

## Catheter-directed thrombolysis in inflammatory bowel diseases: Report of a case

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### Abstract

In patients with inflammatory bowel diseases (IBD) the prevalence of thrombosis is 6.2%, the average incidence of thromboembolism (TE) is 3.6 times higher compared to normal population. The TE is a common extraintestinal complication of IBD, squarely associated with the IBD activity. The application of anticoagulant and thrombolytic therapy in severe IBD is an unresolved issue. Herein we report the first case in literature of an active IBD patient with an upper limb acute arterial occlusion and successful catheter-directed thrombolysis (CDT). A 46-year-old male patient is re-

ported who had Crohn's disease for 10 years. His right hand suddenly became cold and painful. Angiography proved acute occlusion of the brachial and radial artery. Vascular surgery intervention was not applicable. Endoscopy showed extended, severe inflammation of the colon. Despite the severe endoscopic findings, frequent bloody stools and moderate anaemia, CDT with recombinant tissue plasminogen activator was performed. The control angiography proved improvement, the radial artery pulse appeared. No bleeding complication was observed. This case supports that CDT-after careful estimation of the bleeding risk-can be effective and safe in patients with severe or life-threatening TE and active IBD.

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**Key words:** Inflammatory bowel disease; Crohn's disease; Thromboembolism; Catheter-directed thrombolysis; Gastrointestinal haemorrhage

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### INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) the two main forms of inflammatory bowel diseases (IBD) are systemic disorders often associated with extraintestinal

manifestations, complications, and other immune mediated disorders. These chronic inflammatory conditions are characterized by a hypercoagulable state and prothrombotic condition, and accompanied by abnormalities in coagulation. Thromboembolism (TE) is a significant cause of morbidity and mortality in patients with IBD. Recent data suggest that TE is a disease-specific extraintestinal manifestation of IBD, which is developed as the result of multiple interactions between acquired and genetic risk factors. The incidence of systemic thromboembolic events in IBD patients ranges from 1%-7.7%<sup>[1]</sup>, patients having a 3-4-fold overall increase risk for venous TE compared to control population<sup>[2]</sup>.

The application of anticoagulant and thrombolytic therapy in severe IBD is an unresolved issue. Generally the management of TE in IBD patients not differs from treatment in non-IBD patients, although there are currently no clear guidelines for the management of IBD-related TE<sup>[3]</sup>.

## CASE REPORT

A 46-year-old male with a past medical history of 10 years' CD, was presented with symptoms of relapse of IBD: weight loss, lower abdominal pain, bloody diarrhoea and arthralgia (CD activity index: 345). He was treated with high dose prednisone due to severe activity of IBD one year before this event. Actually he was on a treatment with azathioprine (2.5 mg/bwkg) and mesalazine (3 g/d), on a stable dose during the last 1 year. He also complained about an acute onset of pain and coldness of his right hand. The physical examination revealed to an acute arterial occlusion of the right hand. No provoking factor could have been detected. The colour-Doppler imaging and the angiography proved the acute occlusion of the right brachial and radial artery (Figure 1A and B). Vascular surgery intervention was not applicable. The laboratory findings showed anaemia (haemoglobin was 85 g/L) and thrombocytosis (platelet count was 409 g/L normal 150-400 g/L), the D-dimer test was positive (1.0 normal < 0.5 Feu/ $\mu$ L). Liver and kidney panels were normal. An acutely performed endoscopy showed extended, severe inflammation of the colon with deep ulcers and signs of chronic activity involving the sigmoid colon. Considering the severity of the occlusion and the risk of a potential limb-loss catheter-directed thrombolysis (CDT) was suggested, despite the severe endoscopic findings, frequent bloody stools and moderate anaemia. After 24 h from onset of symptoms of arterial occlusion endovascular arterial intervention was performed: 5 mg bolus of radial artery pulse appeared (rt-PA) (Actilyse injection, Boehringer Ingelheim International) was injected into the thrombus, followed by a continuous rt-PA infusion through the catheter in a dose of 0.1 mg/bwkg per hour. The treatment was carried on for 9 h and proceeded with enoxaparin (60 mg QD, subcutaneously). The pain and coldness quickly decreased, the radial pulse became palpable. The control angiography proved the improvement (Figure 1C and D). Despite the high risk of bleed no



**Figure 1** Angiographic pictures. A: Occlusion of the right brachial; B: Occlusion of the radial artery; C and D: Angiographic control after local thrombolytic treatment.

bleeding complication was observed. Echocardiography found no source of an embolus. Low-molecular-weight heparin (LMWH) prophylaxis was applied for 3 mo (enoxaparin, 60 mg OD, subcutaneously). No congenital thrombophilia was proved (antithrombin-III: 120% normal: 80-120; protein C: 132% normal: 70-130; protein S: 93% normal: 60-140; activated protein C resistance: 2.51 normal: > 2; FVLeiden: wild type; Factor II 20210A: wild type; Factor VIII: 188% normal: 60-150). Neither lupus anticoagulant nor antiphospholipid autoantibody was detectable. The level of homocystein was also normal. The relapse of the CD was treated with anti-tumor necrosis factor- $\alpha$  (anti-TNF- $\alpha$ ) antibody (infliximab). One year after the biological treatment and continuous LMWH prophylaxis the patient is in remission of IBD and has a complete recovery of the right upper limb arterial circulation.

## DISCUSSION

We report a case of a peripheral arterial TE of the right upper limb in a 46-year-old patient with acute relapse of CD. In the background no provoking factors could have been detected. Thrombophilia evaluation was normal and a source of an embolus was undetectable either. The background of the hypercoagulability that is present in IBD is the altered platelet/endothel cell function and interaction, the elevated level of coagulation factors and the decreased activity of fibrinolysis. In patients with IBD the prevalence of thrombosis is 6.2%, the average

incidence of TE is 3.6 times higher compared to normal population<sup>[1]</sup>. TE events occur mainly in the venous circulation<sup>[1,4]</sup>, but can also develop in the arterial circulation<sup>[5]</sup>. Deep vein thrombosis and pulmonary embolism are the most common types of TE, but thromboses are also reported in unusual sites such as cerebral, innominate, retinal, hepatic and mesenteric veins<sup>[2,6]</sup>. Arterial thromboembolic complications occur less frequently<sup>[7]</sup> and the majority of cases seem to occur post surgery<sup>[8]</sup>. Patients with IBD have a markedly increased risk of acute mesenteric ischemia. IBD patients are more likely to have cardiac arterial thromboembolic disease, regardless of diagnosis or sex<sup>[9]</sup>. CD has an increased risk for cerebral arterial thromboembolic disease with some differences regarding the sex<sup>[10]</sup>. While the risk of gastrointestinal bleeding has to be considered in each case, most patients tolerate anticoagulants at full dose. Thrombolytic therapy is generally preserved for massive, life-threatening thrombosis. So far, only 17 cases of local thrombolytic treatment in IBD patient have been reported<sup>[11,12]</sup>. Until now there has been no case reported about upper limb arterial occlusion and CDT in IBD. In conclusion, moderate-severe active CD has to be considered as a risk factor for systemic TE<sup>[13]</sup>. Practice guidelines strongly recommend the use of thrombosis-prophylaxis in active IBD<sup>[3]</sup>. Arterial thrombosis is a rare, but severe complication of IBD. Considering the severity of the occlusion, in cases of life-threatening TE CDT could be an effective and safe intervention.

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