

Unmasking Eosinophilic Granulomatosis with Polyangiitis: A Case of Rapid-Onset Myositis Following COVID-19 Booster in an Eosinophilic Asthma Patient*

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Abstract

Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare Anti-neutrophil cytoplasm antibodies (ANCA)-associated vasculitis with multi-organ involvement and eosinophilia. We present a 61-year-old male with a history of eosinophilic asthma who developed progressive weakness and muscle aches six weeks after his second COVID-19 booster. Four to six weeks post vaccination, he developed myalgias and weakness, especially in proximal muscles, leading to a severe decline in function. Lab results showed leukocytosis (29.54 cells/mm³); 54% eosinophils; and elevated erythrocyte sedimentation rate (ESR), C-reactive protein, and creatine kinase levels at 13 736 u/L. Anti-myeloperoxidase antibodies were positive, while PR-3, C-ANCA, and P-ANCA were negative. Magnetic resonance imaging of the lower extremities showed intramuscular edema. Muscle biopsies confirmed EGPA. Diagnosed per American College of Rheumatology (ACR)/ European Alliance of Associations for Rheumatology (EULAR) criteria, he received pulse dose IV methylprednisolone with significant improvement. He was discharged on 60 mg prednisone and started on mepolizumab (300 mg subcutaneous once every 4 weeks). Eosinophilic granulomatosis with polyangiitis progresses through stages: asthma, eosinophilia with organ involvement, and vasculitis. This case highlights a unique presentation of rapid myositis without significant involvement of any other organs and vasculitis post-mRNA vaccination. While environmental factors may trigger EGPA, the role of COVID-19 vaccines remains hypothesis-generating. This case underscores the importance of post-market surveillance for rare events, contributing to the understanding of vaccine-related rheumatic disease triggers.

Keywords: ANCA vasculitis, atypical EGPA, EGPA, EGPA-associated myositis

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Introduction

1. Background-EGPA is an ANCA-associated small vessel vasculitis with multi-organ system involvement and eosinophilia.
2. Rationale and knowledge gap-Numerous reports of immune-related diseases were reported post-COVID vaccination, among these, vasculitis is one of the less commonly reported groups with involvement varying between small and large vessel vasculitis.¹ The validity of the association between the vaccination and the disease onset is still up for speculation, but here a case of new onset EGPA after a second COVID booster is presented.
3. Objective-This report aims to encourage/evoke more discussion regarding potential rare triggers like medication and vaccination.

This manuscript is written following CARE Case Report Guidelines Checklist.

Case Presentation

A 61-year-old male with a history of eosinophilic asthma presented to the office for progressive weakness and diffuse muscle aches in early January 2024. Other significant past medical history included non-obstructive coronary artery disease, hyperlipidemia, GERD, and obesity. Before this, on November 2, 2023, he took his second booster COVID vaccination (Pfizer-BioNTech, previous vaccinations as well). He tolerated his first two doses and the booster of the COVID vaccination well. His asthma symptoms began worsening two weeks later. His asthma improved; however, a month later, he developed severe muscle aches in proximal muscle groups, mainly involving the neck, bilateral shoulders, hips, biceps, and thighs, with progression over three weeks. He also complained of jaw claudication and left orbital pain. The pain was

achy in nature and worse with immobility, with some improvement on movement. No relief with pain medications. He denied weight loss, night sweats, or fevers. On further evaluation, labs revealed leukocytosis 29 800/uL, with significant eosinophilia (54% absolute count), C-reactive protein >19 mg/dL, and erythrocyte sedimentation rate 55 mm/hr. Creatinine kinase levels were elevated to 13,736 U/l. Due to this, he was admitted to the hospital for further workup.

On examination, vitals were stable, the patient appeared to be in mild distress due to pain, and the musculoskeletal exam was significant for tenderness to palpation over proximal muscle groups bilaterally, upper and lower extremities, without any joint swelling, rashes, scalp tenderness, or enlarged vessels. Antinuclear antibody testing and rheumatoid factor were negative. A comprehensive metabolic panel showed mild elevation in transaminases with elevated alkaline phosphatase. Anti-nuclear Antibody (ANA) was negative. His anti-myeloperoxidase (MPO) Abs > 8 (Elevated, normal 0-0.9), negative proteinase 3 Ab, cytoplasmic antineutrophil antibody, and perinuclear antineutrophil antibody.

The differential diagnoses included myeloproliferative neoplasms causing hypereosinophilic syndrome, tissue hypereosinophilia, EGPA, and eosinophilic myositis. Eosinophilic fasciitis was least on the differential as the patient did not have any evidence of fasciitis on exam. Oncology was consulted for any possible underlying myeloproliferative neoplasm causing hyper eosinophilia. They decided to wait for

Main Points

- The case reports shed light on a possible trigger with the mRNA COVID-19 vaccine in a patient who presents with a unique presentation of eosinophilic granulomatosis with polyangiitis (EGPA) vasculitis, reporting such events helps in post-market surveillance of vaccines.
- It is a unique presentation of EGPA vasculitis with primarily only muscle involvement, without involvement of other organ systems like peripheral nerves, respiratory, or Gastrointestinal tract.
- The patient was also followed for twelve months since discharge to look for involvement of other organ systems, however, both his EGPA vasculitis with myositis and eosinophilic asthma have been well controlled currently on mepolizumab only.



Figure 1. (A and B) Magnetic resonance imaging showing diffuse patchy intramuscular edema and enhancement throughout the anterior and posterior compartment thigh musculature (Coronal (a) and Sagittal (b) sections).

an MRI of the abdomen and lower extremities and a muscle biopsy as scheduled before proceeding with a bone marrow biopsy. Magnetic resonance imaging of the lower extremities revealed diffuse patchy intramuscular edema and enhancement throughout the anterior and posterior compartments of thigh musculature bilaterally, as shown in the images (Figures 1 and

2). Left deltoid and quadricep muscle biopsy was consistent with necrotizing vasculitis with granulomas containing eosinophils (Figures 3 and 4). Temporal artery biopsy was performed due to complaints of jaw claudication and left orbital pain, but was without evidence of active vasculitis. His chest radiography was normal, and radiographs of sinuses were not obtained.

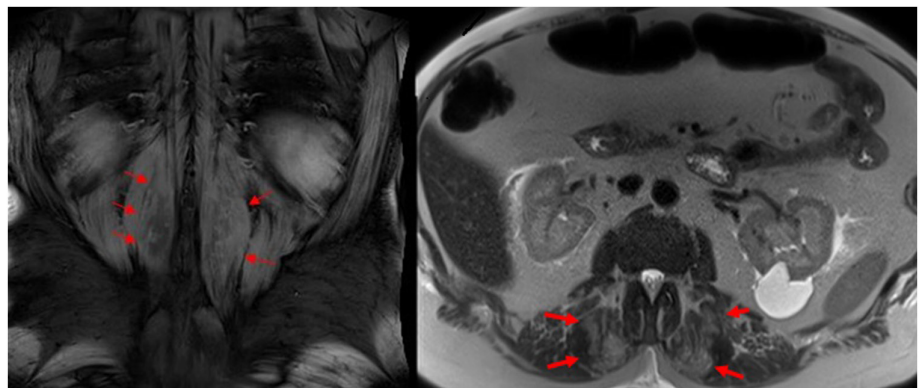


Figure 2. (A and B) Magnetic resonance imaging showing edema in the bilateral erector spinae musculature (axial and coronal sections).

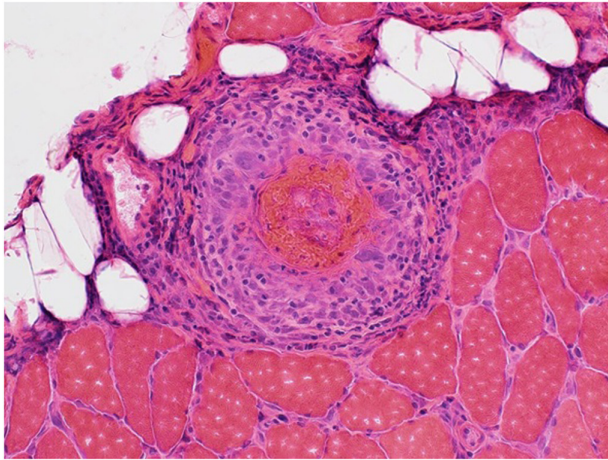


Figure 3. Hematoxylin and eosin-stained sections showing presence of a single arteriole showing several surrounding lymphocytes and eosinophils and a multinucleate histiocyte.

He was diagnosed with EGPA based on ACR/EULAR 2022 diagnostic criteria with long-standing asthma (+3 points), eosinophilia >10% (+5 points), and biopsy findings of vasculitis with associated myonecrosis (+2 points).² With consistent biopsy findings and meeting diagnostic criteria for EGPA, further testing with bone marrow biopsy was not pursued.

The patient was started on IV methylprednisolone 500 mg on day 1, then 250 mg/day on days 2 and 3. He has significant improvement in symptoms and an improvement in eosinophilia to 16% along with a down-trending CK to 4081U/l. As there is no involvement of CNS, GI, pulmonary, or renal systems, it was classified as non-severe EGPA. Therefore, steroids were tapered down to 60 mg prednisone once daily on discharge.

Follow Up

About 60 mg of prednisone was continued till he received his first dose of mepolizumab

150 mg/month, 10 days after hospital discharge. Prednisone was tapered starting from 60 mg to 40 mg after 2 weeks. This was further tapered to 32 mg and 16 mg of methylprednisolone in the next month. Mepolizumab dose was increased to 300 mg/month as the patient continued to experience myalgias on prednisone taper. While being on an increased dose of mepolizumab, his dose of methylprednisolone was decreased to 12 mg for 3 weeks, followed by 8 mg for the next 3 weeks and 4 mg for the next 3 weeks. After that, he continued on mepolizumab and was taken off steroids. He has been followed in the clinic for the last 12 months after his discharge. His symptoms of myositis associated with EGPA have not recurred, outpatient Creatine Kinase levels have been within normal limits, and associated symptoms of eosinophilic asthma and chronic rhinosinusitis have also significantly improved. Informed consent was obtained from the patient before writing this manuscript.

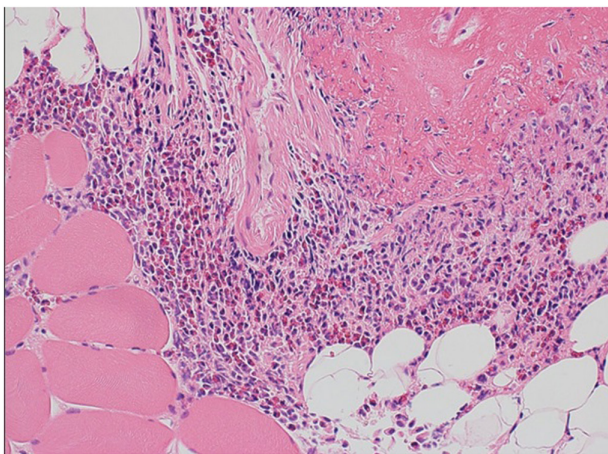


Figure 4. Several small arterioles within the perimysium show mild to moderate surrounding chronic lymphoid inflammation, infiltrating lymphocytes and macrophages within the vascular wall, and patchy fibrinoid necrosis.

Discussion

Eosinophilic granulomatosis with polyangiitis, previously known as Churg-Strauss, is a subtype of ANCA-associated vasculitis characterized by necrotizing granulomatous vasculitis of the small and medium vessel arteries. Patients classically present with long-standing asthma and peripheral eosinophilia, and 30%-40% of patients have p-ANCA positivity.³ The mean age of diagnosis is 50 years, with equal distribution between both genders.⁴

Eosinophilic granulomatosis with polyangiitis is postulated to progress through 3 stages. Initially, an allergic prodromal phase with chronic sinusitis and asthma, which lasts for months to years, followed by an eosinophilic phase with peripheral eosinophilia and initiation of multi-organ involvement, usually involving the lung, GI tract, and cardiac tissues. The last is the vasculitis phase, which is sometimes associated with paradoxical improvement of asthma and usually presents with constitutional symptoms associated with peripheral neuropathy, usually presenting as mononeuritis multiplex, renal, and skin involvement.^{5,6} This is where the patient has a unique presentation; he had long-standing asthma followed by a likely trigger of the mRNA vaccine and a rapid presentation of EGPA vasculitis with mainly myositis component without significant involvement of lung, neural, cardiac, renal, or skin.

A PubMed search with keywords "EGPA" AND "COVID-19 vaccine" resulted in 7 searches, out of which 4 case reports were of new onset of EGPA after COVID mRNA vaccines (Table 1).

For this patient, an initial pulse dose of steroids was used with a taper, and mepolizumab was tried to maintain remission. Mepolizumab is a targeted monoclonal antibody against IL-5. It was initially used for severe eosinophilic asthma, but later the MIRRA (Mepolizumab in Relapsing or Refractory EGPA) trial revealed the benefits for EGPA patients.¹¹ Most of the case reports mentioned above have adequate clinical response, except the case report of Mahdi et al,⁹ where neural involvement was difficult to treat and required multiple trials of treatment.

Different environmental factors can trigger EGPA such as medications, infections, allergens, and vaccines. The development of EGPA primarily involves Th2 activation, followed by Th1 and Th17 activation, and a reduced Treg response. As the disease advances, B-cell participation leads to the production of MPO antibodies and positivity for p-ANCA.⁶ COVID m-RNA vaccine encodes for the spike protein

Table 1. Four cases of new-onset EGPA after COVID-19 vaccine that we could find on PubMed.

Case Report	Age of the Patient and Gender	Onset of Symptoms After Vaccination	Organ Systems Involved	Treatment
Nappi E et al ⁷	63, Male	Received ChAdOx1 anti-SARS-CoV-2 vaccine 6 months prior and then presented 1 day after booster dose of anti-SARS-CoV-2 vaccine	Cardiac, neurological, and pulmonary	Pulse dose steroids followed by cyclophosphamide
Ibrahim et al ⁸	79, female	Thirty-five to 45 days after second dose of mRNA-1273 (Moderna)	Lung, skin, and neural	Prednisone 60 mg followed by azathioprine
Mahdi et al ⁹	53, Male	Ten days after first booster of Pfizer-BioNTech mRNA	Neural, renal, and skin	Pulse dose steroids, rituximab trial followed by trial of cyclophosphamide and intravenous immunoglobulin
Hwang et al ¹⁰	71, female	Two days after first dose of Pfizer-BioNTech mRNA	Neural and skin	Pulse dose steroids and cyclophosphamide

(S2-P), which is then produced by the host cells, leading to the development of both T and B-cell responses.¹²

The potential for the influenza vaccine to induce vasculitis, including large, medium, and small vessel vasculitis, has been investigated.¹³ Machado et al¹⁴ studied the vaccine registry of COVID-19 vaccines in rheumatological diseases; the results were largely positive, with very few rare adverse effects.¹⁴ Given the infrequency of EGPA and the recent introduction of mRNA vaccines for COVID-19, there is a pressing need for increased reporting of such clinical occurrences. This would not only spur further research but also aid in the development of clinical guidelines for individuals predisposed to rheumatological diseases. Given that individuals with rheumatic diseases were initially excluded from vaccine development trials, case reports play a crucial role in post-market surveillance within these patient populations.¹⁵ The biological plausibility of cross-reactivity or rapid activation of immune cells with B-cell and T-cell response and the temporal relationship between new mRNA vaccines and the rapid onset of EGPA is hypothesis-generating but does not establish causality.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Informed Consent: Verbal informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.M., V.B., J.N.; Design – A.M., J.N.; Supervision – A.F., J.N.; Resources – A.F., J.N.; Materials – A.F., J.N.; Data Collection and/or Processing – A.M., V.B., S.A.; Analysis and/or Interpretation – A.M., S.A.; Literature Search – A.M., V.B.; Writing Manuscript – A.M., V.B., S.A.; Critical Review – J.N., A.F.

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