

## Recurrent and Bilateral Deep Vein Thrombosis in a Crohn's Patient

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Clinical assessment of patients presenting with a thromboembolic event necessitates an evaluation of probable risk factors including immobilization, occult neoplasms, prior surgery, or an existing hypercoagulable disorder. Although a significant body of evidence suggests inflammatory bowel disease as a risk factor for TE events, clinical guidelines to date are yet to include this condition as a risk factor. We report a patient with Crohn's disease who developed recurrent deep vein thrombosis (DVT).

### Patient Description

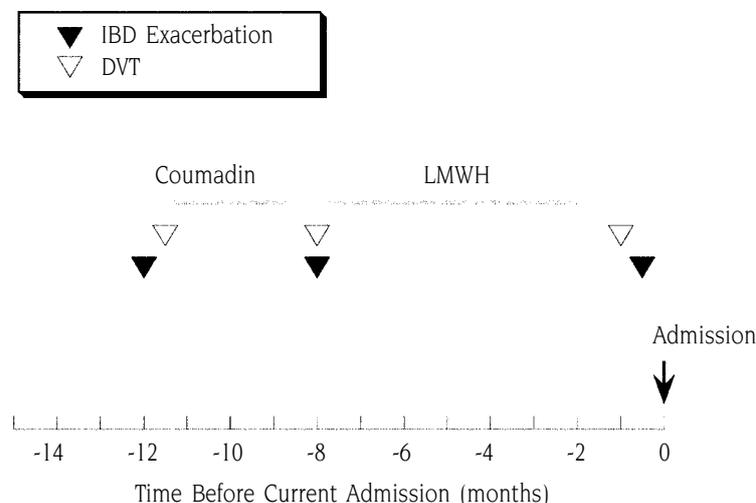
A 59 year old woman with Crohn's disease and a previous history of right leg DVT was admitted for a 3 week complaint of bilateral swelling below her knee and mild difficulty in walking. Two weeks prior to her present admission she had been hospitalized for exacerbation of her bowel disease with a diagnosis of small bowel obstruction, which was treated conservatively. On admission, physical examination revealed mild to moderate bilateral swelling and mild calf tenderness. The diagnosis of DVT was confirmed by Doppler ultrasound. Laboratory tests were unremarkable except for elevated D-dimer (391 µg/ml). Tests for hypercoagulable states including homocysteine, antithrombin-III, β<sub>2</sub>-glycoprotein I, protein S, protein C, anticardiolipin antibodies, lupus anticoagulant, anti-β<sub>2</sub>-glycoprotein I antibodies, activated protein C resistance (Factor V Leiden), prothrombin G20210A mutation and the C677T variant of methylenetetra-

rahydrofolate reductase were all within normal range. The patient denied smoking and any family history of TE events. Menstruation was normal until the age of 49 and the patient did not use hormone replacement therapy.

Eight years prior to the mentioned hospitalization the patient had been diagnosed with Crohn's disease. No extra-intestinal manifestations were ever documented. During the year prior to the current event, she reported five exacerbations of her Crohn's disease, three of which required hospitalization. At that time (8 and 12 months prior to her current admission), the patient was diagnosed with DVT of the right tibial and popliteal veins, with recurring thrombosis after anticoagulant therapy [Figure]. Interestingly, exacerbation of the bowel disease and recurrence of the thrombosis coincided [Figure].

### Comment

As in the patient presented here, the impression by clinicians that IBD patients have an increased risk for TE events has prompted several studies aimed at determining this relationship. Two large cohort studies have shown that the overall incidence of TE events is about 6.5% in both Crohn's disease and ulcerative colitis patients, with a threefold increase in the chance for a systemic TE event as compared to the general population [1,2]. However, the fact that in autopsies the incidence of systemic thromboembolism is nearly sixfold higher than seen in clinical studies [3] suggests that a large proportion of the cases remain undiagnosed. These figures raise the possibility that thromboembolism is a more common extra-intestinal manifestation than previously believed.



Sequence of bowel exacerbation events (black triangles) and DVT (white triangles). Only bowel exacerbations that required hospitalization are indicated. Anticoagulation therapy with coumadin or low molecular heparin (LMWH) is indicated by a grey horizontal line.

TE = thromboembolic  
 DVT = deep vein thrombosis  
 IBD = inflammatory bowel disease

IBD patients have increased risk for both focal microthrombi in the vasculature of the inflamed intestine and systemic TE events, which leads to extensive morbidity and mortality. Systemic TE events occur mainly in the venous circulation but can also develop in the arterial circulation. Deep vein thrombosis and pulmonary embolus are the most common types of TE, but thromboses are also reported in unusual sites such as cerebral, innominate, retinal, hepatic and mesenteric veins [1].

The degree of activity and the extent of inflammatory intestinal disease in Crohn's patients correlate well with the patient's risk for a TE event. In two large cohort studies, about 70–90% of Crohn's patients who experienced a TE event had at least one clinical manifestation of active bowel disease, and in turn, normalization of the hypercoagulable state attenuated inflammation [1,4]. The present case is an extreme example of the tight coupling between active bowel inflammation and a hypercoagulable state, as evidenced by the synchronization between exacerbations

in bowel disease and the occurrence of TE events [Figure].

It is well recognized that the development of a thrombotic process in IBD patients does not involve a single component of the clotting system but is multifactorial, including hyperhomocysteinemia, antiphospholipid antibodies, spontaneous platelet aggregation, endothelial dysfunction, hypofibrinolysis and increased level of the coagulation components [5]. In addition, the degree of bowel inflammation is a critical factor that contributes to hypercoagulability. Yet, the fact that it is absent in other chronic inflammatory diseases such as celiac disease and rheumatoid arthritis emphasizes its multifactorial nature [1].

We conclude that patients with IBD are at increased risk for thromboembolic events. As such, modifiable risk factors should be minimized, early mobilization should be encouraged, and supplementation with folate and vitamins B6 and B12 should be prescribed to control the homocysteine level. Furthermore, since exacerbations of bowel inflammation in these patients coincide with TE events, we sug-

gest that clinicians be aware of the risk during and following these events.

## References

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