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CASE REPORT

CASE REPORT OF PERIPHERAL ARTERIAL THROMBOSIS IN YOUNG FEMALE PATIENT WITH ULCERATIVE COLITIS

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ABSTRACT

Vascular thrombosis is a rare but well-recognized extra intestinal manifestation of ulcerative colitis. Thrombosis usually involves the peripheral veins and less commonly the cerebral veins and the arterial system. A case of a 26-year-old woman is presented with an acute flair of ulcerative colitis and developed extensive arterial thrombosis. Good clinical improvement was achieved after treatment with steroids, sulfasalazine, and anticoagulation with enoxaparin followed by warfarin. Early recognition of thrombotic complications is essential in initiating lifesaving therapy.

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INTRODUCTION

Inflammatory bowel disease (IBD) is an idiopathic disease caused by a dysregulated immune response to host intestinal microflora. The two major types of inflammatory bowel disease are ulcerative colitis (UC), which is limited to the colonic mucosa. There is a genetic predisposition for IBD, and patients with this condition are more prone for malignancy.

Following symptoms may be associated with inflammatory damage in the digestive tract

- Diarrhea: mucus or blood may be present in the stool;
- Constipation, obstipation
- pain or rectal bleeding may be present, severe urgency and tenesmus
- Abdominal cramping and pain: occur periumbilically or in the left lower quadrant in moderate to severe ulcerative colitis
- Nausea and vomiting

Extraintestinal manifestations of idiopathic inflammatory bowel disease (IBD) have been reported in 25% to 36% of patients (Danzi, 1998).

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The usual extra intestinal manifestations are sacroilitis (14%) and peripheral arthritis (10.7%), whereas ocular (8%), mucocutaneous (2.7%), and vascular (2%) manifestations are rare (Kochhar *et al*., 1991). More than 60% of the vascular complications are accounted for by peripheral venous thrombosis or pulmonary embolism. Unusual sites of thrombosis include mesenteric, portal, and cerebral veins. Arterial thrombosis is extremely uncommon (Suarez Crespo *et al*., 1997; Constans *et al*., 1993). We report a young woman presenting with an exacerbation of ulcerative colitis associated with thrombosis involving the peripheral arterial system, all occurring in the course of the same episode of illness.

Case report

A 26-year-old woman was admitted with complaints of severe left upper limb pain, tingling in left upper limb, feeling of cold of 3-4 days duration. She had been symptomatic for 6 months with a history of passage of 1-2 loose stools per day that were occasionally associated with blood. She was not on any form of treatment, including oral contraceptives. She belonged to a low socioeconomic stratum and was a vegetarian. A month prior to admission in this institute, she developed an increased frequency of loose stools of up to 6–8 times per day, almost all of which were associated with blood since yesterday. She also complained of low-grade fever. She was investigated at a local hospital. Sigmoidoscopy revealed diffusely edematous, hyperemic, and friable rectal and sigmoid mucosa and the

presence of small suppurative ulcers. A biopsy of the involved areas revealed acute inflammation, cryptitis, and crypt abscesses. A diagnosis of idiopathic ulcerative colitis was made, and she was started on regular treatment. The frequency of her stools decreased to 1–2 per day, and there was no associated blood in them. On examination, the patient was conscious, thin, malnourished, and pale. Her blood pressure was 110/60 mm Hg, pulse rate was 110/min, pulse was abscent in left carotid, axillary, brachial, radial and ulnar arteries. Examination of the affected limb showed pale, painful and tenderness. and respiratory rate was normal. Cardiovascular, Central nervous system, respiratory, and abdominal examinations were within normal limits. Investigations revealed a hemoglobin of 10.1g/dL, platelet count of $4.63\times 10^5/mm^3$and total leukocyte count of $10900/mm^3$. Her urine analysis, serum electrolytes, serum creatinine, and blood urea nitrogen were all within normal limits. Her prothrombin time was 14.2 seconds (control, 13.2 seconds) and activated partial thromboplastin time was 30 seconds (control, 30 seconds). antiphospholipid antibodies were within normal limits.ANA blot was negative, P-ANCA and C-ANCA was negative. APLA antibody was negative. Lupus anticoagulant test was negative. RA factor was negative. Work up for ankylosing spondylitis was negative. Colonoscopy showed pan ulcerative colitis.

Colour Doppler of Left Upper Limb

subacute complete thrombosis within visualized left subclavian artery and proximal part of left axillary artery with absent colour flow with few collaterals around these thrombosed arteries. Proxymaql part of left common carotid artery and also shows near total thrombosis. Distal part of left axillary artery, radial artery, ulnar artery show very low velocity. Monophasic colour flow within it ranging from 10 cm/sec to 18 cm/sec.

Treatment: Her treatment included anticoagulants-enoxaparin and warfarin. antiplatelets, mesalamine, oral budesonide, IV antibiotics and oral probiotics. Over a period of 10 – 12 days, she responded to the treatment and improved. She was started on subcutaneous enoxaparin 40 mg twice daily and later switched over to warfarin after an overlap period of 5 days. Her pain and swelling subsided; her international normalized ratio was maintained at 2.5 on a usual dose of warfarin (4 mg); and she was discharged. On follow-up, warfarin was continued. She has had no recurrence of symptoms over the last 2 months.

DISCUSSION

Increased coagubility is well-recognized feature of ulcerative colitis but it is rare complication (Kochhar *et al*., 1991). The first report of throm boembolic phenomena complicating IBD was by Bargen and Barter (Bargen and Barker, 1936) in 1936. Since then, several studies have highlighted this association. In one large study, over an 11-year period, thromboembolic complications occurred in 1.3% of patients with IBD (Talbot *et al*., 1986). Sixty-six percent of them had either deep vein thrombosis or pulmonary embolism with a mortality rate as high as 25%. Peripheral arterial thrombosis is another rare complication with a reported incidence of less than 1 in 1000 patients with IBD. The vessels noted to be involved include the aortoiliac, femoropopliteal, and digital arteries (Suarez Crespo *et al*., 1997; Constans *et al*., 1993). It generally occurs as a postoperative complication and has been found to be more common in Crohn's disease than ulcerative colitis. Thrombosis involving multiple sites is an extremely rare feature in IBD. In the study by Jackson and associates, (Jackson *et al*., 1997) 5 of 52 patients with ulcerative colitis and thrombosis had thrombotic episodes involving 2 different sites or at different occasions. Three of them had 3 different thrombotic events. Themajority of patients with IBD do not have demonstrable specific coagulation defects, although acquired deficiencies of antithrombin III and protein S have been reported. Although underlying activated protein C resistance is the most important cause of thrombosis in the general population, it has not been found to be more common in patients with ulcerative colitis, but when present it increases the risk of thromboembolism. Studies on procoagulant activity in patients with active disease have shown elevation in levels of platelets, factors V and VIII, fibrinopeptides, and fibrinogen (Wakefield *et al*., 1990). These have been shown to normalize with response to treatment. Endotoxin-induced microclot formation and monocyte-derived tissue factors have also been implicated in the pathogenesis (Wakefield *et al*., 1990). The precise cause-effect relationship of these factors remains unclear. Active inflammation may not have a causal role in many of the thrombotic events, yet systemic effects of submucosal inflammation should also be considered. It remains conjectural whether mild or subclinical mucosal inflammation is capable of generating sufficient procoagulant activity to result in thromboembolic events. In ulcerative colitis, the majority of the patients do not have active disease at the time of thrombotic episodes, whereas the reverse is true in Crohn's disease (Jackson *et al*., 1997). Treatment of thrombosis in patients with ulcerative colitis is not clearly defined due to the lack of adequate controlled trials. The role of heparin in ulcerative colitis is controversial. Anecdotal reports of benefit with heparin have been reported (Wakefield *et al*., 1990; Gaffney *et al*., 1995; Folwaczny *et al*., 1997).

The underlying mechanism cannot be attributed to the anticoagulant effect alone, as warfarin has not been found to have similar effects (Wakefield *et al*., 1990). The glycosaminoglycans that constitute heparin have been postulated to have anti-inflammatory actions and to potentiate the activity of the peptide growth factors necessary for mucosal regeneration and repair (Gaffney *et al*., 1995). Heparin has been suggested to have a possible role in refractory ulcerative colitis (Wakefield *et al*., 1990; Folwaczny *et al*., 1997). Low-molecular-weight heparin has also been successfully used in an anecdotal case (Evans *et al*., 1997). However, a recent multicenter, randomized, controlled trial has found no benefit of using heparin in ulcerative colitis and reported an increase in significant bleeding complications (Srivastava *et al*., 2002). The administration of either unfractionated or low-molecular-weight heparin for the treatment of ulcerative colitis is currently not justified by the very limited and conflicting data available (Panes *et al*., 2000). On the other hand, their use can be justified in those with associated thrombotic complications. Anticoagulant treatment of venous thromboembolism has been the standard of care for over 50 years and remains the standard of care; however, it has recently been called into question (Cundiff, 2004). In this case, anticoagulant treatment accounting for the resolution of the venous and arterial clots can be debated. Increasing the hydration, mobilizing the lower extremities, and time were probably the most effective treatments. Because of the recent life-threatening hemorrhagic cerebral infarct and contraindication of anticoagulants in active major bleeding,

one has to be cautious with the use of anticoagulants. The duration of therapy in such situations is based on the general guidelines on the management of thrombophilic states. Thrombolytic agents, including streptokinase and urokinase, have been used in patients with ulcerative colitis who have venous thrombosis, even in those with active gastrointestinal bleeding (Van Woert *et al*., 1990; Pogliani *et al*., 1982). Concomitant use of drugs, such as sulfasalazine and azathioprine, for ulcerative colitis have been shown to result in warfarin resistance requiring significant increases in warfarin dosage. (Teefy *et al*., 2001; Havrda *et al*., 2001) Treatment with glucocorticoids affects blood coagulation, and a reduction of fibrinolytic activity may occur during long-term treatment, thus predisposing to venous thrombosis. (Paradis *et al*., 1985) This case highlights the tendency for widespread thrombosis in ulcerative colitis and the need for early recognition and appropriate management of these complications.

Conclusion

A 26 yr old female, a case of ulcerative colitis with flair dignosed to have major arterial thrombotic complication which significantly improved symptomatically and clinically on conservative management.

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