CLINICAL VIGNETTE

Depression, Antidepressants, and a Case of Spontaneous Mesenteric Artery Thrombosis

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A 70-year-old female with well controlled rheumatoid arthritis on etanercep and depression on escitalopram, presented to her gastroenterologist with fatigue, poor appetite, weight loss, and 10 days of severe, constant right upper quadrant (RUQ) abdominal pain. She had prior cholecystectomy with persistent RUQ pain which resolved after ERCP for choledocholithiasis. Years later, she returned to her gastroenterologist with 10 days of RUQ pain and weight loss. Initial evaluation including, CMP, CBC, KUB, abdominal ultrasound, and repeat ERCP were negative.

Due to ongoing pain, she was evaluated at a local ER where labs were significant for: DDimer 1190, INR 1.37, protein C activity 44% (low), protein S activity 41% (low). CT of the abdomen and pelvis showed "extensive thrombus in the superior mesenteric vein extending to the level of the portosplenic confluence… thrombus in the main portal vein extending into the right and left portal veins" without evidence of bowel ischemia. CT Chest, MRI abdomen, as well as numerous cancer markers including CA 19-9, CA 27-29, CA 125, SPEP/UPEP, Jak2, and LDH were negative. Age appropriate malignancy screening including mammogram and colonoscopy were also negative. Subsequent hypercoagulable evaluation including Prothrombin Gene G20210A mutation, Phosphatidylserine antibody, Lupus Anticoagulant, Factor V Leiden, protein C and S, beta 2 glycoprotein antibody, DDRVT, cardiolipin antibody panel, homocysteine, a Paroxysmal Nocturnal Hemolysis panel, Anti Thrombin III activity, and repeat Protein C&S activity after resolution of the acute thrombosis were all normal or negative. The only significant finding was a short PTT (<22 seconds), a known independent risk factor for thrombosis.

The patient was treated with subcutaneous noxaparin, transitioned to Rivaroxaban, initially 20mg daily, reduced to a prophylactic dose of 10mg daily with full resolution of symptoms. Repeat MRA showed no mesenteric venous thrombosis. Subsequent Ddimers were normal, even when off anticoagulation for several weeks. For her anxiety/depression, the patient was eventually switched to a combination of mirtazapine and buspirone.

Discussion

Our patient with depression on SSRI and well controlled RA on etanercept illustrates the importance of thinking about both arterial and venous thrombosis in the differential of acute, unexplained abdominal pain. No malignancy or hematological causes were found after extensive hypercoagulable evaluation. Her rheumatoid arthritis may have placed her at increased risk,[1] but there is also evidence that her depression and/or SSRI may have increased risk for thrombosis.

Serotonin has a mild effect on platelet activation and synergistically works with ADP or thrombin to promote platelet activation through aggregation of procoagulant proteins on the cell surface.[2] In comparison with controls, patients diagnosed with major depressive disorder showed increased platelet aggregating response to arachidonic acid, increased expression of Factor V, Fibrinogen, and GPIB, as well as increased fibrin formulation (among other pro-thrombotic markers)[3]. After 24 weeks of treatment with escitalopram, the majority of these changes had normalized. Patients hospitalized for acute coronary syndrome with moderate depression, had increased platelet aggregation as well as an association with elevated inflammatory markers.[4] Others presented case reports where escitalopram may have increased the risk of central retinal vein occlusion and venous thromboembolism.[5,6] A large prospective showed a 40% increased rate of venous thromboembolism (VTE) in patients on either SSRI's or other psychotropic drugs with different mechanisms of action, suggesting that the underlying risk factor may be severe depression itself (at least in cases in which the depression necessitated medications)[7]. Similarly, pooled observational evidence found that depression and anti-depressant use were each associated with VTE.

Further biochemical and clinical studies are needed to help further elucidate the role of depression and anti-depressants in the human coagulation system. Given the evidence, it may be reasonable to consider thrombosis in the differential diagnosis in patients with depression, especially if they are on anti-depressants.

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