Mesenteric Venous Thrombosis

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Case Presentation

A 32-year-old man with ulcerative colitis requiring total colectomy and ileostomy developed intermittent, severe abdominal pain and fevers 2 days postoperatively. His examination was remarkable for a temperature of 97.2°F, heart rate of 76 bpm, and blood pressure of 134/80 mm Hg. His abdominal examination was notable for diffuse, moderate tenderness on palpation without rebound or guarding. He underwent computed tomographic (CT) scan of the abdomen and pelvis, which demonstrated thrombosis of the superior mesenteric vein (Figure 1). A vascular medicine specialist was consulted.

Overview

Mesenteric venous thrombosis (MVT) describes acute, subacute, or chronic thrombosis of the superior or inferior mesenteric vein or branches. MVT may present with acute abdominal pain or may be an asymptomatic incidental finding on abdominal imaging. MVT accounts for 1 in 5000 to 15 000 inpatient admissions and 1 in 1000 emergency surgical laparotomies for acute abdomen.[1] The incidence of MVT has increased over the past 40 years, likely as a result of the greater use of abdominal CT.[2]

Age at presentation varies, depending on the underlying pathogenesis of MVT, although it is most common in the fifth and sixth decades of life. There is a slight male predominance.[1] The true incidence of chronic MVT is likely to be underestimated because it is often asymptomatic. Two large series demonstrated that chronic MVT accounts for 24% to 40% of total cases of MVT.[3]

Risk Factors and Pathophysiology

Risk Factors

MVT often results from a combination of hypercoagulability, endothelial injury, and stasis, any of which may be part of a local or systemic process (Table). In patients with inherited hypercoagulability, MVT can occur spontaneously as an idiopathic event or after brief or relatively minor insults. In others, it can develop as a result of inflammation caused by inflammatory bowel disease, intra-abdominal infection, or abdominal trauma. Abdominal surgery, which can result in both endothelial injury and inflammation, also precipitates MVT. Malignancy is present in 4% to 16% of acute MVT cases.[1] Up to 37% of MVT cases appear to be idiopathic.[1]

Pathophysiology

Inflammation and other local factors often contribute to thrombus formation in large mesenteric veins, whereas systemic hypercoagulability is more likely to be responsible for thrombus formation in smaller vessels.[1] Normal mesenteric venous drainage mirrors the mesenteric arterial circulation. At rest, the bowel can tolerate marked reductions in blood flow because only 20% of capillaries are needed to provide adequate oxygen delivery to tissues.[4] Even in periods of stress, the intestinal mucosa can augment oxygen extraction. However, with prolonged ischemia resulting from thrombotic occlusion, the ability of the intestinal capillaries to adequately provide oxygen is exhausted. Consequently, an inflammatory reaction occurs that can result in intestinal mucosal necrosis and ultimately disruption of the

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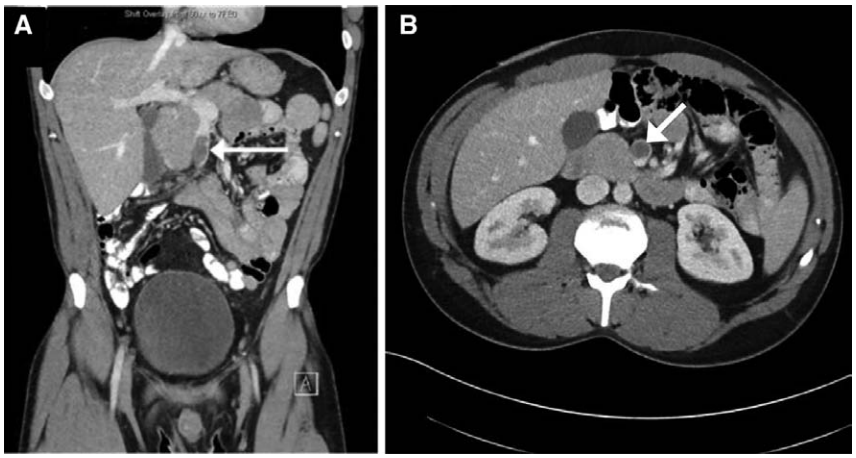

Figure 1. Computed tomography (CT) of the abdomen, coronal view, documenting thrombus in the superior mesenteric vein (white arrow; **A**). Axial view on CT confirms superior mesenteric vein thrombosis (white arrow; **B**).

mucosal barrier. Intestinal bacteria may subsequently translocate into the bloodstream and abdominal cavity, resulting in sepsis, hemodynamic collapse, and multiorgan system failure.[4]

The acuity, anatomic location, and extent of thrombus formation influence the prognosis of MVT. MVT involves the superior mesenteric vein in 95% of cases and the inferior mesenteric vein, which supplies the well-collateralized distal colon, in only 4% to 6% of cases.[1] Acute MVT is typically caused by new-onset symptomatic thrombosis of the superior mesenteric vein or its branches without collateralization. It can affect the ileum (64%–83%), jejunum (50%–81%), and duodenum (4%–8%).[1] In subacute MVT, venous occlusion produces ischemia, but sufficient venous collateralization enables recovery of blood flow. In chronic, nonocclusive MVT, collateral vessels form over time and provide alternative routes for venous drainage. These well-formed collaterals can delay the onset of ischemia.

Clinical Presentation

The symptoms of MVT are often nonspecific. Severity depends on the rapidity of thrombus formation and the extent and location of vessel involvement. Acute MVT often presents with abdominal pain similar to that of arterial mesenteric ischemia, with the initial ischemic stage characterized by sudden-onset, cramping abdominal pain. Acute occlusion of the portal vein rather than the superior mesenteric vein causes abdominal distension, ascites, and diffuse abdominal tenderness. If treatment is delayed, ischemia-induced disruption of the mucosal barriers occurs, resulting in peritonitis or sepsis with eventual hemodynamic instability and multiorgan system failure.[5] Between 6% and 29% of patients with acute MVT are hemodynamically unstable on presentation.[6]

In subacute and chronic MVT, patients may be asymptomatic or present with only vague, intermittent abdominal pain owing to the presence of collateral vessels. In 1 study, >50% of patients with subacute MVT reported a history of intermittent abdominal pain for up to a month before seeking medical evaluation.[1] Patients with chronic MVT may also present with bleeding related to portal hypertension.

Diagnosis

Unfortunately, significant delays often occur between presentation and the diagnosis of MVT because of the nonspecific nature of symptoms. For example, pain resulting from MVT after abdominal surgery is often mistakenly assumed to be postoperative discomfort. Pain in the setting of inflammatory bowel disease is often attributed to disease exacerbation. A high index of suspicion and rapid diagnosis are critical to prevent delays in therapy and adverse outcomes.

Clinical Examination

The abdominal examination can vary significantly, from nonspecific discomfort during palpation to pain out of proportion to the examination. During the initial stages of ischemia, pain can be intense and constant, unchanged with palpation, and without associated peritoneal signs. Fever is typically absent or low grade (99°F–100°F) unless peritonitis or sepsis has developed. As ischemia progresses to necrosis, peritoneal signs evolve, including involuntary guarding, rebound, and abdominal wall rigidity.

Laboratory Evaluation

No single laboratory marker is sensitive or specific for the diagnosis of MVT. Although high serum lactate levels and metabolic acidosis correlate with increased mortality, normal serum lactate and pH do not exclude MVT.[7,8] Profound leukocytosis, often exceeding 20 000 cells/μL, may be the only initial laboratory abnormality.[9] Three separate studies demonstrated that stool samples are positive for blood in 80% to 100% of patients with MVT.[1] D-dimer testing is nonspecific and may be elevated as a result of another abdominal process such as infection or inflammation and has not been well studied in the evaluation of MVT.

Imaging

Computed Tomography

Contrast-enhanced CT angiography is the diagnostic imaging study of choice for MVT.[10] The characteristic finding for MVT is the presence of a filling defect within a mesenteric vein. Other nonspecific findings include bowel wall thickening, indistinct bowel margins, ascites, and a thickened mesentery. Imaging should include the entire abdomen, with contrast timing for both the arterial and venous phases.[5] The sensitivity and specificity of CT angiography are 93% and 100%, respectively, with positive and negative predictive values between 94% and 100%.[11]

Table. Conditions Predisposing to MVT

Thrombophilia
Heritable
Deficiency of protein C or S or antithrombin III
Factor V Leiden mutation
Prothrombin gene mutation
Sickle cell disease
Acquired
Hematologic conditions
Polycythemia vera
Myelofibrosis
Myeloproliferative disease
Monoclonal gammopathy
JAK2 mutation
Anti-phospholipid antibodies
Paroxysmal nocturnal hemoglobinuria
Disseminated intravascular coagulation
Heparin-induced thrombocytopenia
Essential thrombocythemia
Nonhematologic conditions
Hyperhomocysteinemia
Malignancy (particularly intra-abdominal)
Hormonal contraceptive or replacement therapy
Pregnancy/postpartum state
Nephrotic syndrome
Inflammation
Intra-abdominal
Pancreatitis
Inflammatory bowel disease
Trauma
Surgery (most commonly splenectomy)
Infection
Stasis
Cirrhosis
Congenital venous anomaly
Heart failure
Congestive splenomegaly
Idiopathic

MVT indicates mesenteric venous thrombosis.

Magnetic Resonance Venography

Magnetic resonance venography has the advantage of reduced radiation exposure and can be used in patients with allergy to iodinated contrast. However, patients with acute MVT and severe abdominal pain may have difficulty undergoing the longer magnetic resonance venography examination. For patients with chronic MVT who have less severe symptoms, magnetic resonance venography is an excellent imaging modality.

Other Imaging Techniques

Nuclear scintiangiography is rarely used in the contemporary evaluation of MVT and is limited by its poor sensitivity and lack of availability. Often technically limited in patients with acute abdominal pain, Doppler ultrasound may detect large thrombus but is unable to detect thrombus in smaller vessels. With the wide availability of CT, mesenteric angiography is now rarely used to diagnose MVT.

Treatment

The goal of initial treatment for acute MVT is to prevent intestinal infarction by reperfusing the affected bowel. Initial treatment for all patients should include bowel rest, nasogastric suction, intravenous fluids, prophylactic antibiotics, and parenteral anticoagulation such as intravenous unfractionated heparin or an injectable agent such as low-molecular-weight heparin. Advanced therapeutic options, including fibrinolysis, thrombectomy, or bowel resection, are reserved for patients with hemodynamic instability or refractory symptoms (Figure 2).

Anticoagulation

Systemic anticoagulation is the mainstay of treatment for MVT. Anticoagulation prevents thrombus propagation, expedites bowel reperfusion, and decreases resultant morbidity and mortality. Immediate initiation of intravenous heparin on diagnosis prevents the recurrence of thrombosis after intestinal resection by up to 12% and decreases mortality when recurrence occurs by up to 37%.[1] Anticoagulation results in venous recanalization over time.[6] Intravenous unfractionated heparin is preferred over low-molecular-weight heparin in patients who may potentially undergo surgical intervention or receive fibrinolytic therapy.

Anticoagulation is prescribed in acute, subacute, and chronic MVT. Several small, retrospective investigations have demonstrated the benefit of anticoagulation in acute MVT.[12] However, these patients may require further intervention such as thrombolysis or surgery to prevent death. In chronic MVT, anticoagulation may promote recanalization and prevents new thrombosis. One study in patients with chronic MVT showed that 93% of patients treated with anticoagulation either partially or completely recanalized the occluded vessel.[13] Few data are available for patients with portal hypertension resulting from chronic MVT, although heightened consideration should be given to the risk of bleed in those with esophageal varices.

For long-term management, anticoagulation with warfarin with a targeted international normalized ratio of 2.0 to 3.0 is the standard of care. Novel oral anticoagulants have not been studied extensively for MVT.[14] The recommended duration of anticoagulation is 6 months for patients with provoked and reversible causes. Patients with underlying thrombophilia or unprovoked (idiopathic) MVT often require extended duration anticoagulation.[6]

Fibrinolysis

Catheter-directed fibrinolysis may be considered in patients with severe acute MVT refractory to anticoagulation.[6] Even in the absence of radiographic thrombus resolution, catheter-directed fibrinolysis results in symptomatic improvement and lower rates of bowel resection and its associated complications.[6,15] Despite an overall improvement in patient condition, the rate of complications with catheter-directed fibrinolysis, mainly bleeding, is estimated to be as high as 60%.[6] For this reason, catheter-directed fibrinolysis is usually recommended only in patients with refractory symptoms despite anticoagulation but in whom surgical intervention is not necessary. Contraindications for catheter-directed fibrinolysis include a history of stroke or intracranial hemorrhage, primary

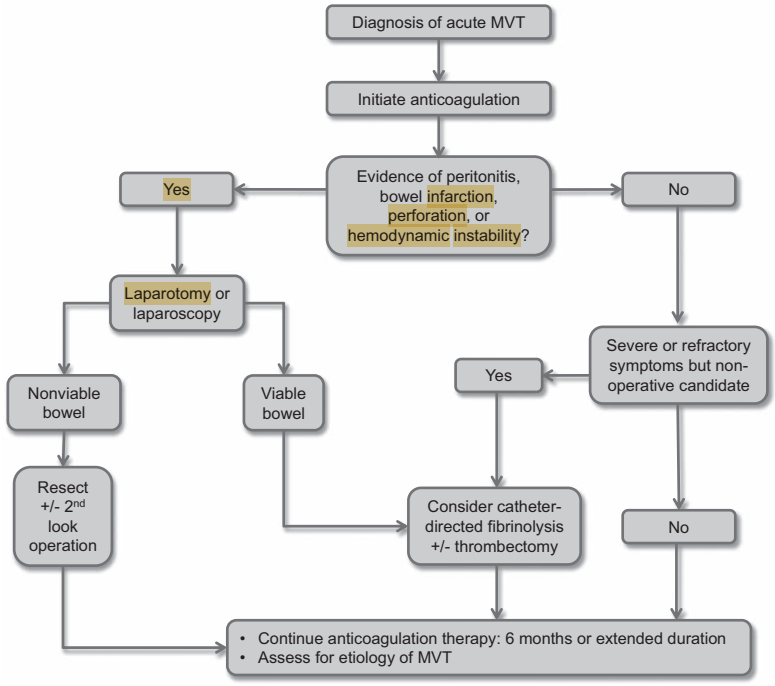

Figure 2. Integrated algorithm for the management of acute mesenteric venous thrombosis (MVT).

or metastatic central nervous system malignancy, active or recent bleeding, recent surgery, recent trauma, and mesenteric infarction.[15]

Thrombectomy

Catheter-assisted thrombectomy may be considered as an adjunct to fibrinolytic therapy and anticoagulation, especially in cases of large-vessel thrombosis when it can rapidly improve venous patency. Options include percutaneous mechanical thrombectomy, angioplasty and stenting, and suction thrombectomy. Thrombectomy is likely most effective in the setting of acute thrombus.[6]

Surgery

Recent investigations suggest that nonoperative management results in improved survival and fewer complications compared with surgical intervention.[16] However, surgery is still indicated in cases of MVT that results in hemodynamic instability, peritonitis, and bowel infarction.[16] The surgical procedure includes either laparotomy or laparoscopy with direct visualization of the length of the intestine. Segments of bowel deemed nonviable are resected, but areas of bowel with questionable viability are usually left intact. This more conservative strategy is favored over wide-margin bowel resection because of the long-term risks associated with short bowel syndrome.[1] Because it is possible that viable bowel can further infarct, many surgeons perform a second-look operation within 12 to 48 hours postoperatively to reassess any areas of bowel previously in question. Up to 50% of patients having a second-look operation will require further resection.[6]

Prognosis

Despite advances in treatment of thromboembolic disease over the past 40 years, acute MVT has an average 30-day mortality of up to 32.1% in severe cases.[17] Prognostic indicators include patient age, known comorbidities, and time to diagnosis and revascularization. Mortality is <10% in rapidly diagnosed and treated cases. If time to treatment is delayed by 6 to 12 hours, the mortality rate rises to 50% to 60%. For cases in which treatment does not occur until >24 hours from symptom onset, mortality ranges between 80% and 100%.[5] Surprisingly, nonocclusive forms of MVT compared with occlusive subtypes have higher mortality rates, likely because their atypical clinical presentation results in delays in therapy.[5] In patients with chronic MVT, 5-year survival rates are 78% to 82%. Prognosis in chronic MVT is influenced by the nature and severity of the underlying condition.[18]

Recurrence of MVT after bowel resection is as high as 60%, with the majority of cases recurring at the site of bowel anastomosis.[15] Some recent data suggest that the use of fibrinolytic therapy with or without thrombectomy offers a lower recurrence rate.[19]

Case Conclusion

The patient was started on enoxaparin self-injections 1 mg/kg twice daily as a bridge to warfarin and then discharged home once free of pain with outpatient vascular medicine follow-up. His MVT was most likely secondary to the postoperative state and hypercoagulability and inflammation related to his inflammatory bowel disease. In the vascular medicine clinic, he denied any abdominal pain. He received 6 months of anticoagulation with warfarin and an international normalized ratio target of 2 to 3. At the 1-year follow-up, his ulcerative colitis was in remission, and he had not experienced any recurrence of MVT.

Disclosures

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