ISCHEMIC COLITIS ASSOCIATED WITH PROTHROMBIN 20210 GENE MUTATION

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Ischemic colitis associated with Prothrombin 20210 Gene Mutation is not described in the English literature. We present the case of a woman who developed an ischemic colitis with no other risk factor than the mutation.

R.T. is a 60-year-old Caucasian female who had been quite healthy until she developed some left lower pelvic discomfort over a year prior to her diagnosis. She was evaluated by gastroenterology and had normal CT scans. Colonoscopy was performed, demonstrating colitis in the sigmoid colon. Biopsies of the colitis were consistent with a diagnosis of ischemic colitis. CT angiography performed with attention to the GI vessels was normal. Echocardiogram was normal. Because she had no history of vascular disease she underwent testing for hypercoagulable states. The following tests were performed.

Anticardiolipin ab IgG, IgA, IgM types= negative

B_2 Glycoprotein 1 ab= negative

Lupus Anticoagulant = negative

D-dimer=1.0 (<0.5)

Factor V Leiden= absent

Antithrombin, Protein S and Protein C levels = normal

Homocysteine= normal

PT, APTT, fibrinogen= normal

Prothrombin Gene mutation 20210A= heterozygous

Cholesterol = 170, LDL = 82, HDL = 67

Exercise Tolerance Test= no evidence of ischemia

Family history was positive for arterial but not venous thrombosis. Her sister and father suffered cerebrovascular infarctions at the ages of 58 and 60.

The patient did not use cigarettes and took no medicines or estrogens. She had undergone two surgeries, including a caesarean section and exploratory laporotomy for infertility, without resulting deep vein thromboses.

Her physical exam demonstrated a totally normal exam without cardiac arrhythmia or murmur.

The patient has no risk factors for thrombosis other than Prothrombin Gene Mutation 20210A. We discussed with her the options of full anticoagulation or aspirin therapy and she chose aspirin therapy alone.

Discussion

Inherited thrombophilia results from a genetic mutation that produces an increased risk of venous thromboembolism. Factor V Leiden, Prothrombin Gene Mutation 20210A and deficiencies in protein S, protein C, and antithrombin account for most of the causes, with rare cases resulting from dysfibrinogenemia (1,2).

Prothrombin is the precursor of thrombin which converts fibrinogen to fibrin, the end-product of the coagulation cascade. Prothrombin is a vitamin K-dependant protein that is synthesized in the liver and circulates with a half-life of approximately three to five days.

Prothrombin G20210A results from a point mutation on the prothrombin gene on chromosome 11p11-q12. The mutation is caused by a substitution of adenine for guanine at position 20210 in an area of the

gene that is not translated and therefore does not affect the structure of Prothrombin. Instead, the mutation leads to increased plasma levels of prothrombin and increases the risk of venous thrombosis 3-4 fold over the patient's lifetime (3).

The molecular mechanism by which the nucleotide G20210A transition raises plasma prothrombin levels may result from altering the efficiency of mRNA processing and/or the decay rate of prothrombin mRNA (4,5).

This prothrombin mutation is the second most common inherited predisposition to hypercoaguability. The prevalence is widely variable according to geographic distribution of the prothrombin gene mutation. The proportion of the white population heterozygous for the allele varies from 0.7% to 6.5%, with the highest prevalence rates reported in Spain (2,3,5,6,7,8,9,10).

In southern Europe the prevalence is almost twice as high as northern Europe: 3.0 vs 1.7% (12). In African or Asian population the prothrombin gene mutation is extremely rare (10,11).

Heterozygous carriers of the G20210A prothrombin gene mutation have an increased risk of deep vein and cerebral vein thrombosis. The G20210A prothrombin gene mutation has been found with greater frequency in patients with venous thrombosis than controls in a number of studies (2,3,6,7,8,9). Two meta-analyses have come to differing conclusions concerning whether the presence of the prothrombin gene mutation is or is not associated with an increased risk for DVT recurrence (12). The prothrombin gene mutation may also increase the risk of venous thrombosis in patients with acquired risk factors, such as pregnancy (13), and is a risk factor for cerebral venous thrombosis with or without exposure to oral contraceptives (14,15).

In general, it has been difficult to establish an association between the inheritable hypercoagulable disorders and arterial thromboses. However, the prothrombin gene mutation has been demonstrated as a risk factor for myocardial infarction, particularly in young women. The reasons for this increase in arterial thromboses and an apparent male/female disparity are unknown (16,17). This unexplained association between arterial thrombosis and prothrombin gene mutation in women may have some bearing in this case. Until this report there has been no case associating the prothrombin gene mutation with thrombotic events involving the intestines reported.

With this patient we describe the first case of ischemic colitis associated with the mutation of prothrombin G20210. Long term follow-up will be necessary to discern the adequacy of treating her with aspirin alone.

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