-79/rc

Peer Review File: Available at https://acr.amegroups.com/article/view/10.21037/acr-24-79/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-24-79/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent for publication of this case report and accompanying images was not obtained from the patient or the relatives after all possible attempts were made.

References

1. Villa-Forte A. Eosinophilic granulomatosis with polyangiitis. Postgrad Med 2023;135:52-60.
2. Fagni F, Bello F, Emmi G. Eosinophilic Granulomatosis With Polyangiitis: Dissecting the Pathophysiology. Front Med (Lausanne) 2021;8:627776.
3. Greco A, Rizzo MI, De Virgilio A, et al. Churg-Strauss syndrome. Autoimmun Rev 2015;14:341-8.
4. White J, Dubey S. Eosinophilic granulomatosis with polyangiitis: A review. Autoimmun Rev 2023;22:103219.
5. Kitching AR, Anders HJ, Basu N, et al. ANCA-associated vasculitis. Nat Rev Dis Primers 2020;6:71.
6. Pyo JY, Lee LE, Park YB, et al. Comparison of the 2022 ACR/EULAR Classification Criteria for Antineutrophil Cytoplasmic Antibody-Associated Vasculitis with Previous Criteria. Yonsei Med J 2023;64:11-7.
7. Li Y, Chen Z, Zhu S, et al. Negative anti-neutrophil cytoplasmic antibodies and eosinophilic granulomatosis with polyangiitis accompanied by cough variant asthma: a case report. Ann Palliat Med 2021;10:11209-15.
8. Chaaban N, Joshi A, Melanie R, et al. Eosinophilic granulomatosis with polyangiitis related endocarditis detected on cardiac imaging. Quant Imaging Med Surg 2023;13:1209-12.
9. Shelton A, Parikh S, Mims C, et al. A challenging case of granulomatosis with polyangiitis with cardiac involvement: a rare case report. AME Case Rep 2023;7:8.
10. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2) LEN and AllerGen). Allergy 2008;63 Suppl 86:8-160.
11. Bousquet J, Toumi M, Sousa-Pinto B, et al. The Allergic Rhinitis and Its Impact on Asthma (ARIA) Approach of Value-Added Medicines: As-Needed Treatment in Allergic Rhinitis. J Allergy Clin Immunol Pract 2022;10:2878-88.
12. Bousquet J, Hellings PW, Agache I, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) Phase 4 (2018): Change management in allergic rhinitis and asthma multimorbidity using mobile technology. J Allergy Clin Immunol 2019;143:864-79.
13. Ledford DK, Wenzel SE, Lockey RF. Aspirin or other nonsteroidal inflammatory agent exacerbated asthma. J Allergy Clin Immunol Pract 2014;2:653-7.
14. Leukemia and Lymphoma Group, Chinese Society of Hematology, Chinese Medical Association. Chinese expert consensus on the diagnosis and treatment of eosinophilia (2017). Zhonghua Xue Ye Xue Za Zhi 2017;38:561-5.
15. Agarwal R, Muthu V, Sehgal IS, et al. Allergic Bronchopulmonary Aspergillosis. Clin Chest Med 2022;43:99-125.
16. Seth D, Poowuttikul P, Pansare M, et al. Allergic Broncho-Pulmonary Aspergillosis. Pediatr Ann 2021;50:e214-21.
17. Groh M, Pagnoux C, Baldini C, et al. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA) Consensus Task Force recommendations for evaluation and management. Eur J Intern Med 2015;26:545-53.
18. Emmi G, Bettiol A, Gelain E, et al. Evidence-Based Guideline for the diagnosis and management of eosinophilic granulomatosis with polyangiitis. Nat Rev Rheumatol 2023;19:378-93.
19. Moiseev S, Novikov P. Five Factor Score in patients with eosinophilic granulomatosis with polyangiitis (Churg-Strauss; EGPA): to use or not to use? Ann Rheum Dis 2014;73:e12.
20. Akiyama M, Kaneko Y, Takeuchi T. Rituximab for the treatment of eosinophilic granulomatosis with polyangiitis: A systematic literature review. Autoimmun Rev 2021;20:102737.
21. Bettiol A, Urban ML, Bello F, et al. Sequential rituximab and mepolizumab in eosinophilic granulomatosis with polyangiitis (EGPA): a European multicentre observational study. Ann Rheum Dis 2022;81:1769-72.
22. Koike H, Nishi R, Yagi S, et al. A Review of Anti-IL-5 Therapies for Eosinophilic Granulomatosis with Polyangiitis. Adv Ther 2023;40:25-40.
23. Berti A, Atzeni F, Dagna L, et al. Targeting the interleukin-5 pathway in EGPA: evidence, uncertainties and opportunities. Ann Rheum Dis 2023;82:164-8.
24. Detoraki A, Tremante E, Poto R, et al. Real-life evidence of low-dose mepolizumab efficacy in EGPA: a case series. Respir Res 2021;22:185.
25. Furuta S, Iwamoto T, Nakajima H. Update on eosinophilic granulomatosis with polyangiitis. Allergol Int 2019;68:430-6.

doi: 10.21037/acr-24-79

Cite this article as: Xie H, Zhang X, Zhang J, Liu M, Che X. The diagnosis of eosinophilic granulomatosis with polyangiitis has been 'masked' by asthma: a case report. AME Case Rep 2025;9:31.