

CLINICAL VIGNETTE

Cerebrovascular Accident and Venous Thromboembolism in a Patient with Granulomatosis with Polyangiitis

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An 84-year-old female with history chronic hypoxemic respiratory failure and bronchiectasis presented to the emergency department (ED) with gross hematuria that started suddenly that day. She was recently discharged from hospital one week prior. She was hospitalized with *campylobacter* induced gastroenteritis, acute kidney injury and a right posterior tibial and popliteal deep vein thrombosis (DVT) and was discharged on apixaban. Her apixaban regimen was 10 milligrams (mg) twice daily for seven days followed by five mg every 12 hours. She denied fever, hemoptysis, flank pain or dysuria. She reported slight worsening of her chronic cough and increased chest congestion. Vital signs were unremarkable, her physical exam did not reveal any significant abnormalities. Initial laboratory findings, white blood cell count (WBC) of 9200 /uL, Hb 10.3 g/dL, Platelets 540,000 /uL, sodium (Na) 132 mmol/L, potassium (K) 5.4 mmol/L, creatinine 4.62 mg/dL, lactic acid of 1.6 mmol/L. Her prior baseline serum creatinine was 1.43 mg/dL. She had turbid urine with 3+ blood, 1+ protein, 500 leukocytes/uL, no bacteria or nitrites, and no casts. Computed Tomography scan (CT) of her abdomen and pelvis ruled out an obstructive uropathy. CT chest showed small areas of ground glass and airspace opacification in right and left upper lobes when compared to her recent CT chest. Apixaban was held on admission and a foley catheter was placed in the ED. Immunologic studies included showed positive Anti-nuclear antibodies (ANA) and cytoplasmic Anti Neutrophil Chemotactic Antibody (ANCA) titer of 1:160. After admission she continued to have hematuria and worsening renal function. Renal biopsy revealed extensive necrotizing and crescentic glomerulonephritis with focal necrotizing arteritis/arteriolitis, consistent with granulomatosis with polyangiitis (GPA).

On hospital day 6, she suddenly became unresponsive to verbal or tactile stimuli. Stroke code was activated, and brain CT angiography revealed markedly decreased enhancement of the distal vertebral arteries and basilar artery with intraluminal thrombi in the distal basilar artery, P1 segments bilaterally. CT brain perfusion studies showed a large area of abnormal perfusion involving the brainstem and bilateral cerebellar hemispheres. Emergent mechanical thrombectomy was performed with complete recanalization of the basilar artery and P1 segments. Despite recanalization, residual clot remained in the distal left P2/P3 segments that were unable to be retrieved. Post-thrombectomy MRI brain revealed left occipital lobe and bilateral thalamic ischemia. Echocardiogram revealed a patent foramen ovale and lower extremity venous doppler ultrasound showed right deep vein thrombosis. Heparin infusion was started, and she was also started on Infliximab infusion for GPA treatment. Hematuria resolved a few days later and she was transitioned to back to oral apixaban. She continues to have a slow neurological recovery.

Discussion

ANCA-associated vasculitis (AAV) is a rare group of auto-immune diseases that affect small to medium sized vessels. These include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EPGA) and pauci-immune vasculitis. The characteristic feature of the disease is presence of circulating autoantibodies to the neutrophil protein's leukocyte proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA).¹ GPA has high mortality and morbidity and can lead to stroke and myocardial infarction. GPA patients have two-to-four-fold

higher risk of venous thromboembolism compared to the general population.²

GPA is a systemic inflammatory disease histologically characterized by the presence of granulomas, necrosis, and vasculitis. It usually affects medium sized vessels which includes upper and lower respiratory tract and kidneys (as in this case), but any other organ can be involved. Patients usually present with fever, chills, hematuria, or sinusitis.² Patients with GPA have a significant increased risk of myocardial infarction and ischemic stroke compared to the general population. The retrospective review of medical records of 125 patients at Toulouse University Hospital from 1981-2015, ischemic reported stroke as one of the main complications of AAV.³ Venous thromboembolism (VTE) was another significant contributor to morbidity and mortality in GPA patients. A Canadian matched cohort study by Marozoff et al compared patients with GPA to the general population and reported that GPA patients are two-fold more likely to develop deep venous thrombosis and four-fold more likely to develop pulmonary embolism. Although, the pathogenesis is not completely understood, it is hypothesized that systemic inflammation upregulates procoagulants, downregulates anticoagulants and inhibits fibrinolysis which leads to endothelial dysfunction and venous thromboembolism formation.⁴

Our patient suffered an ischemic stroke. It is possible that the right lower extremity deep venous thrombus (DVT) might have traversed the PFO and caused the posterior circulation infarct. However, it is important to realize that GPA creates a hypercoagulable state that increases risk of stroke and poor outcomes.⁵

Patients with GPA have a significantly increased risk of VTE, myocardial infarction and ischemic stroke. Monitoring for these complication and vigilance in modifying risk factors are particularly important in this patient population, especially early after GPA diagnosis.

REFERENCES

1. **Fauci AS, Haynes BF, Katz P, Wolff SM.** Wegener's granulomatosis: prospective clinical

and therapeutic experience with 85 patients for 21 years. *Ann Intern Med.* 1983 Jan;98(1):76-85. doi: 10.7326/0003-4819-98-1-76. PMID: 6336643.

2. **Englund M, Merkel PA, Tomasson G, Segelmark M, Mohammad AJ.** Comorbidities in Patients with Antineutrophil Cytoplasmic Antibody-associated Vasculitis versus the General Population. *J Rheumatol.* 2016 Aug;43(8):1553-8. doi: 10.3899/jrheum.151151. Epub 2016 Jun 1. PMID: 27252425.
3. **Mourguet M, Chauveau D, Faguer S, Ruidavets JB, Béjot Y, Ribes D, Huart A, Alric L, Balardy L, Astudillo L, Adoue D, Sailer L, Pugnet G.** Increased ischemic stroke, acute coronary artery disease and mortality in patients with granulomatosis with polyangiitis and microscopic polyangiitis. *J Autoimmun.* 2019 Jan;96:134-141. doi: 10.1016/j.jaut.2018.09.004. Epub 2018 Sep 17. PMID: 30236485.
4. **Marozoff S, Mai A, Dehghan N, Sayre EC, Choi HK, Aviña-Zubieta JA.** Increased risk of venous thromboembolism in patients with granulomatosis with polyangiitis: A population-based study. *PLoS One.* 2022 Jun 17;17(6):e0270142. doi: 10.1371/journal.pone.0270142. PMID: 35714116; PMCID: PMC9205510.
5. **Trieste L, Palla I, Baldini C, Talarico R, D'Angiolella L, Mosca M, Turchetti G.** Systemic vasculitis: how little we know about their societal and economic burden. *Clin Exp Rheumatol.* 2012 Jul-Aug;30(4 Suppl 73):S154-6. Epub 2012 Oct 16. PMID: 23072925.