

LOWER EXTREMITY ARTERIAL OCCLUSION: A RARE COMPLICATION OF INFLAMMATORY BOWEL DISEASE.

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Abstract

Context: the association between active inflammatory bowel disease and thromboembolic complications has long been known. However, Arterial thrombotic accidents in inflammatory bowel relapse and active phases are rare.

Case Report: We report two cases of arterial thrombosis events in inflammatory bowel disease context, both of them were operated with favorable outcome.

Conclusion: The pathogenesis of Thromboembolic complications in IBD has not been delineated; the proposed mechanisms include Hypercoagulability and inflammatory phenomena. We'll explain mechanisms and physiopathology of thromboembolic events and prevention possibilities.

Key Words: inflammatory bowel disease, arterial thrombosis, coagulation, surgery.

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INTRODUCTION

Extradigestive manifestations in inflammatory bowel diseases (IBD) are common [1]. They can be revealing or dominate the prognosis more than bowel disease itself. Among these events, the thromboembolic accidents are known since 1936 [2], whose the severity and frequency were highlighted over the years. Arterial thrombosis is much rarer, cerebral vessels are especially interested [3] and sometimes the limb arteries. We report two cases of arterial thrombosis of the lower extremities in IBD context and we'll explain mechanisms and physiopathology of thromboembolic events and prevention possibilities.

CASE ONE:

A 41 year male chronic smoker (moderate smoking: seven cigarettes per day) was admitted to emergency department with a history of left leg

pain and paralysis. He had a past history of an ileocolic Crohn disease under treatment (corticosteroids and Salazopyrine) (Figure 1).

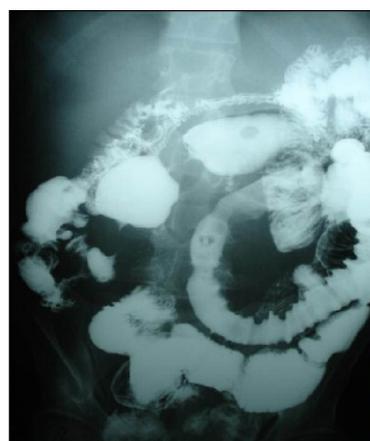


Figure 1: Barium enema showing diffuse stenosis and many areas of expansion and superficial ulcerations.

The clinical examination revealed a cold, pale and painful left leg and deep sensory loss with absent

peripheral pulses but normal ones on the right. Echo Doppler was suggestive of left common femoral and popliteal occlusion. Angiography detected the presence of an intraluminal suspended femoral clot, popliteal and ankle arteries occlusion (Figure 2).



Figure 2: Angiography showing the presence of an intraluminal suspended femoral clot.

The patient was fully anticoagulated with intravenous heparin. A transthoracic echocardiogram was also performed and did not detect any proximal source of emboli. The patient was then operated on: under general anesthesia, a left iliofemoral embolectomy associated to a selective left popliteal, tibial, and peroneal embolectomy and intraoperative intraarterial thrombolysis of tibial vessels. During the operation, no flow was found in distal arteries (tibial artery, dorsalis pedis artery) and a four quadrant fasciotomy was performed on left leg. There was no muscle reactivity to electrical stimulation. We considered that it was an exceeded acute ischemia and the leg amputation became imperative. A postoperative Doppler at 6 hours has confirmed total thrombosis of the leg and foot arteries with no flow in the ankle arteries. Leg amputation was performed 24 hours after femoral embolectomy.

After discharge the patient underwent laboratory tests looking for diabetes and thrombophilia that were unremarkable. These included factor II and V mutation, disorders of plasminogen activation, ATIII deficiency, protein C and protein S deficiency, and homocysteine serum levels. Extensive autoimmune testing looking for autoimmune disorders potentially responsible for thrombotic events including anti-lupus erythematosus, antinuclear, antimitochondrial, and anti-phospholipids antibodies were all negative. There was an important inflammatory syndrome

with a VS 100 mm/ first hour, CRP 43 mg / l an an hyperhomocysteinimiamia. lipid and thyroid function tests were normal. Platelet count was 235,000 / mm³.

CASE TWO

A 37 year male with known history of ulcerative colitis and no vascular risks factor, was admitted to the medicine ward in our hospital as a case of critical right limb ischemia. He had diarrhea and abdominal pain for the last 14 days. Two months forward, he complained right leg cramps and nighttime foot pain. Abdominal examination revealed bleeding and rectal syndrome associated with pain in the right lower abdominal quadrant. Barium meal and Colonoscopy studies were reviewed and were suggestive of malignant colon (tubular colon and ulcerative budding process in rectum segment). Colic Biopsy has found liberkuhnien adenocarcinoma. Contrast Enhanced Compute Tomography was only suggestive of dilated large bowel loops and ulcerative rectal process; there was no lever or other abdominal metastasis. Total colectomy with iléo-anal anastomosis with proximal ileostomy was performed first and vascular management has been reported five days later.

Vascular examination has found no popliteal and distal pulse in right limb. He was noted to have no measurable ankle brachial index (ABI) by non-invasive studies. An angiogram was performed, showing healthy common iliac arteries and abdominal aorta, and a complete occlusive of the proximal superficial femoral artery (SFA) and popliteal artery (Figure 3).

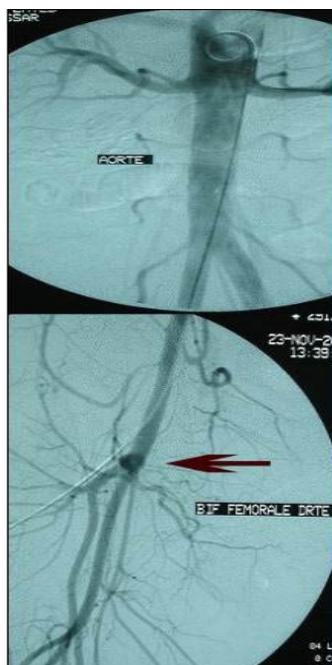


Figure 3: Angiogram showing healthy common iliac arteries and abdominal aorta, and a complete occlusion (←) of the proximal superficial femoral artery (SFA).

There was a runoff to the posterior tibial and dorsalis pedis artery was depicted in delayed collateral circulation. Because the clinical symptoms were intense, femoro-popliteal bypasses using reversed saphenous vein should be done for limb salvage upon this pathology in an urgent basis. Concomitant oral medications were as follows: 200 mg/day of cilostazol, 300 mg/day of sarpogrelate hydrochloride, 100 mg/day of aspirin, 75 mg/day of clopidogrel. His ischemic symptoms in the lower extremities, such as rest leg pain and intermittent claudication, were dramatically disappeared after surgical revascularization. The patient was discharged on the 25th post-operative day. Doppler echography at two months after operation demonstrated good patency of the bypass, and no recurrence of peripheral ischemia or colic tumor were observed during 18 months of follow-up period.

DISCUSSION

Thromboembolic complications of IBD are well recognized and were first described in ulcerative colitis (UC) in 1936[2]. Although pulmonary embolism and lower limb deep vein thrombosis are the most common thromboembolic phenomena seen in IBD. But, case reports of thrombosis of most other veins and arteries can be found in the

literature. In arterial location, thromboembolic events are not uncommon in IBD [4]. The overall prevalence of all clinically patent forms has been estimated at 1.2 to 6.4% [1, 4]. Most often, they occur in the postoperative period and are correlated in 73% cases to degree of disease activity [1]. They affect preferentially cerebral and coronary territories and more rarely the lower limb arteries [5, 6].

The pathogenesis of Thromboembolic events in IBD has not been delineated; the proposed mechanisms include Hypercoagulability and inflammatory phenomena. It has been suggested that thrombosis and ischemia might be involved in the pathogenesis of IBD. Indeed, ischemic conditions were found in inflammatory bowel both in UC [7] and Crohn's disease (CD) [8]. Recently, it has become increasingly clear that inflammatory and thrombotic processes are linked, and current evidence suggests that thrombosis has some involvement, if not in the initiation, at least in the maintenance of the inflammatory process in IBD. A pathogenic sequence was proposed since 1989 in Crohn disease: a series of changes comprising vascular injury, focal arteritis, fibrin deposition, arterial occlusion, and then microinfarction or neovascularization [9]. The study of intestinal vasculature showed changes ranging from intravascular fibrin deposition to complete thrombotic occlusion, vascular fibrin deposition occurred at the site of granulomatous destruction of mesenteric blood vessels [10], and positive immunostaining for platelet glycoprotein IIIa occurred in fibrinoid plugs of mucosal capillaries in CD [11].

Several studies have provided evidence for a malfunction of primary hemostasis: platelet count, platelet activation and aggregation [1,12]. Increased thromboplastin generation [13] and increased fibrinogen, factor VIII, and platelets have been described in patients with IBD [14,15,16]. Then, thrombosis in IBD is generally considered to be hypercoagulability. Fibrin microclots were observed in blood from patients with active chronic ulcerative colitis and Crohn's disease, and addition of endotoxins increased the formation of fibrin. This phenomenon was not seen in healthy patients or patients who had healed after colectomy and may explain why thromboembolism occurs in some patients during exacerbation of IBD [17]. Vitamin K-dependent protein C and protein S are important anticoagulants that inhibit activated factor VIII and V, and a 30 to-60% reduction in protein C levels has been recorded after operations and certain infections [18]. Currently, these proteins are not

measured in routine hemostatic surveys. Prolongation of the prothrombin time has been recognized in patients with IBD [16], and vitamin K deficiency caused by malabsorption, and thereby deficiency in protein C and protein S, might be an important factor in the spontaneous occurrence of thrombosis in IBD.

Fibrinolysis tests in IBD have shown decreased in t-PA (tissue plasminogen activator) and increased t-PA-inhibitor and euglobulin lysis time [1,19]. Fibrinolysis malfunction may be related to endotoxin productions and cytokines (iL-1) [13, 19]. Cytokines (Tumor necrosis factor-alpha, for example) play a pivotal role in the pathogenesis of IBD, and, more recently, their manipulation has led to new developments in the treatment of both UC and CD [20,21] They also have important interactions with the coagulation cascade and hence might contribute to the prothrombotic state associated with IBD.

In IBD hypercoagulability state has many other causes: Hyperhomocysteinemia, for example, is known to predispose to thrombosis, and patients with IBD are more likely to have hyperhomocysteinemia than control subjects [22,23]. Hyperhomocysteinemia in IBD might be due to multiple possible causes, such as deficiencies of vitamin B12 as a result of terminal ileal disease or resection; B6, which is commonly reduced in IBD [24]; and/or folate as a result of therapy with sulfasalazine [25] or methotrexate[26].

In both active and quiescent phases of IBD, three dysfunctions are often associated: disturbance of primary hemostasis, activation of coagulation and hypofibrinolysis, who state that thrombotic events are multifactorial and multigenic [1,4,19]. Unfortunately, no reliable predictive test can predict the thrombotic accidents, then; prophylaxis is particularly difficult. Regarding the indication of heparin, for some years there has been interest in the role of heparin as a specific treatment for active UC and, to a lesser extent, CD. Some randomized studies claimed marked benefit from the use of unfractionated heparin in the treatment of UC [27,28]. However, few years later, similar studies [29] have report that heparin was not only ineffective, but it was also associated with significant bleeding. Low molecular weight heparin, by contrast, does not appear to be useful in treating active UC. Recent randomized studies showed only a marginal benefit [30]. No other antithrombotic therapy has been effective in randomized controlled trials in IBD. There have been no studies with aspirin, either as a therapeutic

agent or as a prophylactic against systemic thrombosis.

DISCLOSURE STATEMENT

All authors do not have any financial relationship with a biotechnology manufacturer, a pharmaceutical company, or other commercial entity that might pose a conflict of interest with the manuscript.

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