

CASR REPORT

From Pulmonary Embolism to Inflammatory Bowel Disease; Give Tunnel Vision up

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Abstract

Inflammatory bowel disease (IBD) is a multisystem disorder with gastrointestinal tract involvement. These patients have the higher risk for thromboembolic events compared to normal population. This report describes a unique case of pulmonary embolism as a first manifestation of inflammatory bowel disease.

Key words: Inflammatory bowel disease; pulmonary embolism; venous thrombosis

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Introduction:

Inflammatory bowel disease (IBD) is a multisystem disorder with gastrointestinal tract involvement. This disease is usually characterized by specific features like chronic or nocturnal diarrhea, abdominal pain, weight loss, fever and rectal bleeding. This disease can correlate with systemic and extra-intestinal complications (1). Elevated thrombin-antithrombin complexes, prothrombin fragments, and D-dimer levels and their increases with disease activity are other evidence pointing toward the relation between inflammation and coagulation. These factors lead to higher risk of thromboembolic events in IBD patients compared to normal population (2-4). The incidence of systemic thromboembolic events in IBD ranges from 1%–7.7% and 39%–41% in clinical and postmortem studies, respectively. Similar to other patients, deep vein thrombosis (DVT) and/or pulmonary thromboembolism (PTE) are the most common thrombotic events. Cerebral, portal, mesenteric, and retinal veins thrombosis have fewer occurrences (5). These events are associated with increased risk of mortality and require improved awareness and prevention (6). This report describes a unique case of pulmonary embolism as a first manifestation of inflammatory bowel disease.

Case report:

A 46-year-old female was referred to the department with pain and edema of her right leg. She was a known case of hypertension and hyperlipidemia and had a history of left leg DVT about two years ago. In previous admission she was discharged on warfarin but after few months of

treatment, warfarin had been stopped due to active peptic ulcer disease. Collagen vascular markers such as anti-nuclear antibody (ANA), anti-double stranded DNA (anti-dsDNA), anticardiolipin and lupus anticoagulant antibodies were negative in first admission which were requested due to recurrent abortions (three times) in her past medical history. Doppler ultrasound was performed to evaluate her leg pain and edema. Findings revealed popliteal and superficial femoral vein thrombosis.

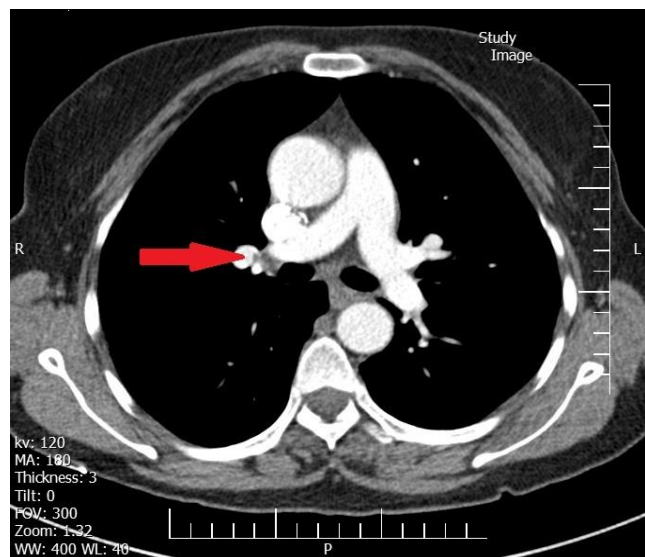


Figure 1: Chest computed tomography angiography of patient, arrow pointed the location of embolus in the right main pulmonary artery.





Figure 2: Colonoscopy views of patient's sigmoid (left) and rectum (right), arrow pointed to location of patchy ulceration compatible with inflammatory bowel disease.

She was admitted again and anticoagulant therapy was started. During her admission, dyspnea was developed; so pulmonary computed tomography angiography (CTA) was performed and pulmonary emboli was demonstrated (Figure 1). In addition to dyspnea she was complaining of abdominal pain and non-bloody diarrhea. Thrombosis of intra-abdominal vessels was ruled out with magnetic resonance venography (MRV). Since her abdominal pain was resistant to analgesics and she had a past surgical history of appendectomy, abdominal CT scan was performed which showed sub-mucosal bleeding and thickness of jejunum indicating probable IBD diagnosis. The patient underwent colonoscopy due to abdominal pain, past medical history, intermittent non-bloody diarrhea, and abdominal CT findings. Unexpectedly, patchy ulceration was seen coincident of IBD (Figure 2). The patient was treated by intravenous unfractionated heparin and discharged on warfarin. Follow up in out-patient clinic for international normalized ratio (INR) level monitoring (target between 2 and 3) was arranged.

Discussion:

Venous thromboembolism incidence differs from 1.3% to 6.2 % and has a mortality rate of 8% to 25% in IBD population. Most of thromboembolic events occur in IBD patients who are younger than 50 and is more common in females compared to males (7). Like IBD pathogenesis, the mechanism of hypercoagulability state is not fully understood. Despite the role of inflammation in activation of coagulation cascade, it seems that this higher incidence rate of thrombosis in IBD is not linked to inflammatory process and evidence in literature has been considered IBD as an independent risk factor for thromboembolism (table 1) (8, 9). Some studies have implicated platelet activation by endothelial dysfunction and hyperhomocysteinemia activation of the coagulation cascade (10). Inherited causes of thrombophilia such as factor V Leiden mutation, prothrombin gene mutation, inherited hyperhomocysteinemia, MTHFR gene polymorphism, deficiency of protein C and S, antithrombin III mutation does not associate with thrombotic events in patients

with IBD. For patients who are diagnosed with venous thromboembolism (VTE), work-up is often necessary to indicate the underlying cause. The first diagnostic steps are rectal examination, fecal occult blood testing and colonoscopy to rule out malignancy which is a strong risk factor for VTE. In absence of inherited causes, acquired one may play a crucial role, but all of them including prolonged immobilization, surgery, fluid depletion, steroid therapy, central venous catheters, smoking and oral contraceptive were absent in our patient (4, 11-13). Bleeding tendency makes the treatment of these patients so difficult. Heparin has been implicated in the therapeutic management of ulcerative colitis with thromboembolism. Two studies showed controversial role for heparin. One of them revealed benefits of use but another failed to repeat this finding and was associated with increased risk of bleeding. Evidence is not enough to utilize low molecular weight heparin. Thrombolytic agents can be life saver in IBD patient with massive PTE. Cardiogenic shock and/or right ventricular dysfunction are the main indication of administration. Vitamin k antagonists should be used with caution due to risk of causing large hemorrhage. Considering above; management of these patients needs multi specialist consultation (14). Based on new consensus, testing for hereditary or acquired hypercoagulability states is not necessary in IBD patients with VTE. In the absence of another provoking factor in clinical remission state of IBD, anticoagulant therapy at least for 3 months has been recommended with periodic reevaluation. There is no recommended follow up time for these patients but based on new consensus echocardiography and CTA can be repeated for reevaluation of anti-coagulation therapy. It seems that persistent use of anticoagulant is not obligatory in patients with good right ventricular function or no evidence of PTE in mentioned investigations (15). However, there is no difference between the management of an acute thrombotic event in patients with IBD and other patients. Patients with diagnosis of PTE need electrocardiography and echocardiography evaluation. In patients with massive saddle emboli, evidence of right heart strain or hypertension is an independent predictor of mortality. Hence, thrombolysis should be considered. Currently, there is no preferred medication and low-molecular-weight heparin (LMWH) or un-fractionated heparin (UFH) have equal effects (16).

Conclusion:

Inflammation and coagulation have been implicated in the pathogenesis of numerous diseases like IBD. Imbalance between prothrombotic and protective mechanisms leads to thrombosis and pathologic blood coagulation. Therefore, finding and treatment of probable underline causes of thrombosis should be considered in all VTE patients referred to the emergency department.



Table 1: Review of the literature (IBD and Thrombotic events)

Authors	Publication date	Major presentation
Wlodarczyk et al. (17)	2014	In this paper authors report three cases of VTE in IBD patients.
Temel et al. (6)	2013	Two case of pulmonary thromboembolism active inflammatory bowel disease patients.
Merrill and Millham (18)	2012	Patients with IBD are at increased risk for developing post-operative DVT or PE.
O'Connor et al. (19)	2009	Case of a patient with ulcerative colitis who has had recurrent thromboembolism.
Choi et al. (7)	2008	Case of a man who was hospitalized with massive PE and deep vein thromboembolism and subsequently was diagnosed with underlying ulcerative colitis.
Kafkas et al. (14)	2008	Massive PE in a patient with ulcerative colitis.
Jin et al. (20)	2005	Exacerbation of ulcerative colitis and developed extensive arterial and venous thrombosis.
Katsanos et al. (21)	2005	Patients with CVT and IBD were significantly younger than CVT patients without IBD (review and analysis of 65 case reports of IBD patients with CVT).
Solem et al. (22)	2004	Venous thromboembolism is a serious complication of IBD.
Bernstein et al. (23)	2001	IBD patients have a threefold increased risk of developing DVT or PE.

IBD: inflammatory bowel disease; VTE: venous thromboembolism; DVT: deep vein thrombosis; PE: pulmonary embolism; CVT: cerebral vein thrombosis.

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All authors passed four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors.

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