A Case of Granulomatosis with Polyangiitis

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Introduction

Granulomatosis with Polyangiitis is a necrotizing, granulomatous, ANCA-associated vasculitis typically characterized by the presence of nasopharyngeal involvement, pulmonary pathology, and rapidly progressing, often crescentic, glomerulonephritis, though the presentation varies.

A 53 year-old gentleman with no notable past medical history presented with two months of self-described sinusitis and lower extremity joint pain with no family history of autoimmune disease.

Objective

A 53 year-old man presented with complaints of conjunctivitis, fever, and lower extremity joint swelling worsening in the past two months. The conjunctivitis was bilateral and without exudate, and his fever waxed and waned but was unresponsive to Tylenol or NSAIDS. He denied any kind of joint trauma, or known infections. He reported having been diagnosed with a viral conjunctivitis and being given tobramycin as well as dexamethasone eye drops. The conjunctival injection and pain abated with the eyedrops but returned upon their discontinuation. Further investigation revealed the patient had been having clear sinus discharge during this time. He denied any hemoptysis but admitted to a minimally-productive cough with clear sputum coinciding with his nasal discharge.

On admission he was hypertensive at 155/107 mmHg, tachycardic at 136 beats per minute, but had otherwise no significant findings.

His physical exam recealed bilateral conjunctival injection without exudate. No nasal polyps were appreciated. He had no tonsillar enlargement or exudate and no obvious mucosal lesions. There was no appreciated lymphadenopathy. Examination of the lungs revealed bilateral basilar crackles. There was minimal lower extremity pitting edema and he ha bilateral petechiae on his calves. The patients strength and range of motion was preserved in all his extremities.

His creatinine was Creatinine 1.35mg/dL. Urinalysis showed blood, with 25-50 RBC per Gigh-Powered Field, 30mg/dL of protein, and 6-10 WBC per HPF. Quantitative D-Dimer was 6.28 mg/L.

He had an unrevealing chest x-ray, but his CTA of the chest showed and 8cm vertical mass beginning at the medial right lower lobe at the azygos esophageal recess.

With the his abnormal finding on imaging and complaints of productive cough, pulmonology and nephrology were consulted. The images were reviewed and it was determined that the findings were more consistent with an infiltrate than a mass .

Given that his workup and symptoms were consistent with kidney, lung, and sinus involvement, a rheumatological workup was recommended due to a high suspicion of vasculitis.

Rheumatology ordered ANCA, ANA, Rheumatoid Factor, and Anti-CCP tests, as well as a repeat urinalysis, and started the patient on 0.5 mg/kg of prednisone, which the patient stated improved his musculoskeletal symptoms. The repeat urinalysis showed Blood, with over 100 RBC, 30mg/dL of protein, and 6-10 WBC per HPF with the random total protein being 36 mg/dL, and random creatinine of 81.0 mg/dL. The Immunological tests returned a positive titer of 1:320 for c-ANCA, and a renal bisopsy was scheduled. The patient's prednisone was increased to 1mg/kg. The patient's symptoms resolved, and he was sent out for an outpatient rheumatology follow-up to begin induction therapy for Granulomatosis with Polyangiitis.

Discussion

- Epidemiology
- A British longitudinal study between 1988 to 2010 identified the incidence of GPA as being between 7.6 to 18.3 cases per million1. It has been noted that Northern European populations have a higher risk than others2.
- Pathophysiology
- GPA is a necrotizing granulomatous disease thought to be mediated by Anti Neutrophil Cytoplasmic Antibodies with specificity to proteinase 3, a protein involved in the proteolytic generation of antimicrobial peptides3. ANCA are thought to be directly involved in the widespread tissue damage that is the hallmark of this condition, as these antibodies attack small vessels, causing vasculitis4. Given the frequency with which the first symptoms of GPA occur in the respiratory tract, exposure to noninfectious agents or toxins via an inhalational route is a likely inciting event5. Silicates and cigarette smoke, among others, have been proposed as possible sources, but the exact mechanism is still unknown6. B and T cell dysfunction have been shown to play a major part in the pathogenesis as well, with the number of B cells shown to correlate with disease activity7.
- Diagnosis
- The 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides (CHCC2012) Criteria offers a diagnostic standardization, but does not stratify severity of the diagnosis. The diagnosis centers on findings of a Necrotizing vasculitis, with few or no immune deposits, affecting predominantly small vessels.
- It is associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA8. A common triad is nasopharyngeal, pulmonary, and renal involvement. Anyone suspected of having any ANCA-vasculitis should have a biopsy done for confirmation. Stratifying ANCA-positive serology as MPO or PR3 positive, as well the clinical manifestations as above, help differentiate GPA from other ANCA vasculitides9
- Treatment
- Treatment is divided into induction and maintenance therapy, with a further division possible based on the presence of life-threatening symptoms. In the case of the latter, glucocorticoids(1 mg/kg per day tapered over four to six months) with either rituximab (375 mg/m2 per week for four weeks) or cyclophosphamide (5 mg/kg every two weeks for three doses and then every three weeks for three to six months) are begun as an induction therapy10,11.
- When symptoms have resolved, rituximab is the preferred choice for maintenance therapy with alternatives including methotrexate, mycophenolate, and azathioprine depending on the individual patient's comorbitidities12. Treatment is a medical emergency, especially in the setting of rapidly-progressing glomerulonephritis.

Conclusion

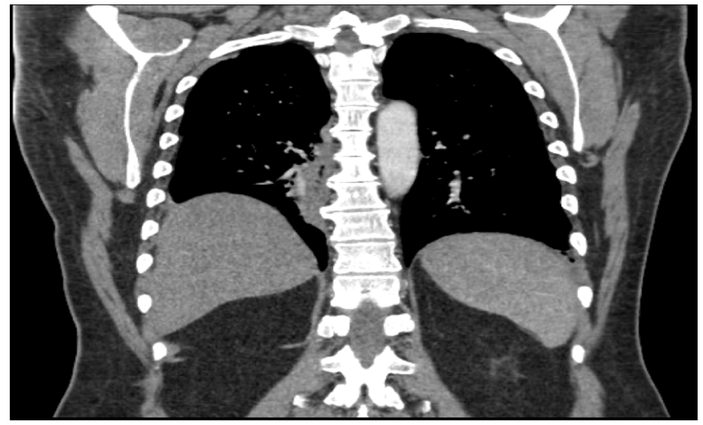

Figure 1. 8 cm mass seen on coronal CTA

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