A Severe Case of ANCA-Associated Small Vessel Vasculitis

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A 31-year-old male with a past medical history of asthma, a recent tooth abscess, and an enlarging scalp wound that grew MSSA and didn’t improve with debridement or antibiotics presented with a two-week history of fevers, arthralgias, scant hemoptysis, abdominal pain and a new purpuric rash and associated fingertip discoloration.

Vital signs at triage were significant for a new oxygen requirement of 4 liters. Physical examination was notable for a deep ulcerated scalp lesion [Figure 1A], bilateral non-painful scleral injection, numerous small palpable purpuras on the lateral thighs [Figure 1B], and splinter hemorrhages of the fingernails.

The initial laboratory workup is noted in Table 1. CT of the chest showed multiple bilateral pulmonary parenchymal nodules and worsening airspace opacities, some with central cavitation [Figure 2]. Interferon-gamma release assay for tuberculosis was indeterminate; however, three sputum stains for acid-fast bacilli were negative, and blood cultures yielded no growth. A transthoracic echocardiogram revealed normal left ventricular function without evidence of valve disease or vegetation. The patient declined to have a transesophageal echocardiogram (TTE). His condition failed to improve despite empiric treatment with broad-spectrum antibiotics.

Additional laboratory workup revealed a positive anti-proteinase 3 (PR3) antibody index at 7.1 AI. Immunofluorescence testing for classic anti-neutrophil cytoplasmic antibodies (c-ANCA) was positive. Rheumatoid factor was also elevated at 99 U/mL. The anti-myeloperoxidase (MPO) antibody index was negative, as was the anti-glomerular basement membrane antibody index. CT of the abdomen and pelvis showed splenic infarct and bilateral wedge-shaped kidney hypodensities concerning for renal infarcts [Figure 3]. A skin biopsy was obtained from the thigh rash, and the final pathology showed exuberant leukocytoclastic vasculitis involving post-capillary venules and medium-sized arteries. Although granulomas were not conspicuous, the findings were consistent with ANCA-associated vasculitis.

Table 1. Initial laboratory workup

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Reference Range</th>
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<tbody>
<tr>
<td>Hemoglobin</td>
<td>8.8 (L)</td>
<td>13.4–16.0 g/dL</td>
</tr>
<tr>
<td>Platelet count</td>
<td>562 (H)</td>
<td>168–382 x10^9/L</td>
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<tr>
<td>White blood cell count</td>
<td>12.3 (H)</td>
<td>4.2–10.0 x10^9/L</td>
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<tr>
<td>Absolute eosinophil count</td>
<td>0</td>
<td>0.0–0.4 x10^9/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.59 (L)</td>
<td>0.64–1.27 mg/dL</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>18 RBC/HPF, Protein: 30 mg/dL (H)</td>
<td>RBC: 0-3/HPF, Protein: &lt;10 mg/dL</td>
</tr>
<tr>
<td>ESR</td>
<td>120 (H)</td>
<td>&lt;15 mm/hr</td>
</tr>
<tr>
<td>CRP</td>
<td>309 (H)</td>
<td>0.00–10.00 mg/L</td>
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*Lab values reveal leukocytosis, anemia, sub-nephrotic proteinuria, hematuria, elevated inflammatory markers, and normal eosinophil count. L=low, H=high.
A diagnosis of granulomatosis with polyangiitis (GPA) was made. Pulse-dose intravenous methylprednisolone was administered, with clinical improvement in respiratory symptoms, scleral redness, and pain. Despite treatment, the upper extremity digits developed progressive skin changes concerning for dry gangrene. Antiphospholipid antibody testing was negative. Several days later, a repeat CT of the abdomen and pelvis was obtained due to a significant hemoglobin drop and abdominal pain, which demonstrated a right renal hematoma with retroperitoneal bleed [Figure 4]. Surgical intervention was deferred in the absence of an acute abdomen and hemodynamic stability. The patient was continued on intravenous methylprednisolone and received induction therapy with 1g of rituximab.

**DISCUSSION**

GPA is a rare disorder classified as small vessel vasculitis that affects the upper and lower respiratory tracts and kidneys and is associated with positive PR3-ANCA. Clinical features often consistent with GPA include arthralgias, petechiae and purpura, splinter hemorrhages, hemorrhagic macules, episcleritis and scleritis, sinusitis, glomerulonephritis, pulmonary fibrosis, pulmonary hemorrhages, and otitis media.1

This is an interesting case because of the significant clotting burden without the classic features we would suspect in severe disease like glomerulonephritis or diffuse alveolar hemorrhage. In recent years, there has been more evidence supporting an increased frequency of thrombosis in ANCA-associated vasculitis, including DVT, PE, and myocardial infarction; however, renal and splenic infarcts are rare and often underdiagnosed, ulcerated lesions are only seen in 9.5% to 35.3% of affected individuals.2-4

With the patient’s poor dentition and recent history of a tooth abscess combined with the appearance of embolic phenomena, we considered infective endocarditis, which can present as GPA5 and positive rheumatoid factor.6 Given his recurrent negative blood cultures, normal TTEs, and failure to improve with antibiotics, it was less likely.

Therapy for GPA is often initiated with combined corticosteroids and cyclophosphamide for remission induction; however, studies show that combination with rituximab is non-inferior to cyclophosphamide in severe cases of ANCA vasculitis and may be superior in relapsing disease.7-9 Many clinicians have transitioned to using rituximab in combination with corticosteroids for remission induction to reduce the risks of infertility, bone marrow toxicity, and secondary malignancy predominantly seen in cyclophosphamide use.8

Once remission induction is achieved, therapies for maintenance therapy are variable but include transition to rituximab, mycophenolate, methotrexate, or azathioprine. The MAINRITSAN trial demonstrated that rituximab is more effective at sustaining remission than azathioprine and methotrexate.10 The duration of therapy is widely dependent on the likelihood of relapse. Notably, individuals with positive PR-3 antibodies have higher rates of relapse.11

**References**


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Disclosures
We confirm that there are no conflicts of interest or disclosures to report for all authors of this study.

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