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TREATMENT RESISTANT EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (CHURG-STRAUSS SYNDROME) WITH NEUROLOGICAL COMPLICATIONS: A CASE REPORT

Case Report

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Conflict of Interest: None | Grant Support & Financial Support: None | Publication Date: 23-01-2025

ABSTRACT

Background: Eosinophilic Granulomatosis with Polyangiitis (EGPA), formerly known as Churg-Strauss Syndrome, is a rare autoimmune vasculitis affecting small- and medium-sized blood vessels. It is characterized by multisystem involvement, including respiratory, dermatological, and neurological manifestations. Neurological complications, such as mononeuritis multiplex and peripheral neuropathy, are reported in up to 70% of cases and can result in significant functional impairment. Standard treatments, including glucocorticoids and cyclophosphamide, may fail in refractory cases, necessitating alternative therapeutic approaches.

Case: A 23-year-old female with a known history of asthma presented with progressive shortness of breath, generalized weakness, and neurological symptoms, including seizures, bilateral leg rashes, and limb paralysis, leading to bed confinement. Initial misdiagnosis and antituberculous therapy delayed appropriate management. Imaging studies, clinical findings, and laboratory investigations confirmed a diagnosis of EGPA with significant peripheral neuropathy and mononeuritis multiplex. Despite six cycles of cyclophosphamide and glucocorticoids, the patient exhibited no improvement, indicating treatment resistance. Monoclonal antibody therapy with rituximab was initiated, resulting in marked improvement in both respiratory and neurological symptoms. The patient remains under regular follow-up, with sustained symptomatic relief and improved functional status.

Conclusion: This case highlights the challenges in diagnosing and managing refractory EGPA, particularly in young patients with atypical presentations and severe neurological complications. The successful response to rituximab underscores its potential as an effective therapeutic option in treatment-resistant cases. It further emphasizes the importance of early diagnosis, multidisciplinary care, and the need for personalized treatment strategies to optimize outcomes for EGPA patients.

Keywords: Autoimmune Vasculitis, Churg-Strauss Syndrome, Monoclonal Antibodies, Mononeuritis Multiplex, Peripheral Neuropathy, Refractory Disease, Rituximab

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INTRODUCTION

Eosinophilic Granulomatosis with Polyangiitis (EGPA), previously known as Churg-Strauss Syndrome, is a rare autoimmune vasculitis affecting small- and medium-sized blood vessels, with an estimated prevalence of 10.7 to 14 adults per million worldwide (1). This condition predominantly presents with a constellation of multisystemic manifestations, including allergic rhinitis, asthma, eosinophilia, purpura, and neuritis, reflecting its complex and heterogeneous nature (2). Neurological involvement is a significant feature of EGPA, reported in up to 60% to 70% of cases. While peripheral nervous system complications such as mononeuritis multiplex or asymptomatic polyneuropathy are common, involvement of the central nervous system or cranial nerves is exceedingly rare and poorly understood (4).

The pathophysiology of EGPA is underpinned by eosinophilic inflammation and immune-mediated damage, yet the precise triggers remain elusive. Standard treatment protocols involve glucocorticoids as the cornerstone of therapy, often supplemented with intravenous cyclophosphamide in refractory cases (5). However, a subset of patients demonstrates suboptimal response to these therapies, necessitating the use of monoclonal antibodies, which have shown promise in emerging clinical trials. Despite advancements in therapeutic strategies, significant challenges persist in managing treatment-resistant EGPA, especially in patients with severe neurological complications. This report discusses a compelling case of a young woman who presented with shortness of breath, generalized weakness, and neurological involvement, ultimately diagnosed as EGPA. The case underscores the critical need for heightened clinical vigilance, timely diagnosis, and individualized treatment approaches for patients with atypical or resistant presentations of this rare and complex condition. The objective is to contribute to the growing body of literature by providing insights into the diagnostic and therapeutic challenges associated with EGPA, emphasizing the importance of multidisciplinary management in optimizing patient outcomes.

CASE REPORT

A 23-year-old married female, previously diagnosed with asthma, presented with a six-month history of progressive shortness of breath and generalized weakness. The shortness of breath, exacerbated by exertion and accompanied by a productive cough, was unrelieved by rest and unassociated with orthopnea, paroxysmal nocturnal dyspnea, or peripheral edema. Alongside generalized weakness, the patient experienced episodes of seizures, leading to the initiation of antiepileptic therapy. Approximately six months before admission, she was empirically started on antituberculous therapy for two months based on a presumed diagnosis of pulmonary tuberculosis, despite the absence of documented evidence. Subsequently, she developed bilateral leg rashes, progressive weakness of the right hand, and involvement of the right upper and both lower limbs, ultimately rendering her bedbound and non-ambulatory. Persistent dyspnea and tachypnea necessitated her transfer to the intensive care unit for advanced management.

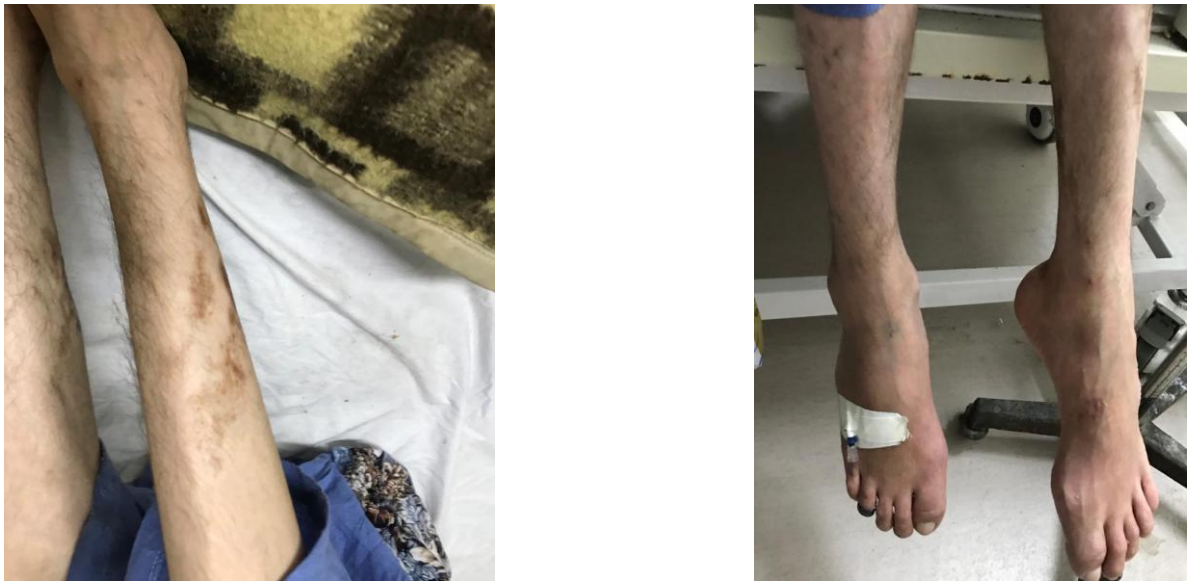

Figure-1 (**A** and **B**): Rashes over the posterior aspect of her right leg as well as the over the medial and lateral aspect of left leg (**Figure-1**).

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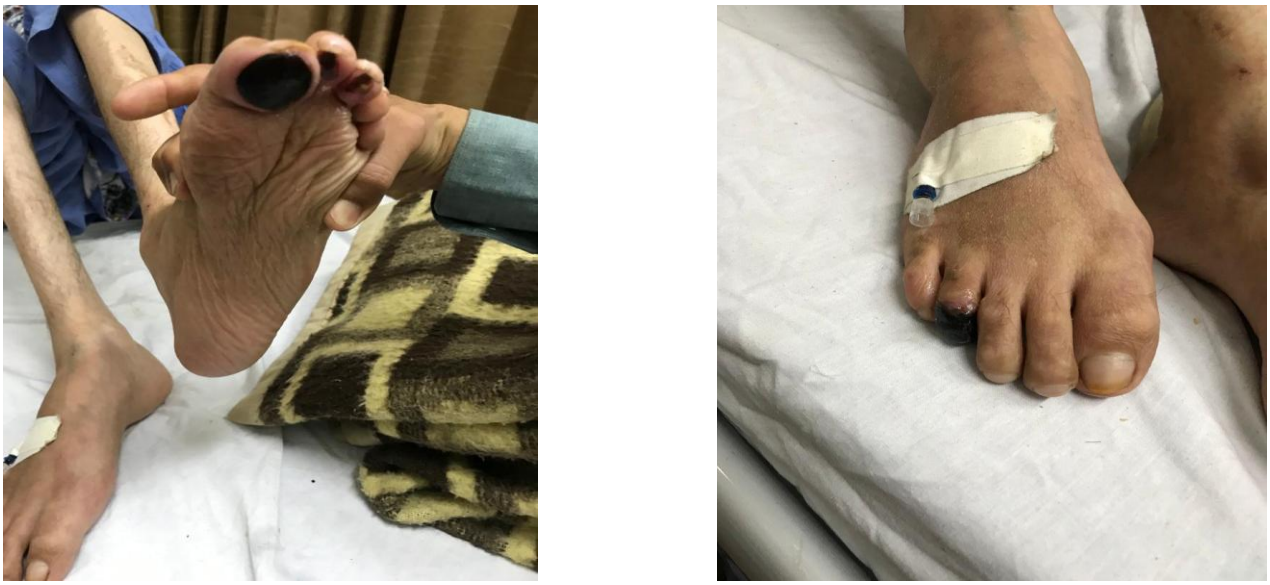

Figure-2 (A and B): The plantar surface of the distal 1st, 2nd and 3rd digits of the left foot showed wet gangrenous wounds and the 4th digit of the right foot showed dry gangrenous changes

On physical examination, her vital signs revealed a blood pressure of 120/80 mmHg, a pulse rate of 120 beats per minute, a respiratory rate of 30 breaths per minute, and an oxygen saturation of 99.4% on 2 liters of oxygen via face mask. Chest auscultation showed bilateral wheezes with crepitations in the left upper lung zones, while cardiovascular examination was unremarkable apart from tachycardia. Musculoskeletal assessment revealed rashes on the posterior aspect of the right leg and the medial and lateral aspects of the left leg. The fourth digit of the right foot exhibited dry gangrenous changes, and the plantar surfaces of the first, second, and third digits of the left foot showed wet gangrenous wounds. Neurological examination highlighted bilaterally reactive pupils, absent plantar reflexes, intact oculocephalic and corneal reflexes, and a Glasgow Coma Scale score of 15/15. Limb-specific findings included decreased tone, bulk, and power below the wrist and ankle joints, absent reflexes and sensations, and impaired proprioception and vibration sense in the affected areas. Coordination remained intact. A detailed summary of the neurological findings is presented in Table 1.

Table-1: Neurological examination of the patient with Churg-Strauss Syndrome

Limb	RUL	RLL	LUL	LLL
Tone	Absent below Wrist joint	Absent below ankle joint	Absent below wrist joint	Absent below ankle joint
Bulk	Decreased	Decreased	Decreased	decreased
Power	4/5 above wrist joint 3/5 on extension at wrist joint 0/5 on flexion at wrist	4/5 above ankle joint 0/5 on dorsiflexion and plantar flexion at ankle	4/5 above wrist joint 3/5 on extension at wrist joint 0/5 on flexion at wrist	4/5 above ankle joint 0/5 on dorsiflexion and plantar flexion at ankle
Reflexes	Absent at wrist joint	Absent at ankle joint	Absent at wrist joint	Absent at ankle joint
Sensation	Absent below wrist joint	Absent below level of calf muscles	Absent below wrist joint	Absent below calf muscles
Vibration	Absent below wrist joint	Absent below wrist joint	Absent below wrist joint	Absent below wrist joint
Proprioception	Absent at level of fingers	Absent at level of digits	Absent at level of fingers	Absent at level of digits
Coordination	Intact	Intact	Intact	Intact

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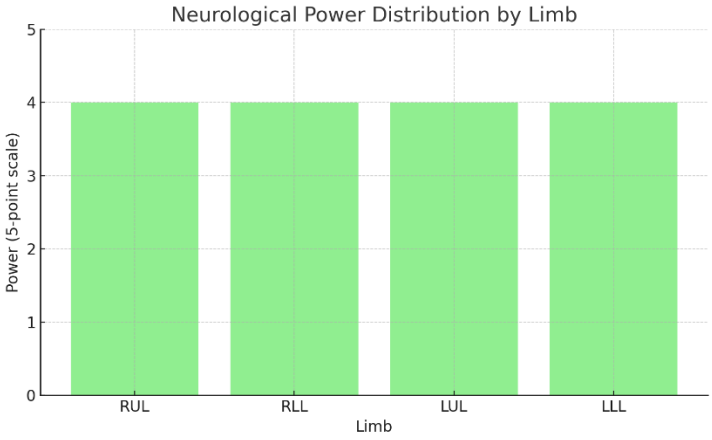
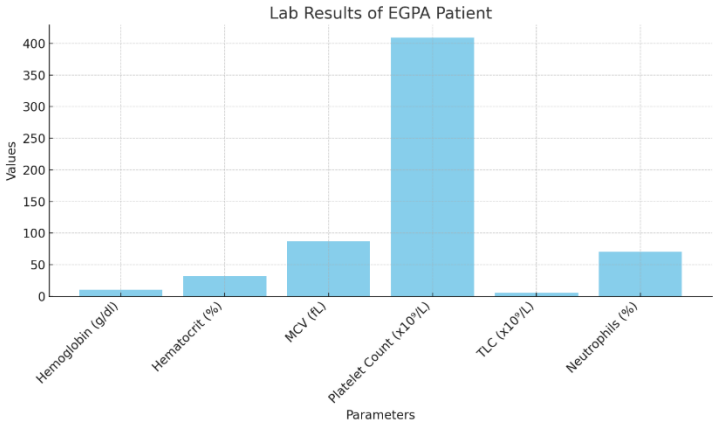
Laboratory investigations revealed a hemoglobin level of 10.5 g/dL, hematocrit of 32%, MCV of 86.7%, platelet count of 409 x 10^9/L, and a total leukocyte count of 5.5 x 10^9/L with neutrophilia (70%). Arterial blood gas analysis showed a pH of 7.32, PO_2 of 169.8 mmHg, PCO_2 of 62.1 mmHg, HCO_3 of 31.3 mEq/L, and oxygen saturation of 99.4%. Additional findings included a serum calcium level of 8.71 mg/dL, serum amylase of 47.8 U/L, HbA1c of 5.9%, procalcitonin of 0.04 ng/mL, and an erythrocyte sedimentation rate (ESR) of 29 mm/hr. The interferon-gamma release assay (IGRA) and viral markers (HbsAg and anti-HCV) were negative.





Imaging studies provided critical diagnostic insights. A chest X-ray revealed hyperinflated lungs, while a Doppler ultrasound of the lower limbs demonstrated normal arterial flow bilaterally. A contrast-enhanced CT scan of the chest showed hyperinflamed lung fields, patchy mosaic attenuation, septal thickening, parastatal emphysema, and large bullae formation, findings consistent with eosinophilic granulomatosis with polyangiitis (EGPA). The patient had previously undergone a standard EGPA treatment regimen in 2020, including six cycles of intravenous cyclophosphamide with mesna and methylprednisolone, followed by maintenance prednisolone at 5 mg daily. Despite completing the therapy, her neurological condition showed minimal improvement, and significant symptoms persisted, indicating treatment resistance. Given the refractory nature of her disease, monoclonal antibody therapy with rituximab was initiated, comprising six cycles, which resulted in notable symptomatic improvement. The patient remains under regular follow-up in the outpatient department to monitor her clinical progress and ensure ongoing management.

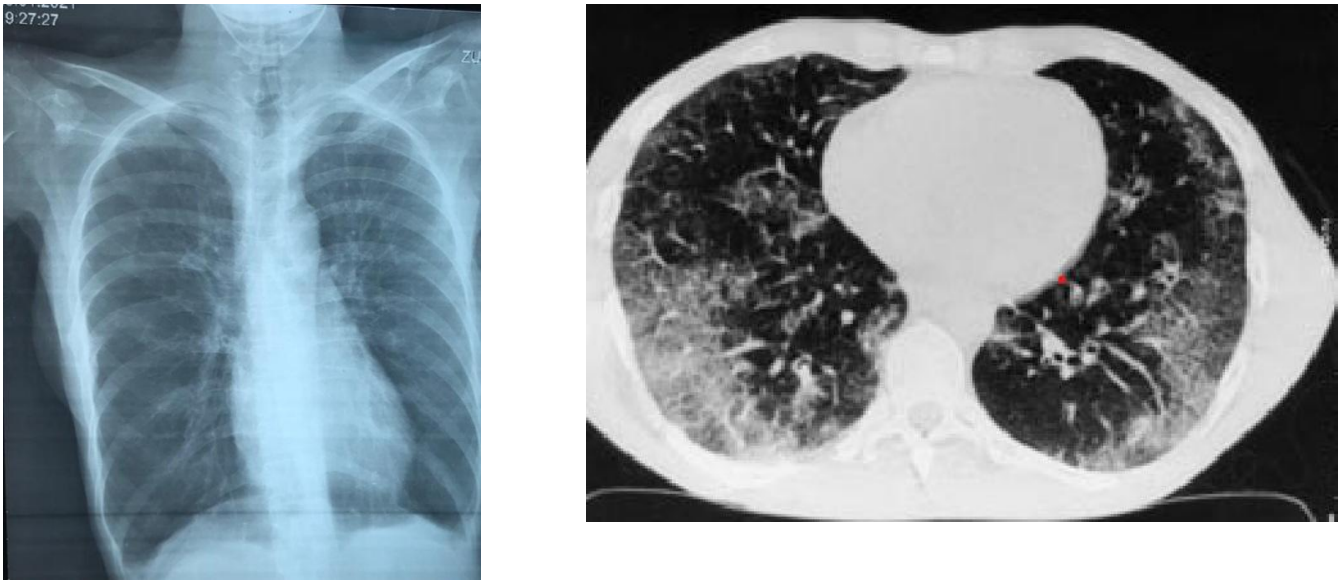


Figure-3 (A and B): **A:** Chest X-ray showing hyperinflated lung fields. **B:** CT Scan chest with contrast showing Patchy mosaic attenuation, septal thickening, paraseptal emphysematous changes in both apices, large bullae formation. Findings suggestive of EGPA.

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DISCUSSION

This case underscores the complexity and challenges associated with the management of eosinophilic granulomatosis with polyangiitis (EGPA), particularly in patients presenting with severe neurological involvement and resistance to conventional therapies. The patient, a young female with a known history of asthma and initial misdiagnosis as pulmonary tuberculosis, exemplifies the multisystem nature of EGPA, including its respiratory, dermatological, and neurological manifestations. The neurological complications, characterized by mononeuritis multiplex and peripheral neuropathy, resulted in profound functional impairment, highlighting the severe disability that can arise in advanced cases of EGPA. Neurological involvement in EGPA is a well-recognized but often debilitating manifestation, occurring in up to 60–70% of cases. This case aligns with existing literature in demonstrating the significant burden of peripheral neuropathy in EGPA patients, which often necessitates intensive care and multidisciplinary management. The failure of initial treatment with glucocorticoids and cyclophosphamide to produce clinical improvement reflects the variability in therapeutic responses seen among EGPA patients. Studies have reported that up to 50% of patients experience relapse or persistent disease activity despite aggressive immunosuppressive regimens, emphasizing the limitations of standard therapy in addressing refractory disease (4, 5).

The introduction of rituximab in this case proved to be a pivotal therapeutic decision. Rituximab, a monoclonal antibody targeting CD20-positive B cells, has shown efficacy in treating refractory EGPA, particularly in patients with inadequate response to cyclophosphamide and glucocorticoids. The significant clinical improvement observed in this patient, both in respiratory symptoms and neurological function, aligns with emerging evidence supporting rituximab as a viable alternative in resistant cases. However, the use of rituximab is not without limitations, including potential adverse effects, high costs, and the need for careful patient selection and monitoring to ensure optimal outcomes. A critical aspect highlighted by this case is the importance of early and accurate diagnosis of EGPA to prevent delays in appropriate management. The initial misdiagnosis of tuberculosis and subsequent initiation of antituberculous therapy could have contributed to the progression of the disease, delaying timely intervention. This underscores the need for heightened clinical awareness, especially in patients with asthma presenting with unexplained systemic or neurological symptoms, and the importance of incorporating comprehensive diagnostic criteria, including eosinophilia and organ-specific findings, to avoid misdiagnoses. The findings of this case demonstrate the potential of rituximab as a promising therapy in refractory EGPA, yet also highlight the broader challenges in managing this complex disorder. Limitations of the study include the lack of long-term follow-up to assess sustained remission and the absence of data on potential predictors of response to rituximab. Future research should focus on identifying biomarkers for treatment response and relapse risk, as well as conducting larger-scale studies to evaluate the long-term safety and efficacy of rituximab and other biologics in EGPA. This case emphasizes the need for individualized, evidence-based treatment strategies in EGPA, particularly for patients with severe or refractory disease. It also underscores the importance of early diagnosis, multidisciplinary care, and the integration of novel therapies such as rituximab in improving outcomes for patients with this rare but challenging vasculitic syndrome.

CONCLUSION

This case highlights the complexities of diagnosing and managing eosinophilic granulomatosis with polyangiitis (EGPA), particularly in young patients with atypical and treatment-resistant presentations. It underscores the critical importance of early recognition and timely intervention to mitigate disease progression and improve patient outcomes. The successful response to rituximab in this patient demonstrates its potential as an effective alternative therapy for refractory cases, offering hope for patients who do not respond to conventional treatments. This case contributes valuable insights into the importance of personalized treatment strategies tailored to individual patient needs and manifestations, reinforcing the need for further research to refine therapeutic guidelines for managing EGPA, particularly in cases involving significant neurological complications.

AUTHOR CONTRIBUTIONS

Author	Contribution
FNU Sunina	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Rekha Bajaj	Methodology, Investigation, Data Curation, Writing - Review & Editing
Maneesh Kumar	Investigation, Data Curation, Formal Analysis, Software
Akash Kumar	Software, Validation, Writing - Original Draft
Sandeep Kumar	Formal Analysis, Writing - Review & Editing
Fizza Reza Sanjani	Writing - Review & Editing, Assistance with Data Curation
Sabih Ahmed	Formal Analysis, Writing - Review & Editing
Raja Taha Yaseen Khan	Writing - Review & Editing, Assistance with Data Curation

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