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Fibrosis, Thrombosis, and Dacrocytosis: An Unusual Case of Male Systemic Lupus Erythematosus

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Keywords

Systemic Lupus Erythematosus; Pancytopenia; vasculitis

PRESENTATION:

A 39-year-old Caucasian male with no prior history of chronic medical disease, but with recently diagnosed Raynaud's phenomenon, and a prior hospitalization for sepsis of unknown etiology, presented with abdominal pain. His chief complaints included: weakness, fatigue, dizziness, and left flank pain. His weakness and fatigue started one week prior to presentation and progressively increased in severity. In addition, abdominal and left flank pain increased in severity over the preceding few days. On the day of presentation, he was somnolent at a social gathering and became pale whereupon his family members urged him to seek medical attention.

Thirteen months prior to his current presentation, he was hospitalized for sepsis which appeared to be transient and self-limiting, though that hospitalization was notable for anemia

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and thrombocytopenia. He was evaluated by a hematologist; however, the etiology of these laboratory findings was never determined. Four months prior to his current presentation, he developed progressively frequent episodes of abdominal pain and pallor in the first 3 digits of the hand bilaterally and he was diagnosed with Raynaud's phenomenon. There was no significant contributory family or social history. Review of systems was notable for recurrent subjective low-grade fever, night sweats, anorexia, early satiety, nausea, and twenty-five pounds unintentional weight loss over the prior several months.

On presentation, vital signs were as follows: temperature 39.8 °C, blood pressure 112/74, heart rate 132 beats per minute, respiratory rate 16 per minute. His initial physical exam was notable for diaphoresis, pallor, severe left upper quadrant abdominal, and left flank tenderness with palpation. Initial tests revealed pancytopenia with hemoglobin of 4.1 g/dL, white blood cell count (WBC) of 2.9 K/uL, and a platelet count of 85 K/uL. He received supportive red blood transfusion until hemoglobin was > 7 g/dL. He was admitted to the hospital general medicine service for further assessment.

DIAGNOSIS:

A computed tomography (CT) study of the abdomen and pelvis identified splenomegaly with multiple regions of hypoattenuation concerning for infarction, and diffuse abdominal and pelvic lymphadenopathy (Figure 1). Arterial Duplex of the abdomen revealed severe non-atherosclerotic stenosis of the celiac artery suggestive of vasculitis (Figure 2). A peripheral blood smear was notable for anisocytosis, polychromasia, and dacrocytes (Figure 3). A reticulocyte study was determined to be 6.2% translating to a reticulocyte index of 0.83 (low). His direct antiglobulin test (DAT) was positive suggestive of Coombs autoimmune hemolytic anemia (AIHA). These data suggested a hypoproliferative and hemolytic etiology for his severe anemia. He also continued to experience intermittent febrile episodes despite a normal paroxysmal nocturnal hemoglobinuria (PNH) immunophenotyping, and an unremarkable infectious workup including aerobic and anaerobic blood cultures, urinalysis, Hepatitis A, B, and C, HIV 1&2, Parvovirus, CMV, and EBV.

A rheumatologist was consulted following a positive anti-nuclear antibody (ANA) test with a titer > 2650 in a speckled pattern coincident with positive anti-RNP, anti-Smith, anti-Centromere B, and a positive lupus anticoagulant antibody assay. Notably negative results were: anti-double stranded DNA, anti-SCL-70, and anti-RNA polymerase III. As such, our patient met 3 clinical and 5 immunologic criteria required for a diagnosis of Systemic Lupus Erythematosus (SLE) using the Systemic Lupus International Collaborating Clinics (SLICC) score¹.

The suspicion for an occult malignancy was high, and additional testing included a right inguinal lymph node biopsy, which revealed only reactive changes. A bone marrow biopsy further revealed a hypercellular marrow with trilineage hematopoiesis and reticulin fibrosis, which raised the possibility of myelofibrosis (Figure 4). Subsequent testing made a diagnosis of occult malignancy less likely. This constellation of symptoms and clinical

results further suggested a diagnosis of autoimmune myelofibrosis (AIMF) in the setting of SLE,

MANAGEMENT:

The patient was initially started on hydroxychloroquine and nifedipine for treatment of SLE and secondary Raynaud's phenomenon, respectively. After lymph node and bone marrow biopsy, he was started on oral prednisone 40 mg daily. He became well enough to return home 3 days after initiation of prednisone and a full 10 days after his initial presentation. Symptomatic and laboratory improvement over several weeks supported the diagnosis of SLE with AIMF.

Upon discharge, he continued treatment with hydroxychloroquine with slow taper of oral prednisone and close follow up with both Rheumatology and Hematology. Overall, his fatigue continued to improve without recurrence of fevers, chills, peripheral vasospasm, or abdominal pain. One month after discharge, his complete blood count improved with hemoglobin 13.4 g/dL, WBC 9.2 K/uL, and platelets 202 K/uL. His three month follow up abdominal Duplex study showed complete resolution of celiac artery stenosis, supporting the resolution of lupus vasculitis.

DISCUSSION:

The presence of multiple aberrant immunologic and vascular phenomena in our patient created a diagnostic dilemma, which was ultimately Systemic Lupus Erythematosus (SLE). This diagnosis is exquisitely rare in male patients.

The combination of hematologic manifestations, and especially increased dacrocytes in peripheral blood, make this patient's presentation unusual. Autoimmune hemolytic anemia (AIHA) is a common manifestation of SLE and among the diagnostic criteria for the disease published by both the American College of Rheumatology (ACR) and the Systemic Lupus International Collaborating Clinics (SLICC).¹ However, SLE associated AIMF is vanishingly rare, with just 48 other cases and only 6 in males ever reported.²⁻⁴ The combination of AIHA and AIMF was only reported once in a male with SLE and Coombs positive hemolytic anemia⁵. Diagnosis of AIMF and differentiating this disorder from primary myelofibrosis is difficult given the lack prior reports. As far as we know, there are no unique antibodies produced by patients with SLE and myelofibrosis.¹ In this setting, bone marrow biopsy is particularly helpful, with AIMF typically showing more reticulin fibrosis and fibroblasts compared to more severe marrow fibrosis in primary myelofibrosis.⁶

Males are an under-studied population in SLE and autoimmune diseases in general. One study of sex disparities in SLE noted more frequent hematological involvement such as hemolytic anemia, lymphopenia, and thrombocytopenia in males.⁷ They also note that Raynaud's phenomenon and lymphadenopathy are less frequently found in male SLE, adding to the unlikeliness of our patient's presentation. Disease severity and long-term outcomes may be less favorable in male SLE.⁷

Once the diagnosis AIHA and AIMF is reached, immunosuppressive medications tend to result in satisfactory resolution. Although there are no controlled studies or guidelines, case-guided literature indicates systemic glucocorticoids are effective first line treatment for both AIHA and AIMF in the context of SLE.^{1, 6} In contrast to primary myelofibrosis, bone marrow changes in AIMF typically regress with treatment⁶. Resolution of anemia in SLE following immunosuppressive treatment may be delayed up to 3 weeks, and the recurrence rate is low.⁶ Because of its reversibility, the ubiquitous use of glucocorticoids in autoimmune diseases, and low frequency of bone marrow biopsy in SLE, AIMF is believed to be underdiagnosed, and careful attention to the evolutionary history of patient symptoms is critical for a timely diagnosis.⁶

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Figure 1.
CT abdomen revealed marked splenomegaly with splenic several areas of hypoattenuation concerning for splenic infarction.

Figure 2.
Duplex ultrasound interrogation of the abdomen demonstrated severely elevated peak systolic velocity of the celiac artery consistent with severe stenosis.

Figure 3. Peripheral blood smear revealed dacrocytes and anisopoikilocytosis concerning for myelofibrosis.

Figure 4. Bone Marrow biopsy revealed A). hypercellularity with a normal myeloid/erythroid ratio; B) Trilineage hematopoiesis and macrophages laden with hemosiderin (yellow arrowhead); C) Increased central and perivascular reticulin fibrosis with focal bundles of thick fibers (red arrowhead); and D) Increased megakaryocyte number (white arrowhead).