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CASE REPORT

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A unique presentation of a rare disease: biopsy proven systemic lupus erythematosus and microscopic polyangitis: an overlap syndrome

Diana Meyler, Abilio Arrascaeta-Llanes, Ravi Gupta and Sanjay Godhwani

Department of Internal Medicine, Long Island Community Hospital, Patchogue, NY, USA

ABSTRACT

Systemic Lupus Erythematosus (SLE) and ANCA-associated vasculitis are classically thought to be separate diseases with different pathophysiologies. An overlap of these diseases has been reported few times in the literature. We present a unique case of a Caucasian male in his third decade of life, without a previous personal or family history of autoimmune disease, with serological and biopsy findings of both diseases occurring simultaneously. ANCA, typically p-ANCA, can be detected in up to 30% of SLE patients and can be higher with renal involvement. Patients with overlap syndrome have increased complications and higher mortality rates than those with either disease alone. Our patient was found to have necrotizing and crescentic glomerulonephritis, most consistent with ANCA vasculitis, specifically microscopic polyangitis with MPO positive staining. The biopsy also revealed abundant immune-complex deposits consistent with WHO class V diffuse membranous lupus glomerulonephritis. These diseases are typically seen in young to middle aged females, and given the rarity of this case, biopsy findings were confirmed by two pathologists from separate institutions. Presentations of autoimmune diseases and vasculitis can be multi-systemic. Immediate action and appropriate work up with a multidisciplinary team is required for optimal patient care. Our patient displayed pulmonary-renal involvement in addition to systemic features such as fevers, myalgia and profound anemia. Considering overlap syndromes, especially in patients with underlying connective tissue disease or systemic vasculitis, is vital for the prevention of excess morbidity in this population.

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Systemic lupus erythematosus; microscopic polyangitis; overlap syndrome

1. Introduction

Systemic Lupus Erythematosus (SLE) and ANCA-associated vasculitis are classically thought to be separate diseases with different pathophysiologies. While both affect the kidneys, SLE leads to an immune complex glomerulonephritis, while ANCA vasculitis causes glomerular necrosis in the absence of immune complex deposition. The presence of both diseases simultaneously has been described in the literature only a handful of times, leading to the possibility of the existence of an overlap syndrome.

2. Case presentation

We present a 26 year old male with no past medical history who reported to the ED with a 3 day history of progressively worsening shortness of breath, hemoptysis, generalized weakness, fever and increasing lower extremity edema. Of note, the patient was discharged from our facility 8 days prior with a diagnosis of pneumonia. Vitals were significant for a fever of 103.3F, tachycardia to 150 beats per minute, blood pressure of 129/53, respiratory rate of 22, and an oxygen saturation of 87% on room air. Upon further questioning, the patient admitted to having intermittent hemoptysis without hematuria, hematochezia, melena or flank pain for the past 6 months. On physical exam, the patient was found to have moderate wheezing and rhonchi in bilateral full lung fields, moderate respiratory distress with use of accessory muscles and 2+ pitting pedal edema extending to the knees. He was alert and oriented to person, place and time and did not have any rashes or skin lesions. His extremities were acyanotic and without clubbing.

Initial blood work revealed anemia with hemoglobin of 6.4 g/dL, acute renal failure with a creatinine of 3 mg/dL (normal previous baseline) and lactic acidosis of 2.8. Urinalysis revealed proteinuria with large blood (50–100 RBC) without bacteria. ABG on admission revealed compensated metabolic acidosis with HCO3 (16), CO2 (22) and a pH (7.47). The patient was admitted to the ICU for acute hypoxemic respiratory failure requiring BiPAP due to vasculitis associated alveolar hemorrhage. Subsequent blood work revealed elevated ESR (83), low C4 (11), borderline low C3 (82), positive p-ANCA (1:160), MPO (22.2), double stranded DNA antibody (62), ANA (1:640). Anti-glomerular basement antibody (anti-GBM), Rheumatoid factor (RF), HIV, Hepatitis A,B,

CONTACT Diana Meyler mdianka@gmail.com Department of Internal Medicine, Long Island Community Hospital

and C and PR-3 were negative. CT chest revealed small bilateral pleural effusions and bibasilar ground-glass opacities. Renal CT was unremarkable. Further urine studies revealed a proteinuria of 11.4 grams in 24 hours. The patient underwent a Video Assisted Thoracostomy (VATS) procedure with biopsy and broncho-alveolar lavage, which showed alveolar hemorrhage syndrome with organizing pneumonia, without granulomatous inflammation. Renal biopsy was obtained which showed focal, necrotizing and crescentic glomerulonephritis, MPO-ANCA associated, superimposed on diffuse membranous lupus glomerulonephritis class V. Throughout the hospital stay, the patient continued to have hemoptysis with anemia, requiring 7 units of packed red blood cell (PRBC) transfusion. The patient was managed with pulse dose IV steroids and underwent 14 sessions of plasmapheresis, followed by cyclophosphamide with improvement in renal function and resolution of hemoptysis. He continued steroid therapy post-discharge and was subsequently treated with Rituximab according to the RAVE protocol. His condition has improved with management and he is being followed closely 1 year post initial encounter.

3. Discussion

SLE is a chronic, multi-systemic autoimmune disease. It is mediated by immune deposition against multiple targets, including ANA, Smith and double stranded DNA antibodies. Frequently involved organs are the skin, kidneys, joints and lungs. Patients often present with flares that may include rashes, arthralgias, pleuritis, or renal insufficiency with proteinuria, depending on the severity. Our patient tested positive for ANA, dsDNA, had low C4 and borderline low C3 with elevated inflammatory markers and biopsy proven Class V lupus nephritis. Our patient met 4 of the 11 lupus criteria based on the 1997 American College of Rheumatology criteria: pleuritis (pleural effusions on CT chest), renal disorder (proteinuria of 11 grams in 24 hours), immunologic disorder(positive anti dsDNA) and positive ANA [1]. Our patient also met 5 of the 17 lupus criteria according to the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria: serositis (pleural effusion on CT chest), renal disorder(proteinuria of >500 mg per 24 hours), positive ANA, positive anti- dsDNA and low complement (low C4 and borderline low C3), as well as biopsy proven lupus nephritis [2]. Through literature review, most reported cases only met 3 of the 11 ACR criteria, which is insufficient for the diagnosis of lupus.

Our patient was found to have necrotizing and crescentic glomerulonephritis, most consistent with ANCA vasculitis, specifically microscopic polyangitis with MPO positive staining (Figure 1). The biopsy also revealed abundant immune-complex deposits consistent with WHO class V diffuse membranous lupus glomerulonephritis (Figure 2). Based on the Chapel Hill consensus conference of 2012, this patient's ANCA- vasculitis is most consistent with the Microscopic Polyangitis subtype due to the presence of necrosis of small vessels without granulomatous

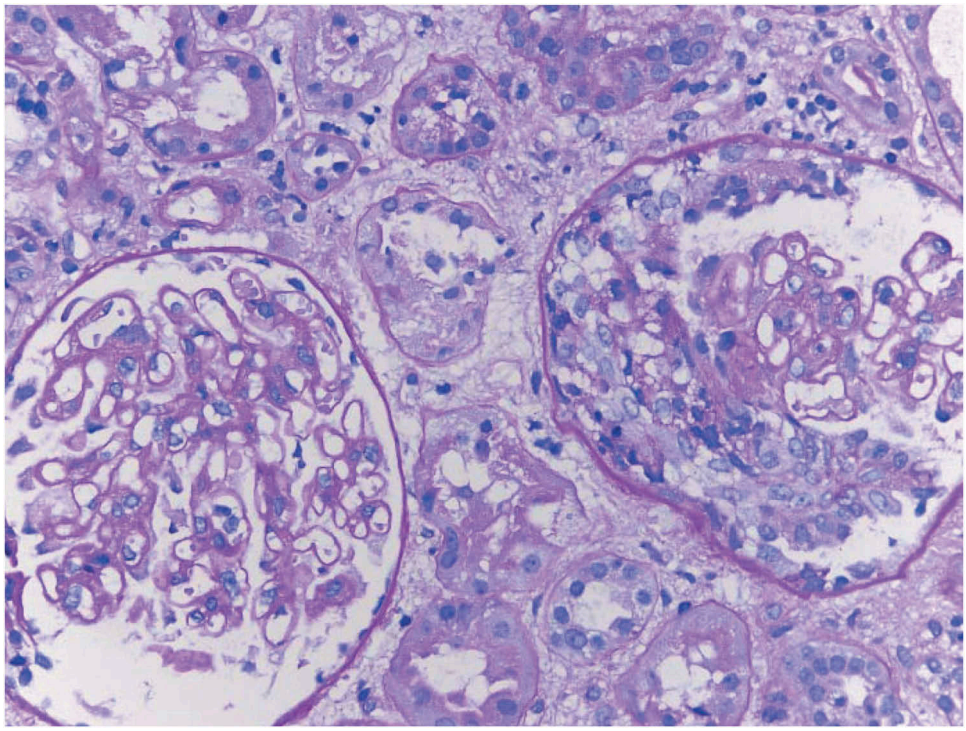

Figure 1. Renal biopsy demonstrating a glomerulus with focal crescentic sclerosis (PAS stain).

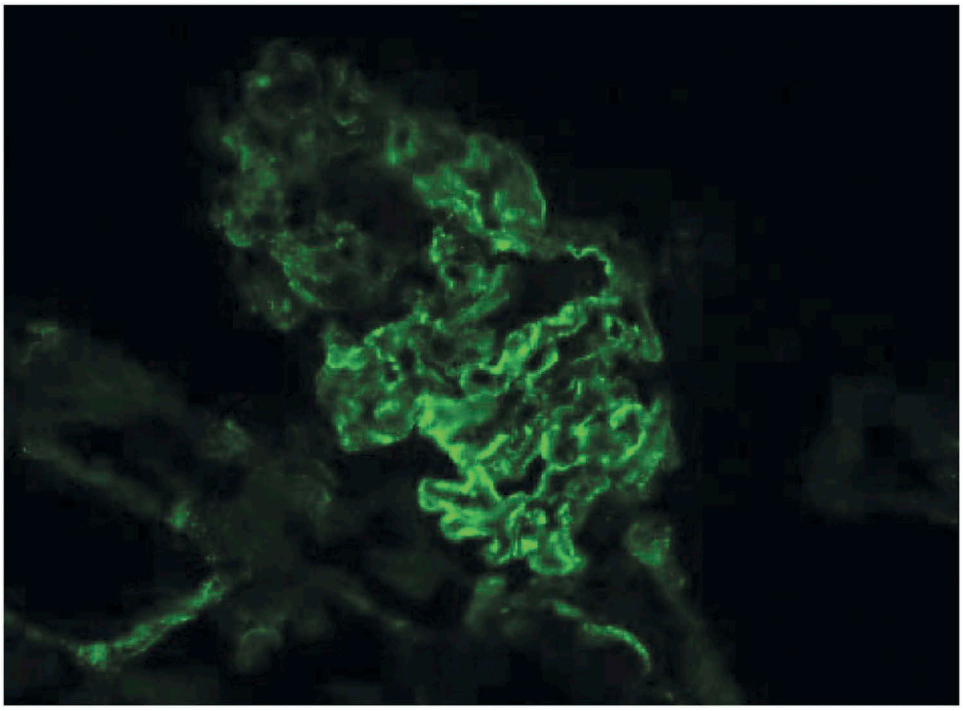

Figure 2. Renal biopsy demonstrating immunofluorescence of nephron with C3 along the glomerular capillary walls and mesangial areas in a global distribution (Immunohistochemical stain

inflammation or eosinophils [3]. The immune deposits present in the biopsy of our patient all relate to the underlying SLE diagnosis, and therefore do not exclude the diagnosis of MPA, which is classically considered to be pauci-immune.

SLE and ANCA-associated vasculitis, separately, are rare rheumatologic diseases. An overlap of these diseases has been reported only a few times in literature. It is a unique entity where neither disease predominates and severity is not determined by the sum of the symptoms [4]. We present a unique clinical case of a Caucasian male in his second decade of life, without a previous personal or family history of autoimmune disease, with serological and biopsy findings of both diseases occurring simultaneously. ANCA, typically p-ANCA, can be detected in up to 30% of SLE patients and can be higher with renal involvement, although this finding is rarely of clinical significance since most patients do not get concomitant vasculitis. This confounding effect can be in part due to a cross reaction with ANA, caused by an artifact in ethanol fixation [5]. ANCA positivity correlates with disease duration, severity of symptoms and response to treatment [6]. Distinguishing ANCA vasculitis from SLE vasculitis may be difficult, as SLE vasculitis can manifest in small vessels and occurs in up to 35% of patients with underlying SLE [5]. Renal histopathological findings are paramount in making the final diagnosis.

Systemic lupus erythematosus and anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis overlap syndrome is a rare disease originally described in 2008. With only a few reported cases in the literature, this case report provides further insight into this rare presentation with renal and pulmonary involvement, and considerably high mortality if not promptly recognized in a timely fashion. A recent literature review by Jarott and collegues found only 8 cases of SLE/ANCA overlap syndrome with renal involvement [7]. Most of the patients in the review were of female sex, and this case report is unique due to its manifestation in a male patient, which, anecdotally, indicates poor prognosis. These diseases are typically seen in young to middle aged females, and given the rarity of this case, biopsy findings were confirmed by two pathologists from separate institutions. Up to 70% of patients diagnosed with overlap syndrome have no previous history of SLE or vasculitis [5]. The most common symptoms at presentation are arthritis, serositis, cytopenias and pulmonary hemorrhage [6]. Rapidly progressive glomerulonephritis, as exhibited in our patient, is an almost universal feature.

Prognosis depends on different factors for each of the aforementioned diseases separately. ANCA vasculitis prognosis depends on creatinine levels at the time of presentation, while the class of lupus nephritis determines SLE prognosis [8,9]. Negative prognostic factors for SLE include male gender and positive lupus anticoagulant [8]. Treatment is divided into two phases: induction of remission and maintenance. Initial treatment is with Cyclophosphamide and high dose IV steroids to reduce inflammation and prevent permanent organ damage. Plasma exchange is often used to rapidly

remove antibodies that may lead to rapidly deteriorating renal function. Once remission is achieved, less toxic immunomodulating agents can be used, such as Azathioprine and Rituximab. Our patient was initially treated with pulse doses of IV steroids, Cyclophosphamide and plasma exchange. He was maintained on tapering PO doses of Prednisone and was eventually transitioned off steroids to Rituximab transfusions as per the RAVE protocol [10].

4. Conclusion

Presentations of autoimmune diseases and vasculitis can be multisystemic. Our patient displayed pulmonary-renal involvement in addition to systemic features such as fevers, myalgia and profound anemia. The association between SLE and ANCA associated vasculitis, while rare, can and does occur. Suspicion should be raised in patients presenting with serological markers of lupus and clinical manifestations of vasculitis, such as pulmonary hemorrhage and rapidly progressive glomerulonephritis. Considering overlap syndromes, especially in patients with underlying connective tissue disease or systemic vasculitis, is paramount for patient outcome. Immediate action and appropriate work up with a collaborative team is required and optimal for patient care.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Diana Meyler http://orcid.org/0000-0001-5612-5636
Abilio Arrascaeta-Llanes http://orcid.org/0000-0001-7768-6109

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