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Case Report

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A Case Report of Eosinophilic Granulomatosis with Polyangiitis in a Pediatric Patient

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ABSTRACT

Introduction: Eosinophilic Granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss syndrome (CSS), is a rare systemic vasculitis of small and medium-sized vessels that primarily develops in middle-aged individuals. It is characterized by asthma, blood eosinophilia, and extrapulmonary manifestations. In childhood, EGPA is extremely rare. Pulmonary and cardiac involvement is predominant in pediatric EGPA, and mortality is substantial. The key to the treatment of EGPA lies in the early diagnosis of the disease. When glucocorticoids and immunosuppressants are used early, they can improve both the symptoms and the overall outlook of EGPA.

Case Presentation: We presented a case of an 8-year-old boy with a history of short-term asthma, marked eosinophilia, and multi-organ involvement. The extremely high eosinophil level in the blood (72.50%) prompted the examination of eosinophilic leukemia before the EGPA diagnosis was made. Subsequently, this disease was successfully treated.

Conclusion: EGPA in children has unique clinical, imaging, and histological characteristics different from those of adults. In pediatric patients, the development and diagnosis of systemic symptoms are often delayed, mainly occurring in the eosinophilic phase, which will lead to specific manifestations. At the same time, we cannot detect a genetic relationship related to EGPA.

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Abbreviation

CSS: Churg-Strauss Syndrome
EGPA: Eosinophilic Granulomatosis with Polyangiitis
CT: Computed Tomography
ACR: American College of Rheumatology

Introduction

Eosinophilic Granulomatosis with polyangiitis, is a rare multi-system disease with unknown etiology, characterized by necrotizing vasculitis affecting small to medium-sized vessels [1]. EGPA is rare in pediatric patients and mainly involves the respiratory tract and necrotizing vasculitis, affecting small and medium blood vessels. Children suffering from EPGA have a shared history of asthma and sinusitis. Clinical manifestations usually involve the lungs, skin, heart, gastrointestinal tract, and peripheral nerves [2]. In addition, patients with EGPA typically have a history of asthma and allergic rhinitis, and the level of eosinophils in the peripheral blood increases significantly [3].

Children rarely suffer from EGPA, and its clinical manifestations can be very diverse [4, 5]. Therefore, the diagnosis of EGPA in children is a difficult task. Clinical criteria for EGPA diagnosis include asthma, blood eosinophilia greater than 1.5 x 109/l, and evidence of vasculitis affecting two or more extrapulmonary organs [6]. Recent research shows that early identification of the disease is essential because a delayed diagnosis can lead to severe organ involvement, which will lead to fatal results for patients [7]. In this study, we report on an 8-year-old boy admitted to the hospital due to fever and cough for 6 days and eventually diagnosed with EGPA.

Case Presentation

An 8-year-old Chinese boy presented at the pediatrics department of a general hospital with a history of high-grade fever and cough for 6 days. He had a prior history of eczema, rhinitis, and asthma and received inhaled corticosteroids for 1 month. The family history was unremarkable. A few days prior to admission, the patient developed fatigue and nasal congestion.

Physical examination showed tach dyspnea with rales and mild expiratory wheezing. Initial laboratory studies revealed the patient's erythrocyte sedimentation rate was 18mm/hour (reference range 1–15mm/h), a peripheral white blood cell (WBC) count was 15.6*10^9/L (reference range 4–14x10^9/L), with eosinophils accounting for 60.0%, neutrophils accounting for 18.0%, lymphocytes accounting for 17.0%, and urine analysis was normal with no detection of proteinuria.

Notably, after 6 days, his eosinophil count increased to 72.5%, with an absolute eosinophil count of 21.32*10^9/L, a WBC count of 29.4*10^9/L (Figure 1), and immunoglobulin E (IgE) was higher than 2000 KU/L. Extensive cultures and blood tests showed that bacteria, viruses, parasites, and fungi that cause infectious diseases were not present.

Figure 1: Changes in Blood Regular Test

Time	Admission Day 1	Day 2	Day 4	Day 7	Day 10	Day 12
WBCs(10^9/L)(3.5-9.5)	15.6*10^9/L	17.9*10^9/L	24.2*10^9/L	29.4*10^9/L	29.8*10^9/L	8*10^9/L
Neutrophil(%)(40-75)	18.00%	11.20%	13.60%	12.00%	21.80%	65.80%
lymphocytes(%)(20-50)	17.00%	20.60%	16.70%	12.90%	9.90%	26.30%
Monocytes(%)(3-10)	5.00%	2.40%	2.70%	2.50%	2.50%	4.10%
Eosinophil(%)(0.4-8)	60.00%	65.70%	66.90%	72.50%	65.80%	3.70%
Basophil(%)(0.0-1.5)	0.00%	0.10%	0.10%	0.10%	0.00%	0.10%
RBCs(10^12/L)(4.30-5.80)	4.68*10^12/L	4.05*10^12/L	4.2*10^12/L	4.5*10^12/L	4.24*10^12/L	4.48*10^12/L
Platelets(10^6/L)(125-350)	296*10^9/L	253*10^9/L	275*10^9/L	284*10^9/L	235*10^9/L	250*10^9/L
CRP(mg/dL)(<1.00)	1.6mg/dl	1.4mg/dl	<0.02 mg/dl	0.01mg/dl	0.04mg/dl	0.11mg/dl

A chest radiography shows bronchial infiltration. A computed tomography (CT scan) of the chest showed tiny nodules of the left oblique fissure subpleural and pulmonary fundus (Figure 2). Electro-echocardiogram and abdominal ultrasound revealed no abnormalities. No biopsy was performed due to the patient's parents' concerns.

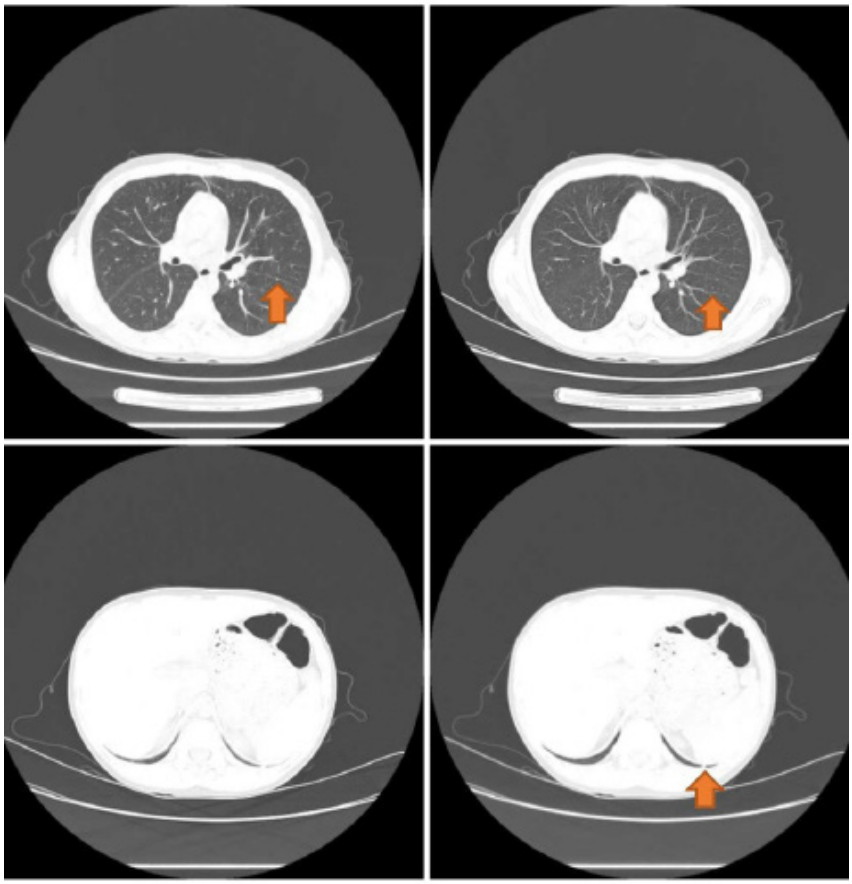

FIgure 2: The texture of both lungs increased, and the subpleural and lung bottom of the left oblique fissure showed tiny nodules. Multiple small lymph nodes in both axillary areas

Bronchoscopy revealed eosinophils in bronchoalveolar lavage fluid, which accounted for 6% (Figure 3). A bone marrow aspiration was performed, and the eosinophil percentage was counted at 45%. Both clinical symptoms and test results fit with the diagnosis EGPA.

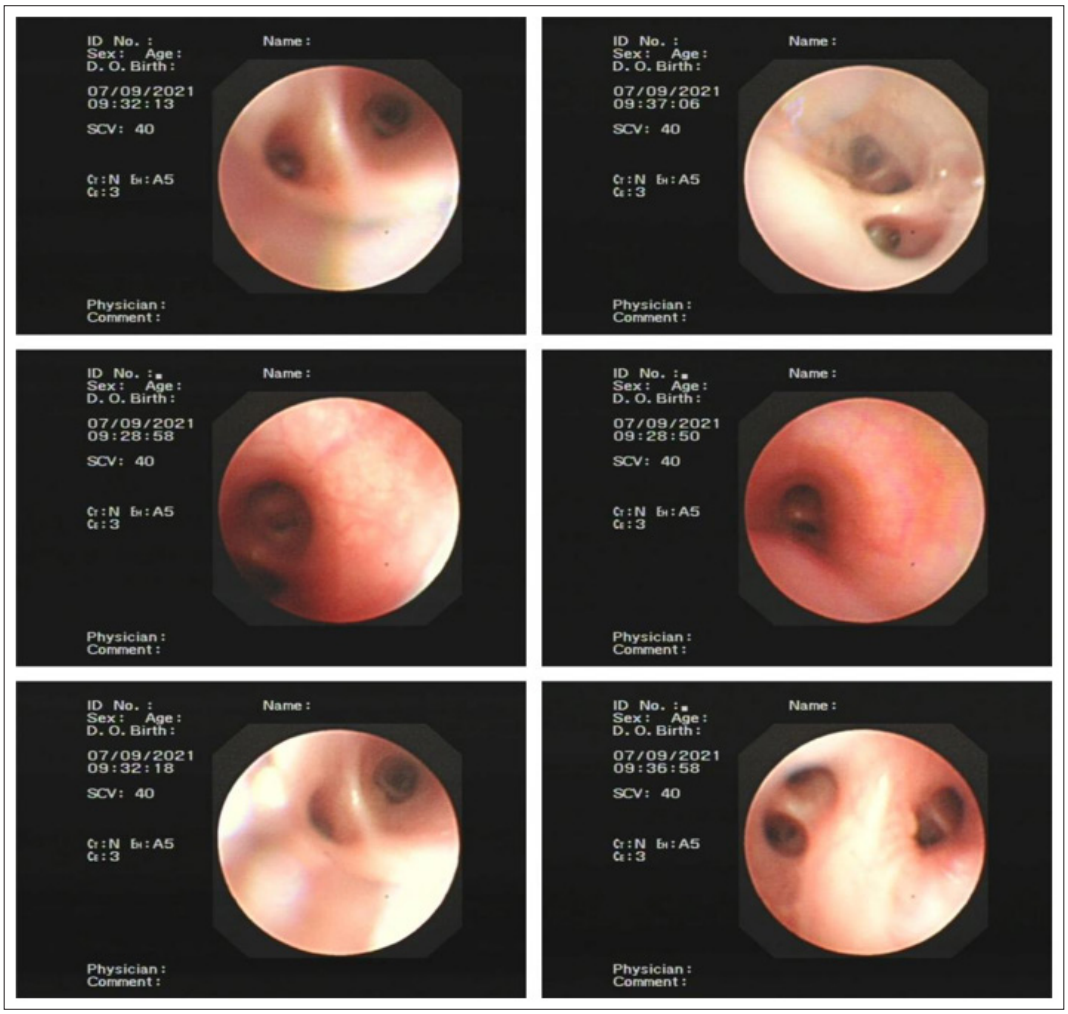

Figure 3: Mucosal hyperemia, medium number of viscous secretions, and phlegm-like substances were visible, and no obvious abnormal light spots were observed. Left lower bronchial lavage, right upper bronchial lavage. Examination indicated that bronchial inflammatory changes

Subsequently, high-dose corticosteroid pulse therapy was started, followed by oral prednisolone with a daily dose of 30 mg (1.2 mg/kg/day). As a result, the blood eosinophilic count dropped from a maximum of 72.50% to 3.70% and all signs of the disease disappeared completely in a few days. The patient was discharged from the hospital in excellent condition. The patient is now in good clinical condition with normal spirometry tests and a chest X-ray.

Discussion

We described a pediatric patient with EGPA characterized by extreme eosinophilia with pulmonary and nasal involvement. The diagnosis of this life-threatening disease was difficult because EGPA in childhood is very rare. Furthermore, the number of eosinophils was reduced. This is far beyond the level reported in the literature, suggesting leukemia. However, sometimes it will be diagnosed with a delay, which will lead to severe complications, so early diagnosis is essential for a reasonable prognosis of the disease. In 1990, the American College of Rheumatology (ACR) developed specific clinical criteria for the classification of CSS [6, 8]. Table (1). The ACR criteria include asthma, eosinophilia greater than 10% on differential WBC count, neuropathy, paranasal sinus abnormalities, pulmonary infiltrates, and biopsy containing extravascular eosinophils. When four or more than six ACR criteria are met, a CSS diagnosis is said to have a sensitivity of 85% and a specificity of 99.7% [9]. Many studies have also shown that at least three potential mechanisms are strongly implicated: a) asthma involving Th2 lymphocytes; b) the role of ANCA in the development of vasculitis; c) the role of eosinophils [10]. Unfortunately, although our patient met 4 out of 6 criteria, only the neuropathy abnormality could not be substantiated, and a biopsy was not performed due to patient family concerns.

Table 1: ACR and Lanham Diagnostic Criteria Met By Described Cases of Pediatric CSS

	ACR criteria for CSS	Lanham criteria for CSS
Case Male,8 years old	Asthma Eosinophilia Non fixed pulmonary infiltrates	Asthma Eosinophil count >1.5 x 10^9 /l Vasculitis in two or more extrapulmonary organs (Heart, liver, and paranasal sinuses)

Asthma-like symptoms always exist in CSS. Because of asthma, it is helpful for doctors to distinguish it from other diseases such as polyarteritis nodosa and Wegener's Granulomatosis. For any patient presenting with symptoms of asthma, the diagnosis of CSS can be suspected when complicated by at least one of these three characteristics: the challenge to treat, dependence on steroids, and delayed onset of disease. Two-thirds of CSS patients will also have pulmonary infiltrates visible on the chest X-ray. Chronic sinusitis and allergic rhinitis are common findings, which can be observed in our study case [11].

To find the genetic relationship and traces of EPGA, we tested the genes of patients and their families. The gene test of a patient was normal, but the gene test of their father showed that about 53.247 Kb of the heterozygous fragment was missing in the chr 6: 31949856-32003103 * 1 region (Figure 4). Therefore, the question now is, do gene mutations play an essential role in EPGA?

Figure 4: A heterozygous fragment deletion of about 53.247Kb was detected in the chr6:31949856-32003103 * 1 region, and its source was the father, The genes contained in this region are C4A; C4B; C4B_2, C4B; and C4B_2. The corresponding genes are associated with diseases in the OMIM database.

However, the relationship between gene mutations and CSS has still been lacking in recent studies. However, further research is needed to take the initiative regarding early genetic mutations that can lead to EPGA.

According to studies conducted by Zwerina et al., which covered 33 cases of EGPA in children, sixteen other patients have subsequently been reported [12, 13]. Therefore, 50 cases were selected for summarized studies. The mean age was 10 years (range 2–18 years). Studies show that EGPA is more common in girls than in boys, so the male and female ratio was set at 0.79, i.e., 22 boys and 28 girls. One of the typical clinical characteristics in all patients was pulmonary involvement (90%, including pulmonary infiltrates, pleural effusions, wheezing, and alveolar hemorrhage). Asthma was (88%), sinusitis (76%), and skin involvement was (73%), including rash, nodules, and purpura. Cardiac involvement includes only 22 patients out of 44 with cardiac involvement. Neurological involvement was also noted at a 50% ratio, i.e., 21 out of 42 patients. commonly includes mononeuritis multiplex, bilateral optic neuropathy, and vision loss. When it comes to gastrointestinal and musculoskeletal involvement, the percentages gradually decreased. Gastrointestinal involvement was 45%, including abdominal pain, diarrhea, ulceration, abdominal mass, and hepatic venous outflow obstruction. Musculoskeletal involvement was also 45%, which includes myalgia and arthralgia. Renal involvement was less than the recorded involvement, which was noted only in 21% of patients, i.e., proteinuria, IgA-nephropathy, and hematuria.

All patients received hormonal therapy early, i.e., corticosteroids, usually prednisone 1-2 mg/kg/d. Corticosteroids and additional immunosuppressive treatment were noted in 23 out of 46 patients (50%) from the 1st month to the 26th month. In addition, 8 patients were treated with corticosteroid monotherapy (35%), while 15 patients received additional immunosuppressive therapy (65%), usually cyclophosphamide.

EGPA is a vasculitis associated with significant morbidity and mortality. The key to EGPA treatment lies in early identification. Early use of glucocorticoids and immunosuppressants can change the disease process of EGPA and improve the prognosis and survival rate of the patient [14, 15]. According to recently published studies, data indicates that the EGPA mortality ratio in pediatric patients is very high, and the treatment response is not good. The corticosteroid therapy (prednisone tablets) was initiated at a dose of 30 mg daily (1.2 mg/kg/day), which improved the symptoms, and it played a vital role in reducing the percentage of eosinophils (Figure 5).

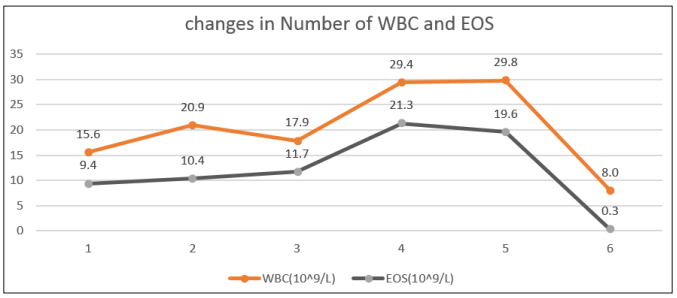

Figure 5: The number of white blood cells (WBC) and eosinophils (EOS) decreased gradually after the treatment of corticosteroids

The mortality ratio of EGPA is substantial. 10 out of 47 patients, i.e., (21%), died after suffering from EGPA in 2–26 months. Among them, 2 patients died within a short time when therapy was stopped or refused. The number of deaths reported due to respiratory, cardiac, and gastrointestinal system failure. Respiratory insufficiency (n =1), sepsis, and pulmonary abscess (n =1). As far as cardiac failure is concerned, the number of deaths recorded was (n =3), whereas cardiac arrest and severe myocarditis were (n =1). Intestinal perforation and septicemia (n = 1). Gastrointestinal inflammation along with necrosis and sepsis were recorded (n = 1). It is essential to mention that we only reported the first case of EGPA in our pediatrics department in the past 20 years. However, EGPA is more common in adults as compared to pediatric patients. Our hospital (Hangzhou First

People Hospital) admits approximately 400-500 asthma patients per year. This data ratio indicates the rarity of EGPA in the Chinese population. So, we cannot exclude the impact of systemic hormone therapy on asthma or hyper eosinophilia. We were suggesting the clinical follow-up of suspected patients.

Conclusion

In conclusion, we report an 8-year-old Chinese boy admitted to our hospital for intermittent fever and cough for six days and later diagnosed with EGPA. The clinical manifestations of EGPA can be diverse. Therefore, early diagnosis of EGPA in children is vital; otherwise, delayed diagnosis can lead to severe organ involvement and fatal results. The Respiratory tract usually involves asthma symptoms, sinusitis, and pulmonary infiltrates. More studies should closely monitor genetic mutations related to EGPA, and more and more research studies should be conducted to find a link between C4A; C4B; C4B_2, C4B; C4B_2 and EGPA However, further research is needed to be carried out to take the initiative regarding early diagnosis of EGPA and its prognosis.

Data Availability Statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Ethics Statement

The studies involving human participants were reviewed and approved by the Hangzhou First People's Hospital joint institutional Review Board. Written informed consent to participate in this study was provided by the participant's legal guardian. The legal guardian of any minors whose images or information could be used to identify them gave written permission for this article to be published.

Author Contributions

Saboor Saeed cared for the patient, drafted the initial manuscript, and approved the final manuscript submitted. Jiang Chunming and Zhang YI diagnosed, cared for, and treated the patient. They also drafted and revised the manuscript. Weijian Xi and Jiang Liya helped in the collection of data and patient laboratory reports. Zheng Xuyang performed bronchoscopy and helped to guide the manuscript. Wang Di helped to point out mistakes in the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Potential Conflict of Interest

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

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