Catastrophic Antiphospholipid Syndrome in the setting of Overlap Syndrome

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Case Presentation:

A 35-year-old female with past medical history of Overlap Syndrome (Systemic Lupus Erythematosus, Sjogren's, CREST), primary biliary cholangitis, and pulmonary hypertension with right-sided heart failure presented to the hospital with an 8-day history of shortness of breath and 2-week history of progressive cough and fatigue. On initial evaluation in the ED, she was lethargic, jaundiced, and in respiratory distress, with O2 saturation of 85% and tachycardia to 113. Labs were significant for lactic acid 13.5, WBC 15.8, platelets 29, glucose 64, ALT 46, AST 139, Alk phos 436, GGT 133 with evidence of a combined metabolic and respiratory acidosis (VBG: pH 6.97, CO2 37; CMP: Na 131, K 4.4, Cl 101, HCO3 8). CT Angio of the Chest and Abdomen revealed diffuse tree-in-bud pulmonary opacities, perfusion abnormalities of her liver, and a splenic infarct. There was initially concern for DIC in the setting of septic shock (D-dimer 36,000, PT 31.5, INR 2.7, fibrinogen 297). She received empiric Vancomycin and Zosyn in the ED. However, her blood cultures remained negative. She was admitted to the ICU in the setting of her respiratory distress and AMS. Rheumatology and Hematology were consulted for evaluation of Thrombotic thrombocytopenic purpura (TTP) versus antiphospholipid disease given her history of Overlap Syndrome. Immunologic labs were consistent with triple positive Catastrophic Antiphospholipid Syndrome (CAPS) (+ANA screen, +Anti-cardiolipin, +b2 GLP, +Lupus anticoagulant, normal ADAMTS-13 activity). However, the patient did not meet definitive criteria for CAPS. The patient completed treatment with 4 days of plasma exchange followed by IVIG therapy, and a steroid course. After the patient stabilized, she began warfarin with heparin bridge for long term anticoagulation. Her discharge was delayed due to difficulty achieving a consistently therapeutic INR. Lovenox was discussed as an alternative, and the patient was discharged on lovenox.

Discussion:

Catastrophic Antiphospholipid Syndrome (CAPS) is a severe subtype of antiphospholipid syndrome (APS) representing just 4.39% of incident APS cases. It is defined by the acute development ($\leq$ 1 week) of thromboses in three or more organs, with positive antiphospholipid antibodies, and confirmation of micro thrombosis in affected organs by histopathology. If patients meet some but not all criteria, such as our patient who had two affected organs, spleen and liver, at the time of diagnosis, they are

characterized as Probable CAPS. It is imperative to start treatment as soon as possible, as CAPS has a mortality of 44% even with intervention. Acute management of CAPS includes corticosteroids, plasma exchange, and IVIG to suppress the cytokine cascade. The anticoagulant of choice in CAPS is unfractionated heparin, which is transitioned to long-term anticoagulation to reduce the risk of future thrombotic events. For APS, warfarin is the preferred long term anti-coagulant with a target INR of 2.0 to 3.0. However, lupus anticoagulant can cause falsely elevated INR due to interactions with phospholipids in the test. If interaction is suspected, it is recommended to compare the venous PT-INR with the point of care PT-INR test to see if a discrepancy exists, and the target INR can be increased to 3.0 to 4.0. If therapeutic INR is not achievable, low molecular weight heparin and DOACs are viable for long-term anticoagulation in CAPS. However, DOACs are not recommended for patients with triple positive APS or arterial thromboses due to increased risk of repeat thrombosis.

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