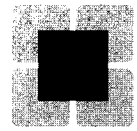

Chronic mesenteric venous thrombosis: difficult diagnosis and therapy

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■ Chronic mesenteric venous thrombosis is an uncommon problem that can occur spontaneously or secondary to trauma, contiguous inflammation, or hypercoagulable states. Diagnosis is often difficult, and therapy is controversial. Surgery and/or anticoagulation may be needed. The authors describe the clinical presentation and management of a patient with this unusual condition.

□ INDEX TERMS: MESENTERIC VASCULAR OCCLUSION; MESENTERIC VEINS; THROMBOSIS □ CLEVE CLIN J MED 1989; 56:823–828

MESENTERIC venous thrombosis was first described as a distinct clinical entity in 1935 by Donaldson and Stout[1] and Warren and Eberhard.[2] Since that time, numerous authors have emphasized the protean clinical presentations of the syndrome and debated the optimal diagnostic and therapeutic approach. In most reported series, thrombosis presented as an acute illness, with mortality rates between 50% and 100%.[3–5] However, in up to one third of patients, mesenteric venous occlusion presented as a subacute or chronic process with symptoms of more than one month's duration.[3]

A number of predisposing factors have been associated with mesenteric venous thrombosis. These include intra-abdominal inflammatory processes, diseases associated with venous stasis, abdominal trauma, primary and secondary hypercoagulable states, and other renal and cardiac disorders.[5] In many instances, no cause has been identified and the terms "primary," "spontaneous," or "agnogenic" have been employed.[6–8] Such cases account for 15%–45% of all reported cases of mesenteric venous occlusion.[9]

Acute mesenteric venous thrombosis often presents as a catastrophic illness that necessitates exploratory laparotomy. The diagnosis is frequently made in the operating room or after pathologic examination of the bowel. When mesenteric venous thrombosis is gradual in onset, the diagnosis may be especially difficult, since patients with subacute or chronic presentations may not have frank bowel infarction. Since the condition is not a common one and symptoms are frequently nonspecific, the diagnosis is often not considered. Conventional plain abdominal radiographs and barium studies are abnormal in up to 70% of patients with mesenteric venous occlusion; however, findings are frequently nonspecific and unhelpful.[10,11] Barium studies of the small intestine may suggest mucosal congestion or ischemia in some, but the sensitivity of such studies is unknown. The utility of angiography has been described in a limited number of patients.[10] Recent reports have emphasized the potential role of computed tomography (CT) and ultrasonography in establishing the diagnosis.[12,13]

We recently encountered a patient with chronic mesenteric venous thrombosis in whom CT provided

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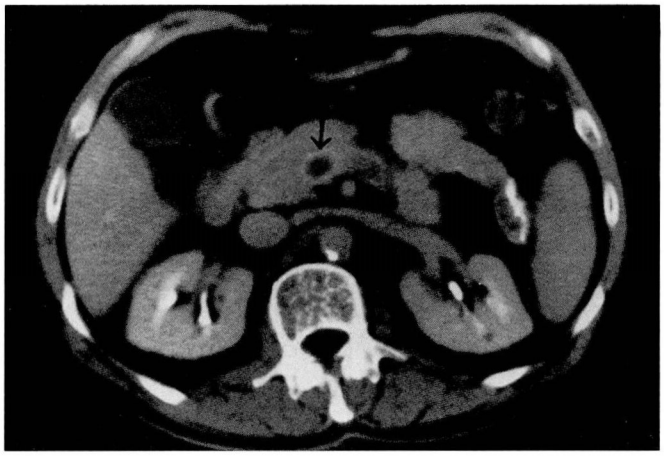

FIGURE 1. CT scan of abdomen at the level of the pancreas showing a low-attenuation area within the superior mesenteric vein consistent with thrombosis (arrow).

the initial clue to the diagnosis. The purpose of this report is to highlight the diagnostic role of CT scans and to review the clinical presentation and management of chronic mesenteric venous occlusion.

CASE REPORT

A 55-year-old white man, a retired coal miner, was referred to the Cleveland Clinic in November 1986 for evaluation of unexplained fever and flank and abdominal pain. His medical history was significant for a myocardial infarction in 1980 and "black lung." In May 1986, he developed left flank pain radiating to the left lower quadrant, fever to 38.3°C, and watery nonbloody diarrhea. On admission to a local hospital, he was found to have leukocytosis and was treated with a one-week course of antibiotics administered intravenously, and his symptoms resolved. All cultures were negative, and the cause of his complaints was not determined. One month following discharge, his symptoms recurred, and he was readmitted to the same hospital, where he received another one-week course of broad-spectrum antibiotics and recovered. All cultures were again negative. He lost 20 lb (9 kg) over the subsequent five months.

In early November 1986, he was admitted to another hospital with recurrent lower abdominal pain, fever to 38.3°C, chills, and watery stools with occasional melena. Diagnostic evaluation included a normal barium-enema examination and upper-gastrointestinal series, normal contrast-enhanced abdominal CT scan, and normal indium-labelled leukocyte scan. Colonoscopy and upper endoscopy studies were normal. Serologic studies for collagen vascular disease were negative. Broad-spectrum antibiotics were given for one week. The patient improved and was discharged on a regimen of oral erythromycin but was readmitted the next day with recurrent fever and abdominal pain. Blood cultures grew *Bacteroides fragilis*, and he received two weeks of intravenous carbenicillin and amikacin for presumed recurrent prostatitis, since he admitted to mild dysuria and frequency. Follow-up CT scans of the abdomen with and without contrast material demonstrated a new lesion adjacent to the pancreas, absent on the prior scan, that was thought to be a duodenal cyst. The patient was referred to the Cleveland Clinic for further evaluation.

Examination on admission disclosed a pale, chronically ill-appearing male in no distress, with a blood pressure of 95/60 mmHg and pulse of 85 bpm without orthostatic changes. The oral temperature was 36.7°C. Pertinent findings included minimal left costovertebral and suprapubic tenderness and a diffusely enlarged, slightly tender prostate. The stools were negative for occult blood.

The hemoglobin level was 11.8 g/dL, hematocrit 34.4%, platelet count 345,000/mm^3 and WBC count 9,400/mm^3 with 78% polymorphonuclear cells, 16% lymphocytes, 5% monocytes, and 1% eosinophils. The alkaline phosphatase level was 164 IU/L (normal, 20–110 IU/L), GGPT 135 IU/L (normal, 0–50 IU/L), and 5′-nucleotidase 50 U/L (normal, 3–15 U/L). SGOT, SGPT, and serum amylase levels were normal. Westergren sedimentation rate was elevated at 52 mm/h. Serum protein electrophoresis and quantitative serum immunoglobulins were normal. The rapid plasma reagin (RPR) test was negative, and urinalysis was unremarkable. Prothrombin time (PT) and partial thromboplastin time (PTT) were 13.7 sec and 25.4 sec, respectively. Fibrinogen, plasminogen activator, protein S, and protein C levels were normal. A circulating anticoagulant was not detected, and there was no evidence of antithrombin III deficiency. Serum viscosity was borderline high at 1.8 (normal, 1.3–1.8), and serum ferritin level was normal at 291 ng/mL.

Review of the most recent abdominal CT scan suggested a superior mesenteric vein thrombosis. Repeat CT scanning at the Cleveland Clinic with and without contrast enhancement confirmed the finding (*Figure 1*). This initial scanning was performed without dynamic imaging. Nevertheless, a rim of contrast material outlined the superior mesenteric vein thrombus, suggesting that occlusion was subtotal. There was no evidence of intra-abdominal collections or retroperitoneal ade-

A,B

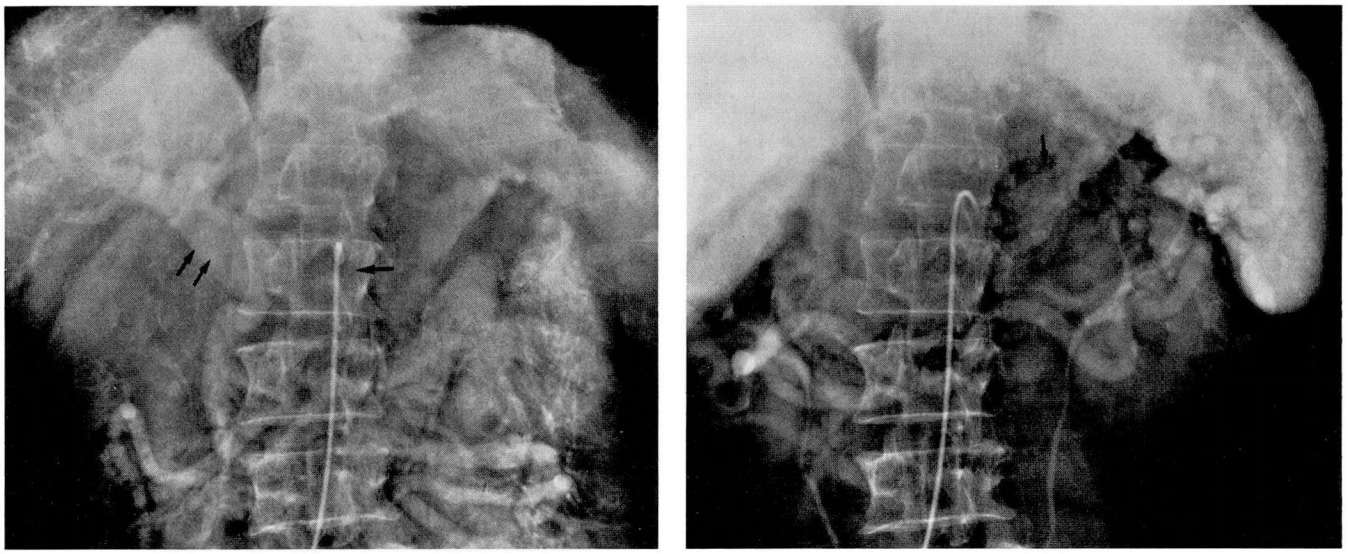

FIGURE 2A. Selective mesenteric angiogram (venous phase) demonstrating occlusion of the superior mesenteric vein with tortuous collateral flow bypassing superior mesenteric vein and reconstituting portal vein (double arrows). Tip of catheter is located in superior mesenteric artery (single arrow). FIGURE 2B. Selective mesenteric angiogram of celiac axis (venous phase) demonstrating multiple venous collaterals from splenic vein occlusion (arrow).

nopathy. A follow-up CT scan one day later with dynamic imaging confirmed the findings. Selective mesenteric angiograms with venous-phase studies demonstrated thrombosis and occlusion of the superior mesenteric and splenic veins with extensive collateralization (*Figure 2*), suggesting that the process was long-standing. A gallium scan was remarkable for diffuse increased uptake in both lungs, consistent with black lung. Bone marrow biopsy and aspirate specimens were normal. Endoscopic retrograde cholangiopancreatography was performed to exclude biliary tract and pancreatic pathology and was normal. Colonoscopy demonstrated three small (2-mm) polyps, which proved to be benign tubular adenomas, but was otherwise normal.

The patient was febrile to 39°C during the first 24 hours of hospitalization, but was afebrile thereafter. Blood and urine cultures were negative. He experienced several episodes of diffuse lower abdominal pain followed by diarrhea, which may have reflected intermittent intestinal ischemia. Cultures of stool were negative, and examinations for ova and parasites disclosed no pathogens. Because the extensive collateralization demonstrated on angiography suggested that the process was chronic, surgical intervention was deemed inadvisable. Medical management with anticoagulation was therefore initiated.

The patient was treated with intravenous heparin sulfate for 10 days and was discharged on a regimen of oral Coumadin (warfarin). He gained 25 lb (11.25 kg) and remained asymptomatic after 1.5 years of follow-up except for very rare episodes of mild abdominal discomfort. Subsequent CT scans with and without contrast enhancement demonstrated resolution of the superior mesenteric and splenic vein thrombosis.

DISCUSSION

Etiology

Mesenteric venous thrombosis can occur alone or in association with a variety of underlying disease processes. These are outlined in *Table 1* and include portal hypertension; blunt abdominal trauma; inflammatory conditions such as intra-abdominal or pelvic abscesses, peritonitis, inflammatory bowel disease, and diverticulitis; and a variety of coagulation disorders. The pathogenesis of mesenteric occlusion in the inflammatory disorders probably relates to contiguous inflammation of the mesenteric veins or release of thrombogenic factors secondary to inflammation. Mesenteric venous occlusion has been associated with a variety of hypercoagulable states,[14] including antithrombin III deficiency,[15] protein C deficiency,[16] polycythemia vera,[17] thrombocytosis, and in association with certain intra-abdominal neoplasms (especially of the pancreas and colon).

Several reports have linked mesenteric venous occlusion with oral contraceptives,[18,19] and isolated cases have occurred in association with pregnancy.[10] Diagnostic evaluation of our patient failed to disclose an associated underlying secondary condition.

The potential pathogenetic significance of protein C deficiency and mesenteric venous thrombosis has been recently emphasized; Green et al[16] documented protein C deficiency in eight consecutive patients with mesenteric venous occlusion. The normal protein C level in our patient excluded this predisposing factor.

The etiology of the patient's *Bacteroides* bacteremia in early November was unclear. This was thought to be an unlikely urinary tract pathogen and to suggest underlying bowel disease. Transient bacteremia could have arisen secondary to intermittent intestinal ischemia, resulting in breakdown of the mucosal barrier. Alternatively, primary septic pylephlebitis was another potential source of bacteremia. Of interest, Harch et al[12] recently reported a patient with *B fragilis* and *Streptococcus* bacteremia in association with idiopathic mesenteric venous occlusion, in whom another focus of infection was not identified.

TABLE 1
CONDITIONS ASSOCIATED WITH MESENTERIC VENOUS THROMBOSIS

- Primary (agnogenic)
- Secondary
  - Abdominal/pelvic processes
    - Trauma
    - Surgery
    - Inflammation—abscess, peritonitis, inflammatory bowel disease, diverticulitis, thrombophlebitis
    - Others—intussusception, volvulus
  - Hypercoagulable states
    - Congenital—antithrombin III deficiency, protein C and S deficiency, homocystinuria, dysfibrinogenemia, hypoplasminogenemia, plasminogen activator deficiency, factor XII deficiency, lupus anticoagulant
    - Acquired
      - Hematologic—disseminated intravascular coagulation, paroxysmal nocturnal hemoglobinuria, sickle cell disease, myeloproliferative syndromes (polycythemia, thrombocytosis, leukemia), thrombotic thrombocytopenic purpura
      - Malignancy—colon, pancreas
      - Hyperviscosity syndromes—myeloproliferative syndromes, paraproteinemias, idiopathic
      - Drugs/agents—oral contraceptives, estrogens, heparin-induced thrombocytopenia, infusion of prothrombin complex concentrates
      - Disorders associated with venous stasis—congestive heart failure/myocardial infarction, advanced age, obesity, portal hypertension
  - Others
    - Liver disease/cirrhosis
    - Nephrotic syndrome
    - Pregnancy
    - Hyperlipidemia
    - Peripheral arterial disease
    - Vasculitis
    - Artificial endothelial surfaces
    - Diabetes mellitus

Diagnosis

The clinical presentation of mesenteric venous occlusion is highly variable. Most patients present with a rapidly progressive illness of several days' duration and have an acute ischemic bowel. Such patients often exhibit leukocytosis, unexplained metabolic acidosis, and complaints of pain out of proportion to findings on physical examination. Emergency laparotomy is frequently necessary and typically discloses thickening of hemorrhagic or frankly devitalized bowel loops. Transection of involved veins may result in extrusion of venous thrombi. Histopathologic examination characteristically demonstrates hemorrhage into bowel wall, mucosal edema, and transmural necrosis in severe cases.[10]

Although most patients present with acute disease, up to one third may be symptomatic for longer than one month prior to seeking medical attention. In such individuals, abdominal pain is almost invariably present and is usually intermittent. As in the cases of acute thrombosis, patients with subacute or chronic disease often complain of pain that is disproportionate to findings on examination. Nausea and emesis are present in about 50%, and diarrhea, hematemesis, or hematochezia may be seen in a minority. Fever is usually low-grade or absent,[10] and mesenteric venous occlusion is an uncommon cause of fever of unknown origin, as was seen in our patient. Stools may contain occult blood in 33%–100% of patients.[1,20,21] Mathews and White[3] suggested an association between prior myocardial infarction and mesenteric venous occlusion. Forty-one percent of their patients had a history of infarct, as was seen in our patient.

The difficulty in diagnosing chronic mesenteric venous occlusion was aptly demonstrated in this case. An extensive radiographic evaluation failed to disclose the diagnosis, which was only appreciated on follow-up CT scan. Several authors have advocated sonography and CT to detect portal venous occlusion.[22–24] Several reports suggest that these techniques may be useful in the diagnosis of superior mesenteric venous thrombosis as well.[12,13] Kidambi et al[13] reported a case in which ultrasonographic findings established the diagnosis of mesenteric venous occlusion. Harch et al[12] recently reported four cases in which CT scans serendipitously showed mesenteric venous thrombosis, as occurred in our patient. Prior studies have emphasized that the presence of gas in the portal system or mesenteric veins should

suggest the diagnosis.[25] In our patient, the thrombus was well visualized and, in fact, a rim of contrast material discernable around the clot suggested that occlusion was subtotal. This may well account for the patient's salutary clinical outcome, since this permitted time for adequate collateralization to develop and did not lead to bowel infarction. The full extent of involvement, however, was not appreciated on CT scans and mesenteric angiography documented the extent of splenic venous thrombosis. The relative sensitivity of ultrasonography and CT compared with angiography in the diagnosis of mesenteric venous thrombosis has not been rigorously assessed.

Management

The management of chronic mesenteric venous occlusion is controversial. Some patients may develop bowel infarction, and this requires prompt and aggressive surgical intervention with resection of involved intestine. In such patients, survival rates have ranged between 27% and 79%,[10] and thrombosis has recurred in up to 29% of patients.[26] Although it is evident that mesenteric occlusion can be catastrophic, slowly progressive thrombosis may develop in some patients and permit the development of adequate collateralization. In such individuals, surgery may not be necessary, and conservative medical therapy may be more appropriate. There are insufficient data in the literature, however, to resolve this issue directly.

The role of anticoagulation has been debated over the last 15 years. Naitove and Weismann[4] reported no mortality in patients who underwent surgery for mesenteric venous occlusion and who were subsequently treated with anticoagulation. Another study described one patient who developed recurrent thrombosis following intestinal resection for mesenteric venous thrombosis while receiving adequate oral anticoagulation therapy.[26] Although most authorities recommend anticoagulation for acute mesenteric occlusion, some investigators think that this is not mandatory in those with chronic thrombosis and adequate collateralization.[12] Heparin has been shown to increase survival in dogs with experimental occlusion of the superior mesenteric vein,[27] but there are no studies corroborating similar benefit in humans. Because our patient experienced intermittent pain, we elected to continue therapy with warfarin. The appropriate duration of anticoagulation has not been defined. In patients with protein C deficiency, however, warfarin should probably be used with caution, since fat and skin necrosis have been reported.[16,28]

CONCLUSION

CT scanning provides a useful noninvasive diagnostic technique in the evaluation of patients with suspected mesenteric venous occlusion. Ultrasonography may also be helpful in the diagnosis. The sensitivity and specificity of these radiologic tests are unclear when compared to conventional angiography. They may be useful, however, as initial screening examinations and may also permit noninvasive assessment of progress during therapy. The management of patients with chronic idiopathic mesenteric thrombosis remains controversial but should be individualized. In patients whose condition is medically stable and in whom adequate collateralization is demonstrated on angiography, a conservative approach with oral anticoagulation may be optimal treatment.

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