



Clinical and radiographic presentation of superior mesenteric vein thrombosis in Crohn's disease: A single center experience

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KEYWORDS

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Abstract

Background: Mesenteric vein thrombosis (MVT) is a rare and frequently underdiagnosed complication of Crohn's disease (CD). This study describes the clinical and radiological characteristics of CD /patients with superior mesenteric vein thrombosis (MVT) diagnosed by CT/MRI.

Patients and methods: The database of Crohn's disease patients treated in Sheba Medical Center between 2005-2010 was searched for MVT diagnosis. Imaging studies of identified patients were retrieved and reviewed by an experienced abdominal radiologist. MVT was defined by superior mesenteric vein obliteration and/or thrombus in the vessel lumen on abdominal imaging. The clinical and radiologic data of these patients were collected from the medical records.

Results: MVT was demonstrated in 6/460 CD patients. Five patients had stricturing disease, and one patient had a combined fistulizing and stricturing disease phenotype. All patients had small bowel disease, but 3/6 also had colonic involvement. No patient had a prior thromboembolic history or demonstrable hypercoagulability. One patient had an acute SMV thrombus demonstrable on CT scanning, the remaining patients showed an obliteration of superior mesenteric vein. Two patients received anticoagulation upon diagnosis of thrombosis. No subsequent thromboembolic events were recorded.

Abbreviations: SMV, superior mesenteric vein; MVT, mesenteric vein thrombosis; PT, portal vein thrombosis; VTE, venous thromboembolism; IPAA, ileal pouch anal anastomosis.

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Conclusions: The incidence of mesenteric vein thrombosis is likely to be underestimated in patients with Crohn's disease. Both CT and MRI imaging demonstrate the extent of enteric disease and coincident SMV thrombosis. In our cohort, thrombosis was associated with stricturing disease of the small bowel. The clinical impact of SMV thrombosis and whether anticoagulation is mandatory for all of these patients remains to be determined.

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1. Introduction

Thromboembolic events are a known complication of inflammatory bowel diseases (IBD). The incidence of venous thromboembolism varies widely in different studies and is reported to range from 7.7% in clinical studies^{1,3,4} to 41% in postmortem studies.²⁻⁴ The most common thromboembolic phenomena are low extremity deep venous thromboembolism (DVT) and pulmonary embolism (PE). Up to threefold increased risk for development of DVT or PE was reported in IBD patients compared to the general population.^{5,6,7} However, additional thromboembolic phenomena such as arterial⁸ and venous mesenteric thromboembolism^{9,10} have also been reported. The clinical presentation of mesenteric vein thrombosis in IBD is non-specific and may be easily confused with signs and symptoms of the underlying disease. With the widespread use of modern imaging technology such as CT and MRI, incidental discovery of a thrombotic mesenteric event (in some cases only during unrelated review of the original imaging study) is not uncommon. In a retrospective study from the Mayo clinic, MVT was identified on 1.7% of CT enterography (CTE) studies of Crohn's disease (CD) patients.⁹ However, there are still only scant data about MVT in CD patients outside the perioperative setting, with the largest case series so far published including only 5 patients.¹⁰

The aim of this study was to describe the clinical and radiological characteristics of CD patients who were diagnosed with MVT in our medical center.

2. Patients and methods

Patients with CD and mesenteric vein thrombosis demonstrated on abdominal CT or MRI were identified by a search of the computerized database and by retrospective review of the medical charts of CD patients treated in Sheba Medical Center between 2005 and 2010. For the purpose of the current study, the CT and/or MRIs of the 6 identified patients with MVT were again reviewed by an expert abdominal radiologist along with their previous and subsequent radiologic evaluations in order to ascertain the original diagnosis. Relevant demographic clinical data were extracted from the charts and electronic databases. The patients' available abdominal imaging studies were reviewed by an expert radiologist (MA). Hypercoagulability workup results were collected when available. Patients with known malignancy and liver cirrhosis were excluded. MVT/PVT was defined as a presence of thrombus in an enlarged mesenteric vein and/or obliteration of the vein ("rat-tail") combined with appearance of mesenteric congestion or mesenteric venous collaterals.

Comparison of categorical variables between the study group and the rest of the CD patients in our database was performed by Fisher exact test. A p value <0.05 was considered significant. The study was approved by the ethics committee of the Sheba Medical Center.

3. Results

3.1. Demographics and clinical characteristics

Six patients (3 males, mean age 32.2 ± 4.4 years) with mesenteric/portal vein thrombosis were identified out of 460 (1.3%) CD patients in our database. The demographic and clinical characteristics of these patients are depicted in Table 1.

The mean duration of CD was 15 years. Five patients had stricturing disease and one patient had fistulizing and stricturing disease. All patients had small bowel and the colon was additionally involved in 3/6 patients. One patient had perianal involvement. The clinical presentation was acute in two patients manifesting with severe exacerbation of abdominal pain with leukocytosis in one patient, without any clinical or laboratory signs implying thrombotic complications. Both patients were referred for abdominal imaging in order to rule out more common complications of their disease such as abscess or perforation. In all other patients the mesenteric vein thrombosis was retrospectively diagnosed upon review of the imaging studies during an unrelated occasion.

None of the patients had had previous thromboembolic events. Complete thrombophilia workup (factor V Leiden, prothrombin mutations, protein C and S deficiency, lupus anti-coagulant/antiphospholipid antibodies) was performed in 2 patients, and was positive for lupus anti-coagulant in one patient who was also receiving oral contraceptives at the time of MVT diagnosis. Thrombophilia workup was negative in an additional patient treated with oral contraceptives.

Two out of six patients received treatment with warfarin (for 2 and 4 years, respectively). The other 4 patients did not receive any form of anti-coagulation therapy. The patients were followed up for 2.25 ± 1.5 years. No recurrent thromboembolic events occurred during the length of follow-up.

3.2. Radiologic findings

"Rat tail" appearance of the obliterated thrombosed lumen of the SMV and mesenteric congestion was demonstrated in 5 patients. A thrombus in the superior mesenteric vein was demonstrated in one patient and was accompanied by segmental portal vein thrombosis. A follow-up scan performed

Table 1 Clinical, demographic and radiologic characteristics of patients with Crohn's disease and portal/mesenteric vein thrombosis.

| N | G* | Age at CD onset, years | Age at MVT/PVT diagnosis, years | History of abdominal surgery | Phenotype | Disease location | Medical treatment at development of MVT/PT | Risk factors | Acute presentation | Real time diagnosis | Main finding on index CT/MRI | Anticoagulation | VTE on follow-up | Progression of findings on follow-up CT/MRI | Follow-up duration, years |
|------------|----|------------------------|---------------------------------|------------------------------|---------------|------------------|--|--------------|--------------------|---------------------|--|-----------------|------------------|---|---------------------------|
| 1 | F | 13 | 32 | No | Strict + fist | Sb + lb | None | OC LAC | Abdominal pain | Yes | Mesenteric vein thrombus, liver infarcts | Warfarin | No | SMV cutoff, mesenteric congestion (2 years) | 2.5 |
| 2 | M | 15 | 32 | Yes | Strict | Sb + LB | None | NA | No | No | SMV cutoff, mesenteric congestion | No | No | No | 1 |
| 3 | M | 19 | 36 | Yes | Strict | Sb + lb | 6-mp | Na | No | No | SMV cutoff, mesenteric congestion | No | No | No | 1 |
| 4 | F | 15 | 26 | Yes | Strict | Sb | none | OC | No | Yes | SMV cutoff, mesenteric congestion | Warfarin | No | No | 5 |
| 5 | f | 16 | 38 | Yes | Strict | Sb | Remicade 6-mp | Na | No | No | SMV cutoff, mesenteric congestion | No | No | Large mesenteric collaterals | 2 |
| 6 | M | 15 | 29 | Yes | Strict | Sb | Remicade 6-mp | Na | | No | SMV cutoff, mesenteric congestion | No | No | No | 2 |
| Average | | | | 15.5 ± 2 | 32.2 ± 4.4 | | | | | | | | | | |
| 2.25 ± 1.5 | | | | | | | | | | | | | | | |

G – gender
 Strict – structuring
 Fist – fistulizing
 Sb – small bowel
 Lb – large bowel
 6-mp – 6 mercaptopurine
 SMV – superior mesenteric vein

after 2 years demonstrated “rat-tail” appearance of SMV and mesenteric congestion. The diagnosis of MVT was established by CT in 5 patients and by MRI in one. In one of the patients primarily diagnosed by CT, similar findings consistent with MVT (SMV cutoff and mesenteric congestion) appeared on a subsequent MRI scan (Figs. 1–3).

4. Discussion

Inflammatory bowel disease is a known predisposing factor for the development of venous thromboembolic events. However, portal/mesenteric vein thrombosis is a rare complication of IBD. The presentation of MVT varies from subtle symptoms indistinguishable from the underlying IBD to full-blown abdominal catastrophe. In our cohort, the imaging finding of mesenteric/portal vein thrombosis was associated with acute presentation in only 2 patients. In 4 patients, MVT was incidentally discovered upon retrospective review of past imaging studies.

In 5/6 of the patients, findings associated with a long-standing process such as SMV cutoff sign and mesenteric venous congestion were demonstrated. A thrombus in the superior mesenteric vein was demonstrated in only one patient. This finding, which is consistent with acute presentation of SMV thrombosis, underwent a transformation into a truncated SMV with mesenteric congestion on a subsequent MRE scan performed 2 years later.

The pathogenesis of mesenteric vein thrombosis is unclear. The increased frequency of thromboembolic events in IBD has been attributed to acquired and/or inherited risk factors. The most important of the acquired factors is probably chronic inflammation resulting in enhanced platelet activation and aggregation, increased levels of intrinsic procoagulants and decreased levels of intrinsic anti-coagulants.^{1,11} A major risk factor for venous thrombosis in IBD patients is surgery. Portal vein thrombi were identified on postoperative CT scans of 45% UC patients after restorative proctocolectomy with available postoperative CT scans, and have also been reported after IPAA construction.¹² In fact, 3/6 patients in our cohort had at least one previous abdominal surgery. However, the abdominal surgery was remote from the time when mesenteric venous thrombosis was diagnosed and preceded it by at least 3 years in all patients. Since it is impossible to accurately date the onset of these MVT events, it cannot be excluded that thrombi had formed perioperatively at least in some of the patients. Other reported acquired factors besides surgery include prolonged hospitalization, hyperhomocysteinemia secondary to vitamin deficiencies,¹³ corticosteroid therapy, venous catheters, smoking and use of oral contraceptives.¹⁴ In the case series by Hatoum et al,¹⁵ 4/6 patients with mesenteric vein thrombosis had risk factors for thromboembolism

other than IBD itself (oral contraception, history of DVT, factor V Leiden, malignancy). In Jackson's case series,¹⁰ four out of eight patients with MVT and IBD had identifiable risk factors



Figure 1 A 30 year old female patient with a 10 year history of Crohn's disease. Acute mesenteric vein thrombosis with follow-up CT after 2 years. a. Coronal reconstruction of CT of the abdomen shows a filling defect in the mesenteric vein (arrow) consistent with acute mesenteric vein thrombosis. b. Two years later an obliteration of the lumen of the superior mesenteric vein showing a “rat tail” appearance (arrow) is demonstrated.



Figure 2 Thirty five year old male patient with an 18 year history of Crohn's disease. Obliterated superior mesenteric vein with "rat tail" appearance (arrow head), mesenteric congestion (long arrow). Dilated distal ileum proximal to stricture due to CD (arrow).

for thrombosis. In our series, complete thrombophilia workup was not available for most of the patients. However, 2 female patients were using oral contraceptives, and one of them was

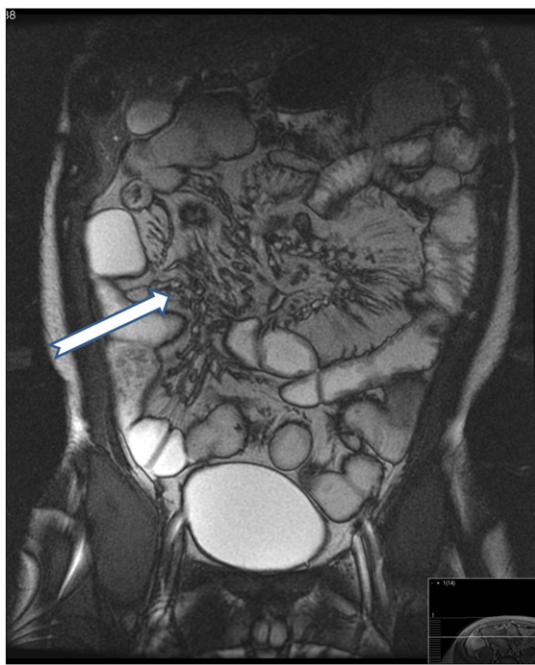


Figure 3 MR enterography in a 35 year man with long standing CD and SMV thrombosis demonstrating marked mesenteric root congestion (arrow).

positive for lupus anti-coagulant. Due to the rarity of this complication and the observational design of this study, we have not been able to address any possible influences of anti-inflammatory therapy on the risk of MVT. Finally, MVT in IBD patients may result from causes unrelated to hypercoagulability per se, such as incessant inflammatory process of the mesentery gradually encroaching and obliterating the MV lumen and/or septic pyelophlebitis episodes.

All patients had involvement of small bowel in their disease (3/6 ileal disease, 3/6 ileo-colonic). Isolated colonic disease was accounted for in 27% of all patients with Crohn's disease followed up at our hospital, and in none of the patients with CD and MVT in the present cohort, but this difference did not reach statistical significance ($p=0.85$). Similar results were demonstrated by Jackson.¹⁰ The association of MVT with small bowel disease probably stems from the anatomy of the intestinal venous drainage.

All our patients had stricturing or stricturing–fistulizing disease and none had luminal phenotype. In contrast, 48% of the 460 patients in our unit database have luminal phenotype of disease ($p=0.03$). The predisposition of patients with stricturing or penetrating disease for MVT could be at least partially explained by extensive local inflammation of the mesentery that tends to be less involved in isolated luminal disease, resulting with involvement of mesenteric vasculature. The severity of disease in patients with MVT could also be an important contributing factor.¹¹ It may also be argued that patients with more severe disease and patients with stricturing phenotype undergo more abdominal imaging studies compared to patients with milder course and/or with inflammatory phenotype, leading to the seemingly increased rate of MVT in this population. Thus, further studies with larger cohorts are necessary to corroborate the association of a stricturing phenotype observed in the present study.

MVT/PVT is easy to miss and is probably underdiagnosed in clinical practice. Of relevance, in a series by Remzi et al.,¹⁶ portal vein thrombi were diagnosed only on remote retrospective review of the imaging studies in 74% of the patients. In concordance with these findings, only 2/6 (33%) of the imaging studies in our patients were diagnosed with MVT in "real time". We have been able to demonstrate mesenteric vein thrombosis by both CT and MRI. Nonetheless, these findings are still limited and cannot serve as testifying that the two imaging modalities are of equivalent accuracy for MVT diagnosis. Indeed, to the best of our knowledge, no recommendations pertaining to the preferred modality for diagnosis of MVT have been published so far.

None of the patients with undiagnosed mesenteric thrombosis received anticoagulation. However, similar to the results from Cleveland Clinic group¹⁵ none of these patients developed VTE for the length of follow-up (median follow-up time – 2.5 ± 3.5 years).

The clinical outcome of IBD patients with abdominal venous thrombosis is variable. In older series a mortality of 50% was described.^{17,18} However, this high mortality rate should be probably attributed to unavailability and inaccuracy of abdominal diagnostic technology in the past, leading to diagnosis of MVT/PVT only in severely ill patients. This contention is supported by the fact that recent reports including patients with subtle forms of PVT suggest a favorable prognosis.^{12,16,18–21}

There is no established treatment strategy for MVT/PVT in IBD patients. Treatment with intravenous heparin or subcutaneous low molecular weight heparin followed by systemic oral anticoagulation for a minimum of six months has been suggested.¹⁷ Percutaneous transhepatic fibrinolysis,²¹ systemic thrombolytic therapy²² and intravascular thrombectomy device²³ have been performed in several cases of acute portal or mesenteric vein thrombosis. However, patients with subtle PVT may suffer few, if any, long-term sequelae when undiagnosed and untreated.¹⁶ In our patient cohort, no recurrent thromboembolic events occurred, even though only 2 patients received anticoagulation therapy.

Our study has several limitations. The number of included patients is small. However, the condition is rare and frequently undiagnosed, as indicated by the fact that the largest case series of patients with CD and MVT/PVT so far reported (excluding post-operative PVT) included 5 patients. Some of the important clinical data such as thrombophilia workup were not available for all patients due to a retrospective nature of the study. Thus, the therapeutic benefit of anticoagulation in patients with incidentally discovered CD and mesenteric/portal vein thrombosis remains to be determined. Patients were identified by chart review rather than inspection of all imaging studies done for CD patients in our hospital. Therefore, it is possible that the true prevalence of MVT/PT in these patients is even higher.

In summary, MVT/PVT is a rare and probably underdiagnosed complication of CD that may be associated with stricture and penetrating small bowel disease. Findings consistent with MVT/PVT can be demonstrated by both CT and MR. Vigilance and awareness of this complication of CD is required from both clinicians and radiologists. Whether anti-coagulation in these patients is mandatory remains to be determined.

Conflicts of interest statement

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Dr. Amitai reviewed the radiologic data and drafted the manuscript. Dr Kopylov collected clinical data and drafted the manuscript. Dr Amitai and Dr. Kopylov contributed equally to the creation of the manuscript. Dr. Lubetzky assisted in collection of the clinical data and contributed important clinical and scientific insights to the manuscript. Prof. Chowers and Prof. Eliakim reviewed the manuscript and provided important scientific and clinical insights. Dr Ben-Horin designed the study and provided a critical review of the manuscript.

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