EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS – A FOUR-YEAR LONGITUDINAL FOLLOW-UP CASE REPORT

EOZINOFILNA GRANULOMATOZA SA POLIANGIITISOM – STUDIJA SLUČAJA SA ČETVOROGODIŠNJIM LONGITUDINALNIM PRAĆENJEM

Slobodan ŠAJINOVIĆ[1,2], Milica POPOVIĆ[1,2], Branimir MIĆANOVIĆ[1,3], Vanja PETKOVIĆ[1,2], Aleksandra Bukvić ŠAJINOVIĆ[1] and Tatjana ILIĆ[1,2]

ORCID NUMBER
Slobodan Šajinović – 0009-0004-0519-3400,
Milica Popović – 0000-0002-0124-9444
Branimir Mićanović – 0009-0003-0482-201X
Vanja Petković – 0009-0001-2173-8640
Aleksandra Bukvić Šajinović – 0009-0003-5578-4412
Tatjana Ilić – 0009-0002-9659-6621

University of Novi Sad, Faculty of Medicine Novi Sad[1]
University Clinical Center of Vojvodina, Novi Sad
Clinic for Nephrology and Clinical Immunology[2]
Clinic for Hematology[3]

Case report
Prikaz slučaja
UDK 616-097:616.1-002]-085
https://doi.org/10.2298/MPNS2508198S

Abstract

Introduction. Eosinophilic granulomatosis with polyangiitis is a rare antineutrophil cytoplasmic antibody- associated small- to medium-vessel necrotizing vasculitis characterized by asthma, eosinophilia, and heterogeneous multisystem involvement. Diagnosis is based on a combination of clinical, laboratory, and histopathological findings, in accordance with current guideline-recommended criteria. Treatment strategies are stratified according to disease severity, with systemic glucocorticoids as first-line therapy and additional immunosuppressive agents reserved for relapsing or refractory disease. **Case Report.** We report the case of a 44-year-old woman with a history of asthma and chronic sinusitis who presented with rapidly progressive leg pain, paresthesias, cutaneous purpura, and constitutional symptoms. Laboratory investigations revealed marked leukocytosis with severe eosinophilia, anemia, elevated inflammatory markers, and strongly positive anti-myeloperoxidase antibodies. Electromyography demonstrated chronic sensorimotor polyneuropathy, while muscle biopsy confirmed acute necrotizing vasculitis. Cardiac involvement was excluded, and renal function and urinalysis remained normal. Given the severity of clinical manifestations, induction therapy with high-dose glucocorticoids and methotrexate was initiated, followed by a structured tapering regimen during outpatient follow-up. Over a four-year follow-up period, the patient achieved rapid clinical improvement, normalization of eosinophil counts, resolution of neuropathic and cutaneous manifestations, and sustained antineutrophil cytoplasmic antibodies negativity. Complete remission was maintained after discontinuation of both glucocorticoids and methotrexate, without evidence of relapse. **Conclusion.** This case illustrated that eosinophilic granulomatosis with polyangiitis without adverse prognostic factors can respond favorably to timely diagnosis and appropriately tailored immunosuppressive therapy. Early initiation of glucocorticoids combined with methotrexate, supported by structured monitoring and guided tapering, resulted in complete and sustained remission with full recovery of neurologic and cutaneous involvement. Durable remission following treatment withdrawal highlights the potential for long-term disease control in selected patients.

Key words: Granulomatosis with Polyangiitis; Churg-Strauss Syndrome; Vasculitis; Purpura; Peripheral Nervous System Diseases; Methotrexate

Sažetak

Uvod. Eozinofilna granulomatoza sa poliangiitisom predstavlja redak nekrotizujući vaskulitis malih i srednjih krvnih sudova asociran sa prisustvom antineutrofilnih citoplazmatskih antitela koji karakterišu astma, eozinofilija i heterogene kliničke manifestacije. Dijagnoza se zasniva na kliničkim, laboratorijskim i histopatološkim nalazima, tumačenim u skladu sa preporučenim kriterijumima. Terapija se određuje prema težini bolesti, pri čemu su glukokortikoidi terapija prvog izbora, a dodatni imunosupresivi se primenjuju kod relaps-refraktorne bolesti. **Prikaz slučaja.** Prikazana je 44-godišnja pacijentkinja sa istorijom astme i hroničnog sinusitisa, koja se klinički prezentovala progresivnim razvojem bola u nogama, parestezijama, pojavom purpuričnih papula i opštim konstitucionalnim simptomima. Laboratorijski nalazi su pokazali izraženu leukocitozu sa eozinofilijom, anemiju, povišene inflamatorne markere i pozitivnu antimijeloperoksidazu antitela. Elektromioneurografija je ukazala na hroničnu senzomotornu polineuropatiju, dok je biopsija mišića potvrdila akutni nekrotizujući vaskulitis. Isključena je kardiološka involucija. Bubrežna funkcija i nalaz urina bili su uredni. Na osnovu procene težine bolesti započeta je indukciona terapija visokim dozama glukokortikoida i metotreksata, uz postepeno i kontrolisano smanjivanje doze. Tokom četvorogodišnjeg praćenja postignuto je kliničko poboljšanje, normalizacija broja eozinofila, povlačenje neuropatskih i kožnih manifestacija i kontinuirana seronegativnost na antineutrofilna citoplazmatska antitela. Potpuna remisija je održana i nakon prekida glukokortikoida i metotreksata, bez zabeleženog relapsa. **Zaključak.** Ovaj slučaj pokazuje da eozinofilna granulomatoza sa poliangiitisom može dobro odgovoriti na blagovremenu dijagnozu i adekvatno prilagođenu imunosupresivnu terapiju. Rano uvođenje glukokortikoida i metotreksata, uz intenzivno praćenje i smanjivanje doze, rezultiralo je potpunom i održivom remisijom, uz potpuni oporavak neuroloških i kožnih manifestacija. Dugoročna stabilnost nakon prekida terapije potvrđuje da je trajna remisija dostižna kod ovih pacijenata.

Ključne reči: granulomatoza sa poliangiitisom; Čurg-Štraus sindrom; vaskulitis; purpura; periferna neuropatija; metotreksat

✉ Corresponding author: Slobodan Šajinović, E-mail: slobodan.sajinovic@mf.uns.ac.rs

Abbreviations

EGPA – eosinophilic granulomatosis with polyangiitis
ACR – American College of Rheumatology
EULAR – European Alliance of Associations for Rheumatology
ANCA – antineutrophil cytoplasmic antibodies
anti-MPO – anti-myeloperoxidase antibodies
HIV – human immunodeficiency virus
NCS – nerve conduction studies
ENT – ear, nose, and throat
FFS – Five-Factor Score

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic necrotizing vasculitis affecting small- to medium-sized blood vessels and extravascular granuloma formation [1,2]. The pathogenesis of EGPA is influenced by genetic and environmental factors [3]. Classically, the disease evolves through three phases, which may overlap and delay diagnosis [4]. Clinical spectrum of EGPA is broad and heterogeneous, influenced by antineutrophil cytoplasmic antibody (ANCA) status [5]. Common manifestations include constitutional symptoms such as fever, fatigue, and weight loss, cutaneous involvement such as palpable purpura, respiratory features including asthma and chronic rhinosinusitis, and involvement of the heart, kidneys, peripheral nerves, musculoskeletal system (arthralgia and myalgia), as well as hematologic and gastrointestinal disorders [2,6]. Diagnosis relies on a combination of clinical presentation, laboratory findings, and histopathological confirmation. Classification and diagnostic guidance are commonly based on the American College of Rheumatology (ACR) criteria and recommendations from the European Alliance of Associations for Rheumatology (EULAR) [1,2,7]. Treatment strategies for EGPA are tailored according to disease severity and the presence of adverse prognostic factors. Patients with non-severe disease are typically treated with glucocorticoid monotherapy, with a high likelihood of achieving remission [2,7]. In contrast, severe disease requires induction therapy with high-dose glucocorticoids combined with intravenous cyclophosphamide or rituximab, followed by maintenance therapy with methotrexate, azathioprine, or mepolizumab. Biologic agents play a central role in relapsing or refractory disease [2,8]. Supportive management also includes careful glucocorticoid tapering, structured follow-up using activity scores, infection prophylaxis, and monitoring for organ damage [1,7]. The aim of this report is to illustrate the clinical course, diagnosis, and successful long-term management of EGPA, emphasizing the importance of early diagnosis and individualized therapy in achieving sustained remission.

Case Report

A 44-year-old woman presented with a 10-day history of progressive lower-extremity symptoms. Initial complaints included pain and cramping in the calf muscles, followed by the gradual onset of heel, plantar, and toe pain. The symptoms progressed to the point that she was unable to climb stairs. During the same period, she developed bilateral ankle swelling. The skin over the lower legs became warm, erythematous, and pruritic. She also reported generalized fatigue, pain in the small joints of the hands, and shoulder pain exacerbates by arm movement. Her medical history was notable for long-standing chronic sinusitis, with persistent nasal obstruction and impaired nasal breathing. She denied recent asthma exacerbations and did not require increased use of maintenance therapy. Prior to admission to the Clinic for Nephrology and Clinical Immunology at the University Clinical Centre of Vojvodina, a complete blood count performed in primary care revealed marked leukocytosis with eosinophilia, accompanied by progressive clinical deterioration and fever up to 38 °C. Empirical antibiotic therapy was initiated. Soon thereafter, she developed intense pruritus around the ankles, leading to excoriations.

Pre-admission laboratory investigations, performed five days before hospitalization, showed white blood cells (WBC) count of 29.35×10^9/L with 41.9% eosinophils, microcytic anemia (Hb 90 g/L), and thrombocytosis (487×10^9/L). Inflammatory markers were elevated, with C-reactive protein (CRP) 76.8 mg/L and ESR 43 mm/h, while procalcitonin was only mildly increased (0.07). Basic metabolic panel, liver enzymes, coagulation parameters, and lipid profile were within reference ranges. Rheumatoid factor was negative. Urine sample was not obtained due to active menstruation. Family history was significant for paternal lung cancer.

Three days prior to admission, the patient was evaluated by a hematologist, started on prednisone 15 mg daily, and urgently referred to the nephrology and immunology department. On the same day, dermatologic examination revealed doughy edema of the ankles and several purpuric papules and plaques on the lower legs and dorsum of the feet **(Figure 1)**.

On admission, the patient was alert, oriented, and communicative. Lung auscultation revealed diffuse low-pitched wheezing. Cardiovascular and abdominal examinations were unremarkable. Physical examination of the lower extremities demonstrated mild pedal edema and pasty swelling of both ankles, with warm erythematous skin, excoriations over both malleoli, and palpable purpuric papules and plaques on the lower legs and dorsum of the feet. Repeat lab-

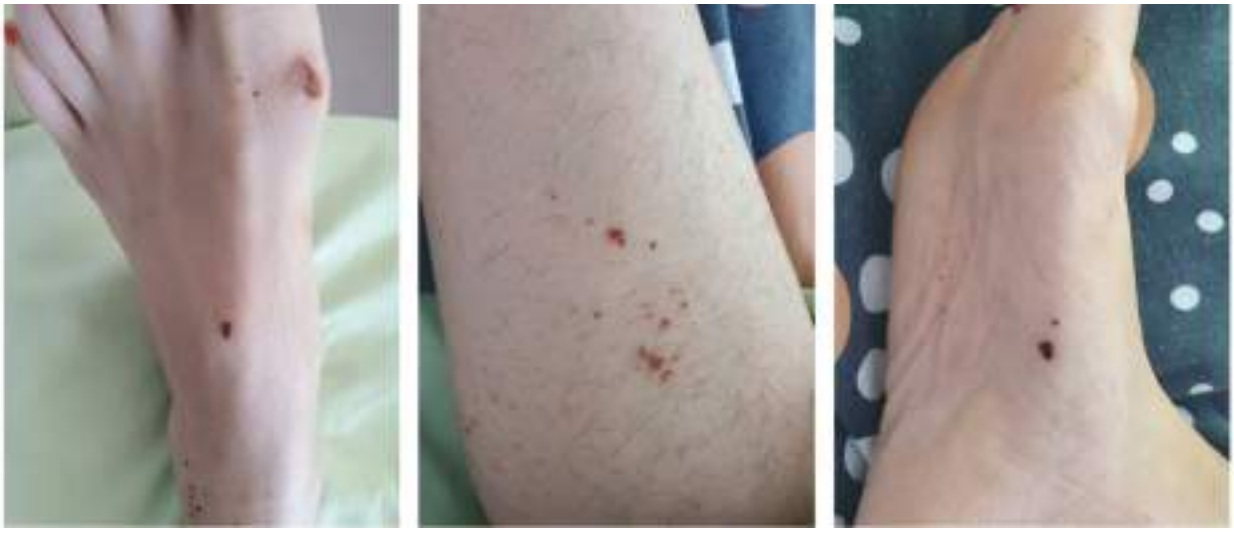
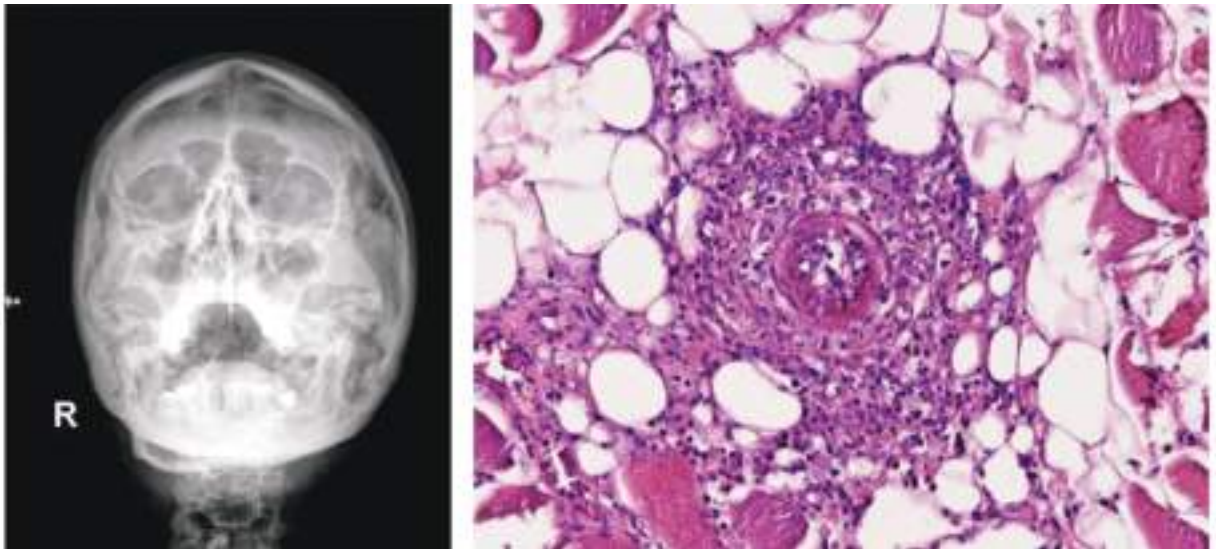


Figure 1. Palpable purpuric papules and plaques on the skin of the lower limbs

oratory testing on admission confirmed persistent leukocytosis (WBC 29.74 × 10^9/L) with 43.2% eosinophils, microcytic anemia (Hb 95 g/L), and thrombocytosis (533 × 10^9/L). Peripheral blood smear showed eosinophilia (44%), anisopoikilocytosis, hypochromia, microcytosis, and anulocytes. CRP was 29.1 mg/L, while procalcitonin had normalized (0.05). Renal function was preserved (creatinine 57 μmol/L; estimated glomerular filtration rate 100 mL/min/1.73 m^2). Iron studies demonstrated low serum iron (3.9 μmol/L) with normal ferritin levels. Immunoglobulin levels were within reference ranges, except for markedly elevated IgE (546 IU/mL). Complement level (C3 and C4) were normal, and the direct Coombs test was negative. Thyroid function tests were normal under replacement therapy. Autoantibodies revealed positive ANCA, with strongly positive anti-myeloperoxidase (Anti-MPO) antibodies (>100 AU/mL), while proteinase 3 (PR3) antibodies were negative. Rheumatoid factor was mildly elevated (74 IU/mL), whereas ANA and anti-cyclic citrullinated peptide (anti-CCP) antibodies were negative. Serologic testing for HIV and hepatitis viruses was negative. Urinalysis obtained during menstruation showed hemoglobin positivity with mild microscopic hematuria and no proteinuria. Repeated urinalysis after menstruation confirmed the absence of proteinuria and hematuria. Given the presence of iron-deficiency anemia, screening for occult gastrointestinal bleeding was performed and was negative. Gynecologic evaluation



Figures 2 and 3. Paranasal sinuses X ray showing mucosal thickening and normal sinuses transparency; Muscle biopsy histopathological analysis revealing acute vasculitis characterized by a dense mixed inflammatory infiltrate with some individual eosinophiles

revealed chronic cervicitis and two uterine myomas, considered the most likely cause of secondary sideropenic anemia. Vaginal flora analysis was unremarkable except for *Candida spp.* isolation. Urine culture and stool parasitological examination were negative. Electromyography (EMG) and nerve conduction studies (NCS) demonstrated chronic, moderately severe sensorimotor polyneuropathy, with absent sural nerve responses and reduced amplitudes in all examined motor nerves except the left peroneal nerve. Mildly slowed conduction velocity was noted in the right tibial nerve. Sinus radiography showed preserved aeration with mild mucosal thickening of the anterior paranasal sinuses **(Figure 2)**. Chest computed tomography revealed no pulmonary infiltrates; only a few bilateral micronodules were observed. There was no mediastinal or axillary lymphadenopathy, pleural effusion, or pericardial effusion. Cardiac ultrasound demonstrated normal chamber dimensions, intact valve morphology, preserved systolic and diastolic function, and no pericardial effusion. Histopathological examination of a skin biopsy revealed chronic superficial perivascular dermatitis. In contrast, muscle biopsy showed acute vasculitis, characterized by a dense mixed inflammatory infiltrate involving the vessel wall with focal vascular necrosis, consistent with active vasculitis **(Figure 3)**. The Five-Factors Score (FFS) was 0.

During hospitalization, induction therapy was initiated with high-dose prednisone (1 mg/kg) and methotrexate 10 mg weekly, along with folic acid supplementation, gastric protection, vitamin D, and B-complex vitamins due to the presence of polyneuropathy. At discharge, structured prednisone taper was prescribed, starting with 60 mg daily for 5 days, followed by 50 mg daily for 7 days, and then 40 mg daily until the first outpatient follow-up visit. Methotrexate was continued at 10 mg weekly, with folic acid 5 mg administered the day after methotrexate intake. Supportive therapy included pantoprazole 20 mg twice daily, vitamin D 2000 IU daily, and Milgamma (B-complex vitamins: B1, B6 and B12) twice daily.

Over a four-year follow-up period, patient demonstrated progressive and sustained clinical improvement. One month after discharge, neuropathic symptoms persisted, although eosinophil counts and inflammatory markers had substantially decreased under high-dose corticosteroid and methotrexate therapy. At subsequent outpatient visit, paresthesias gradually diminished and cutaneous lesions resolved. Inflammatory markers normalized, while mild anemia persisted. Eight months later, the patient reported only residual neuropathic discomfort. Eosinophil counts normalized (8%), inflammatory markers remained within reference limits, and ANCA serology converted to negative, allowing further tapering of prednisone.

Table 1. Timeline of visits with clinical status, key laboratory findings and treatment regimen

Time after discharge	Clinical status	Key laboratory findings	Treatment at the time
1 month	Improving; persistent neuropathic symptoms; skin lesions resolving	WBC 14.35 (Eos 28.9%); Hb 98; CRP 9; ESR 22	Prednisone taper (35→20 mg); MTX 12.5 mg/wk; supplements
4 months	Further improvement; reduced paresthesias; cushingoid	WBC 12.3 (Eos 19%); Hb 94; CRP 5, ESR 15	Prednisone 15→10 mg alt days; MTX 12.5 mg/wk
8 months	Stable; residual neuropathy only	WBC 9.2 (Eos 8%); Hb 100; CRP <5, ESR 7	Prednisone 10→5 mg alt days; MTX 12.5 mg/wk
12 months	Clinically stable; no new skin lesions	WBC 11.1 (Eos 8%); Hb 101; CRP <5, ESR 7, C3 nad C4 normal, ANCA negative	Prednisone 10–5 mg alt days; MTX 12.5 mg/wk
18 months	Improved; neuropathic pain resolved	WBC 10.2 (Eos 7%); Hb 111; CRP 8	Prednisone 5 mg; MTX 12.5 mg/wk
24 months	Asymptomatic	WBC 11.5 (Eos 11%); Hb 115; CRP 7, ESR 10, ANCA negative	Prednisone 5 mg qod; MTX 12.5 mg/wk
32 months	Asymptomatic	WBC 8.5 (Eos 7%); Hb 120; CRP <5, ESR 5,	Prednisone discontinued; MTX 12.5 mg/wk
40 months	Asymptomatic; patient self-discontinued MTX	WBC 7 (Eos 6%); Hb 121; CRP <5, ESR 8, C3 and C4 normal, ANCA negative	No immunosuppression supplements only
48 months	Stable; in full clinical remission without therapy	WBC 7 (Eos 7%); Hb 120; CRP <5, Iron 24 umol/L	None

WBC – white blood cell, Eos – eosinophils, Hb – hemoglobin, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, MTX – Methotrexate

Over the following nine months, the patient remained clinically stable, with complete resolution of neuropathic symptoms and no new vasculitic manifestations. Laboratory findings consistently showed normal eosinophil counts and persistent negative ANCA titers. Two years after hospitalization, the patient remained asymptomatic with laboratory results within reference ranges. Prednisone was discontinued after 30 months. Shortly thereafter, the patient independently discontinued methotrexate due to intolerance; nevertheless, she remained in sustained clinical and serological remission without relapse. Four years after the initial presentation, the patient remained off all immunosuppressive therapy, in complete clinical remission, with low inflammatory markers and stabilized hemoglobin level. A summary of laboratory findings, clinical status, and treatment during the four-year follow-up period is provided in **Table 1.**

Discussion

EGPA affects males and females at approximately equal rates, although some studies report a slight female predominance, particularly among patients presenting with asthma and ear, nose, and throat (ENT) involvement [6,9]. The clinical presentation of EGPA is highly heterogeneous [1,2], with manifestations often appearing at different times, which can delay recognition and result in diagnosis only after the disease has reached a more advanced stage [2]. The disease typically presents in mid-to-late adulthood, with a peak onset between 40 and 60 years of age [6,10], consistent with the age of our patient. Classically, EGPA evolves through prodromal, eosinophilic, and vasculitic phases; however, these stages often overlap, further complicating timely diagnosis [4,11]. The **prodromal phase** is characterized by asthma, allergic rhinitis, and chronic sinusitis, often persisting for many years and frequently accompanied by ENT manifestations [1,12]. This pattern was evident in our patient, who had been treated for bronchial asthma and chronic sinusitis for over 20 years. The patient presented with rapidly progressive lower-extremity symptoms, including pain, cramping, and paresthesias. Neurological involvement in EGPA commonly manifests as distal symmetric polyneuropathy with paresthesia, numbness, and weakness [13,14]. In addition, ankle swelling, small joint pain of the hands, and shoulder pain exacerbated by arm elevation have been described in the literature as a common presentation of EGPA [15]. Matucci et al. reported that up to 20% of patients exhibit arthritis [16]. Purpura is the most common cutaneous lesion in EGPA [2,13,15]. Kataoka and al. demonstrated that purpura is associated with elevated CRP and IL-5 levels, reflecting higher disease activity [17]. Anemia is a relatively common finding in EGPA, however, other causes such as hemolytic anemia or lymphoma should be excluded due to its complex pathophysiology [18]. In our patient, an extensive workup – including peripheral blood smear analysis, Coombs testing, lactate dehydrogenase (LDH) and bilirubin measurements - excluded hemolysis. Gynecological evaluation revealed two myomas and increased menstrual bleeding, identifying chronic blood loss as the most likely cause of microcytic anemia. This condition was likely further exacerbated by inflammation during the EGPA flare [19]. Immunoglobulin levels were within reference ranges except for markedly elevated Immunoglobulin E (546 IU/mL), with a characteristic finding in EGPA, reflecting the underlying Th2-driven eosinophilic and allergic immune response [13]. Given that ANCA-positive patients (strongly positive Anti-MPO>100 AU/mL in our patient) are more prone to vasculitic manifestations such as glomerulonephritis [2,14], renal involvement was carefully assessed, including 24-hour proteinuria measurement, along with multiple analyses of urine and serum urea, creatinine, and uric acid levels, all of which were within normal ranges. Durel et al. reported renal involvement in approximately 25–30% of EGPA patients [20]. Infectious screening for HIV and hepatitis viruses was performed prior to the initiating therapy, as rare associations between chronic viral infections and EGPA have been reported [21]. EMG and NCS confirmed chronic, moderately severe sensorimotor polyneuropathy, characterized by absent sural nerve responses and reduced motor amplitudes in all tested nerves except the left peroneal nerve, a pattern well described in EGPA-related neuropathy [2,14]. In addition to general recommendations, Liu and Srikhantharajah [3,24] highlighted cardiac involvement in EGPA, comprehensive echocardiographic evaluation was performed and showed no abnormalities. Pulmonary imaging revealed no evidence of interstitial lung disease typically seen in hypereosinophilic syndromes [22]. Radiographic evaluation of the paranasal sinuses demonstrated mucosal thickening with preserved sinus transparency, consistent with chronic sinusitis [23]. Histopathological description of tissue samples consisted of neutrophilic infiltrate with abundant eosinophils, vascular wall necrosis and vasculitis, as reported by several authors [24]. In our case, findings were consistent with active vasculitis. Given the absence of adverse prognostic factors (Five-Factor Score (FFS) = 0) and lack of life-threatening organ involvement, induction therapy was initiated with prednisone (1 mg/kg/day) combined with methotrexate (10 mg once weekly), with a planned increase to 12.5 mg weekly

depending on drug tolerability. According to EULAR recommendations, methotrexate is an appropriate option for remission maintenance following glucocorticoid-induced remission is in patients with EGPA [2,7]. Although glucocorticoid monotherapy induced remission in more than 90% of such patients, relapse during dose tapering is common [7], prompting many clinicians to combine glucocorticoids with additional immunosuppressive or biologic agents. While evidence supporting methotrexate or mycophenolate mofetil remains limited – owing to small observational studies and a lack of randomized control trails – methotrexate has demonstrated favorable outcomes in several small cohorts and is widely used as a steroid-sparing agent in non–severe EGPA [2,19]. In our patient, early glucocorticoid tapering was performed in accordance with EULAR [7] guidelines once clinical remission and biomarker improvement were achieved, minimizing long-term toxicity. Sustained remission, normalization of eosinophil counts, and persistent ANCA negativity supported complete glucocorticoid discontinuation, consistent with current guidelines advocating the lowest effective cumulative exposure [2,7,19]. Babapoor et al. indicate that approximately 72% of patients with ANCA-associated vasculitis achieving long-term remission following induction therapy, with nearly 38% remaining off all medications [25]. Remarkably, despite the patient's independent discontinuation of methotrexate due to intolerance, she remained in complete clinical and serological remission one year later.

Conclusion

Eosinophilic granulomatosis with polyangiitis is a rare systemic necrotizing vasculitis characterized by highly heterogeneous clinical manifestations. This four-year longitudinal follow-up demonstrates that the disease can be effectively controlled through early diagnosis and individualized treatment guided by disease severity and prognostic scoring. In the present case, induction therapy with high-dose glucocorticoids combined with methotrexate resulted in rapid disease control, normalization of eosinophil counts, resolution of organ-specific manifestations, and sustained clinical and serological remission. Careful tapering of glucocorticoids minimized cumulative exposure, while methotrexate served as an effective steroid-sparing agent. Medication-free remission was maintained even after methotrexate discontinuation, underscoring the potential for long-term disease control. These findings highlight the importance of early recognition, close monitoring, and guideline-driven, individualized therapy in optimizing long-term outcomes for patients with eosinophilic granulomatosis with polyangiitis.

References

1. Jakes RW, Kwon N, Huynh L, Hwee J, Baylis L, Alfonso-Cristancho R, et al. Burden of eosinophilic granulomatosis with polyangiitis in Europe. ERJ Open Res. 2024;10(4):00912-2023.

2. White J, Dubey S. Eosinophilic granulomatosis with polyangiitis: a review. Autoimmun Rev. 2023;22(1):103219.

3. Fagni F, Bello F, Emmi G. Eosinophilic granulomatosis with polyangiitis: dissecting the pathophysiology. Front Med (Lausanne). 2021;8:627776.

4. Berti A, Boukhlal S, Groh M, Cornec D. Eosinophilic granulomatosis with polyangiitis: the multifaceted spectrum of clinical manifestations at different stages of the disease. Expert Rev Clin Immunol. 2020;16(1):51-61.

5. Springer JM, Kalot MA, Husainat NM, Byram KW, Dua AB, James KE, et al. Eosinophilic granulomatosis with polyangiitis: a systematic review and meta-analysis of test accuracy and benefits and harms of common treatments. ACR Open Rheumatol. 2021; 3(2):101-10.

6. Dolin P, Lucas S, Gamble A, Turner M, Rowell J. Systematic literature review and meta-analysis of the epidemiology and clinical burden of eosinophilic granulomatosis with polyangiitis. Mod Rheumatol. 2025;35(4):697-706.

7. Hellmich B, Sanchez-Alamo B, Schirmer JH, Berti A, Blockmans D, Cid MC, et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. Ann Rheum Dis. 2024;83(1):30-47.

8. Martins-Martinho J, Pereira da Costa R, Abreu T, Ponte C. Successful combination therapy of mepolizumab and dupilumab in a patient with EGPA: a future therapeutic option? Rheumatol Adv Pract. 2024;8(3):rkae093.

9. Liu S, Han L, Li M, Tian X, Zeng X, Lu Y, et al. Sex differences in clinical manifestations of hospitalized patients with eosinophilic granulomatosis with polyangiitis: a retrospective cohort study. J Rheumatol. 2023;50(10):1318-25.

10. Hwee J, Harper L, Fu Q, Nirantharakumar K, Mu G, Jakes RW. Prevalence, incidence and healthcare burden of eosinophilic granulomatosis with polyangiitis in the UK. ERJ Open Res. 2024;10(3):00430-2023.

11. Trivioli G, Terrier B, Vaglio A. Eosinophilic granulomatosis with polyangiitis: understanding the disease and its management. Rheumatology (Oxford). 2020;59(Suppl 3):iii84-94.

12. Hagemann J, Laudien M, Becker S, Cuevas M, Klimek F, Kianfar R, et al. EGPA: eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) as a special presentation of chronic rhinosinusitis with nasal polyps (CRSwNP). Allergol Select. 2024;8(1):18-25.

13. Jakes RW, Kwon N, Nordstrom B, Goulding R, Fahrbach K, Tarpey J, et al. Burden of illness associated with eosinophilic granulomatosis with polyangiitis: a systematic literature review and meta-analysis. Clin Rheumatol. 2021;40(12):4829-36.

14. Koike H, Nishi R, Ohyama K, Morozumi S, Kawagashira Y, Furukawa S, et al. ANCA-associated vasculitic neuropathies: a review. Neurol Ther. 2022;11(1):21-38.

15. Solans-Laqué R, Rúa-Figueroa I, Blanco Aparicio M, García Moguel I, Blanco R, Pérez Grimaldi F, et al. Red flags for clinical suspicion of eosinophilic granulomatosis with polyangiitis (EGPA). Eur J Intern Med. 2024;128:45-52.

16. Matucci A, Vivarelli E, Perlato M, Mecheri V, Accinno M, Cosmi L, et al. EGPA phenotyping: not only ANCA, but also eosinophils. Biomedicines. 2023;11(3):776.

17. Kataoka H, Tomita T, Kondo M, Mukai M. Presence of purpura is related to active inflammation in association with IL-5 in eosinophilic granulomatosis with polyangiitis. Rheumatol Int. 2021;41(2):449-54.

18. Helbig G, Klion AD. Hypereosinophilic syndromes – an enigmatic group of disorders with an intriguing clinical spectrum and challenging treatment. Blood Rev. 2021;49:100809.

19. Fijolek J, Radzikowska E. Eosinophilic granulomatosis with polyangiitis – advances in pathogenesis, diagnosis, and treatment. Front Med (Lausanne). 2023;10:1145257.

20. Durel CA, Sinico RA, Teixeira V, Jayne D, Belenfant X, Marchand-Adam S, et al. Renal involvement in eosinophilic granulomatosis with polyangiitis (EGPA): a multicentric retrospective study of 63 biopsy-proven cases. Rheumatology (Oxford). 2021;60(1):359-65.

21. Osada SI, Kawana S, Saeki H. Non-asthmatic and HCV-seropositive eosinophilic granulomatosis with polyangiitis complicated by multiple intracerebral haemorrhages: a case study. Eur J Dermatol. 2019;29(1):85-7.

22. Nagorni-Obradovic L, Stevic R, Videnovic-Ivanov J, Vucinic-Mihailovic V, Pesut DP, Stjepanovic M. Interstitial lung diseases in women. Med Pregl. 2013;66(Suppl 1):113-7.

23. D'Onofrio M, La Prova D, Galdiero MR, Cantone E, Tremante E, Mascolo M, et al. Early ear, nose and throat manifestations in eosinophilic granulomatosis with poliangioitis: results from our cohort group and literature review. J Clin Med. 2023;12 (22):6967.

24. Micheletti RG, Chiesa Fuxench Z, Craven A, Watts RA, Luqmani RA, Merkel PA, et al. Cutaneous manifestations of antineutrophil cytoplasmic antibody–associated vasculitis. Arthritis Rheumatol. 2020;72(10):1741-7.

25. Babapoor P, Hajialilo M, Rahimi M, Esalatmanesh K, Rahmanpour D, Barahimi A, et al. Predictors of medications-free and long-term remission in anti-neutrophil cytoplasmic antibody-associated vasculitis: real-world evidence. Sarcoidosis Vasc Diffuse Lung Dis. 2024;41(1):e2024011.

Rad je primljen 3. XII 2025.
Recenziran 5. XII 2025.
Prihvaćen za štampu 7. XII 2025.
BIBLID.0025-8105:(2025):LXXVIII:5-8:198-204.