Introduction: The prevalence and clinical spectrum of mesenteric venous thrombosis (MVT) in India is largely unknown. Methods: We retrospectively reviewed the case records of patients with primary mesenteric venous thrombosis seen over a 10-year period, and retrieved information on clinical picture, underlying hypercoagulable states, and outcome. Results: The 28 cases (mean age 41.2 [SD 10.2] years; 19 male) included 13 with acute MVT, 10 with subacute MVT and 5 with chronic MVT. Ten patients had past thromboembolic events (multiple events in five); four patients had isolated superior mesenteric vein involvement and 14 had multiple vessel involvement. Hypercoagulable state was identified in 17 patients, with multiple etiologies in 7 patients. Pre-operative diagnosis was made in all patients. Ten patients needed surgical management; the rest were managed medically initially, but 2 required surgery on follow up. Seven patients died during a follow up of up to 10 years, with in-hospital mortality during index admission in six. Conclusions: Most of the patients with MVT have multiple intra-abdominal vessel involvement and underlying hypercoagulable state. The policy of early treatment with anticoagulation in all, and surgical treatment as per need, achieves low mortality. [Indian J Gastroenterol 2007;26:113-117]

Mesenteric venous thrombosis (MVT) is the third most common site of venous thrombosis, after the lungs and lower limbs. Secondary MVT is more common than 'primary' MVT (idiopathic or due to congenital or acquired primary hypercoagulable state). Most cases are diagnosed at laparotomy or autopsy. A high index of suspicion is required for timely diagnosis.

The prevalence and clinical spectrum of this entity in India is largely unknown. We analyzed the clinical spectrum of primary MVT, prevalence of underlying hypercoagulable states, and outcome of MVT with currently available therapy.

Methods

This retrospective study included patients with confirmed diagnosis of primary MVT seen between April 1994 and April 2004. MVT was diagnosed by demonstration of thrombosis in the mesenteric venous circulation on imaging. Patients with MVT secondary to intra-abdominal inflammation or infection, malignancy, cirrhosis, and post-traumatic, post-sclerotherapy or post-surgical MVT, and decompression sickness were excluded.

Patients were divided into acute (sudden onset of symptoms and symptom duration <15 days, absence of collaterals), subacute (symptom duration >15 days and absence of intestinal infarction or collaterals) and chronic (presence of collaterals on presentation) groups. Patients with clinical suspicion of MVT underwent ultrasonography (USG) with Doppler study, followed by laboratory tests and plain X-ray abdomen. Findings were confirmed on contrast-enhanced dual-phase computerized tomography (CT), magnetic resonance angiography (MRA) (if CT was non-diagnostic or contraindicated) or mesenteric angiography (if definitive management strategy was planned or the diagnosis was in doubt). At diagnosis, blood was collected for investigating hypercoagulable state.

Laboratory work-up included complete blood count, liver function tests, renal function tests, serum LDH and amylase, arterial blood gas analysis, coagulation profile, HIV serology, blood sugar, ascitic fluid examination and blood culture. Tests for hypercoagulable states included protein C, protein S, antithrombin III and factor V Leiden mutation; Ham test and sucrose lysis test for paroxysmal nocturnal hemoglobinuria; lupus anticoagulant and anticardiolipin antibodies; and plasma homocystine levels; bone marrow biopsy was done in patients with abnormal blood cell lines and splenomegaly for diagnosing myeloproliferative diseases.

After resuscitation and supportive care, anticoagulation was started. Surgery was done in acute and subacute cases, with the aim of conserving as much viable intestine as possible. This was done on emergency basis in patients who had signs of intestinal infarction (peritoneal signs or signs of intestinal obstruction or perforation) or massive hemorrhage or when the diagnosis was in doubt. In patients with chronic MVT with recur-
rent upper GI hemorrhage or with intestinal ischemic stricture with recurrent partial obstruction, surgery was planned at a later date. Patients with underlying hypercoagulable states or with past thromboembolic events were treated with lifelong anticoagulation; patients with intake of oral contraceptive (OC) pills and those with idiopathic MVT without past or further thromboembolic events were treated with anticoagulation for at least 3 months. Patients were followed up every 6 months or as and when required.

**Results**

Twenty-eight patients (mean age 41.2 [SD 10.2] years, range 22-78; 19 male) had been diagnosed with primary MVT. Their presenting features are listed in the Table.

Their laboratory tests showed: hemoglobin <10 g/dL (n=6), WBC>12,000 cells/µL (17), transaminase levels >2 times upper limit of normal (4), hypoproteinemia (9), pre-renal azotemia (3), pH >7.2 (4), elevated LDH >2 times upper limit of normal (18) and amylase levels >2 times upper limit of normal (11). Eight patients had sepsis (bacterial 6, fungal 2). Stool occult blood was positive in 12/20 patients.

Ten patients had past history of one (n=5) or more (5) thromboembolic event; these events included deep venous thrombosis in 4 patients, portal venous thrombosis and suspected MVT (jejunal strictures of unknown etiology) in 2 each, Budd-Chiari syndrome (BCS) in 2 and cortical venous thrombosis, pulmonary thromboembolism, cerebral vascular accident due to thromboembolism and aortic thrombosis in one. Three patients had family history of thromboembolic events.

**Etiology of hypercoagulable state**

Of the 23 patients who underwent investigation, 17 had one (n=7) or more (10) identifiable hypercoagulable state; these included protein C deficiency (n=6), protein S deficiency (4), OC pill intake (4), myeloproliferative diseases (2), thrombocytosis (2), factor V Leiden mutation (2), anticardiolipin antibody (2), lupus coagulant (2) and polycythemia (1). None had antithrombin III deficiency, hyperhomocystinemia or paroxysmal nocturnal hemoglobinuria. Of five patients who did not undergo tests for hypercoagulability, three were already on anticoagulant therapy for past episodes of thromboembolism and two died on the day of admission.

**Morphology of vessel involvement**

The vessels found to be involved on imaging and/or at surgery were as follows: superior mesenteric vein (SMV; n=28), portal vein (23), splenic vein (20) and inferior mesenteric vein (2). SMV was involved alone in only 4 patients. Two patients had hepatic vein thrombosis; one of these also had inferior vena cava thrombosis.

**Diagnostic tests**

Plain X-ray abdomen (n=15) showed air-fluid levels in 8 and gas under diaphragm in 2 patients. In 7 patients it showed only air-filled small bowel loops. Small bowel barium series (n=4) showed strictures in 2 and thumb-printing in one patient. Upper GI endoscopy (n=19) showed esophageal varices, portal hypertensive gastropathy and gastric varices in 5, 5 and 3 patients, respectively. Colonoscopy (n=7) showed ileal erythema and nodularity in one patient with active bleeding.

USG did not provide adequate window in 4
patients with acute disease and missed the diagnosis in 8 patients (1 acute, 7 subacute). USG was diagnostic in 16/28 patients (57.1%), CT in 16/17 patients (94.1%), MRA in 2/2 patients and abdominal angiography in 13/13 patients. The findings were: thrombus within venous lumen in 26/28 (92.9%) patients (the other two had venous thrombus as operative finding), thickened and/or dilated bowel loops in 19 (67.8%) patients, bowel stricture in 2 (7.1%) patients, ascites/pleural effusion in 16 (57.1%) patients, and splenomegaly with collaterals at porta or splenic hilum in 5 (17.8%) patients. Additional findings at imaging were splenic infarct in 4 (14.2%) patients and associated arterial aneurysms (renal, splenic or aortic) in 4 (14.2%) patients.

Clinical course
During hospitalization, 3 patients developed jaundice (2 sepsis-related and 1 due to BCS), 3 developed renal failure, and 4 patients developed anemia. Five patients died in hospital (4 acute, 1 subacute); 3 of these could not be investigated for underlying etiology and 2 were idiopathic. Two of these who had received anticoagulants (including one subacute with BCS) died on the second and 14th days of admission – one patient had acute widespread small intestine infarction and underwent jejunal-ileal resection with jejuno-colic anastomosis followed by anticoagulation. Two patients had acute extensive small bowel infarction, could not receive any specific therapy and died on the day of admission. Various complications observed in these patients were peritonitis (3), perforation (2), sepsis (4), shock (3), pulmonary embolism (1), gastrointestinal bleed (1) and hepatic failure in a patient with BCS.

Treatment
Treatment was based on clinical presentation, condition of the patient, and presence of hypercoagulable states. It included short-term anticoagulants followed by surgery and long-term anticoagulants (3 patients with hypercoagulable states), short-term anticoagulant treatment followed by surgery (2 patients, one with OC pills and one idiopathic without past history of thromboembolism), short-term anticoagulant alone (3 patients – 2 with OC pills and 1 with hypercoagulable state with intracranial hemorrhage), long-term anticoagulant alone (9 patients with hypercoagulable state), surgery alone (2 patients who were not investigated for hypercoagulable state), surgery followed by long-term anticoagulant (2 patients – 1 idiopathic with past thromboembolism and 1 with hypercoagulable state), and no surgery and no anticoagulant (2 patients with idiopathic without history of thromboembolism).

At surgery (n=9), the findings included bowel infarction (5), perforation (3), peritonitis (4), jejunal stricture (4) and splenic infarct (1); 8 patients had jejunal involvement and five had ileal involvement. Surgical procedures done were: resection-anastomosis with peritoneal toilet (n=4; all acute), resection-anastomosis of intestinal stricture (3; all subacute), resection-anastomosis with splenectomy and peritoneal toilet (1, acute), and resection-anastomosis of stricture with splenectomy and devascularization (1, chronic). Postoperatively, one patient developed short-bowel syndrome and one developed wound infection and sepsis; both recovered successfully. Angiographic treatment was not done in any patient.

Follow up
In the 23 patients who survived index hospitalization, follow up was available for 6 months to 10 years (mean 4.2 [SD 1.3] years). Five patients experienced recurring abdominal pain. Two of them required resection-anastomosis of jejunal stricture followed by relief of symptoms and 3 patients had relief in pain after dietary modification. Treatment-related complications included gastrointestinal hemorrhage (2), intracranial hemorrhage (1) and incisional hernia (1). Eight patients developed esophageal or gastric varices, 5 developed portal cavernoma, 4 developed lienorenal collaterals and 6 developed splenomegaly. One patient died; he had myeloproliferative disease and developed intracranial hemorrhage on anticoagulant therapy.

Discussion
Our study included only patients with primary MVT. Almost 50% of cases were aged <40 years; hypercoagulable state was identified in 60%, and 35% had past thromboembolic events with multiple events in 50%. Venous thrombus was demonstrated in all cases. Multiple vessel involvement was seen in 86% of patients. Two-thirds of patients were managed medically (11% required surgery on follow up). The overall mortality was 21.4%.

MVT is responsible for 1.5%-15% of cases with mesenteric ischemia.2-4,5,6 The age of presentation ranges from 19 to 81 years and male to female ratio from 0.9:1 to 4:1.3,4,7-11 After abdominal imaging and recognition of hypercoagu-
Primary mesenteric venous thrombosis

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In identifiable states, no identifiable cause is found in 10%-35%. Of identified etiologies, 38%-87% of cases are due to underlying hypercoagulable states. A combination of factors may be involved in causation of MVT. In our series, protein C and S deficiency was commoner than factor V Leiden mutation. This was in contrast to a previous report from India. History of thromboembolic events in the past or in the family, which is present in 19%-60% of cases, gives an important clue to suspect this diagnosis in a patient with unexplained abdominal pain.

The clinical manifestations vary according to the extent of thrombus, the size of vessels involved and depth of bowel-wall ischemia. The only constant finding is pain out of proportion to physical findings. Progression is slow, often with steady low-grade symptoms for >48 hours; 75% of cases have such a clinical profile. Physical findings are dependent on the stage and degree of ischemic injury. Presence of GI bleeding, fever, guarding, rebound tenderness and serosanguinous ascitic fluid indicates progression to bowel infarction.

The absence of specific symptoms, signs or laboratory tests makes the diagnosis of MVT difficult and delay in diagnosis up to 48 hours is frequent. In the past, 90%-95% of cases were diagnosed only at laparotomy, but with advanced imaging technology pre-operative diagnosis is possible in most cases. For diagnosis within 6-12 hours, non-invasive imaging by X-ray, USG, CT or MRI plays an important role. Features of pneumatosis intestinalis, air in portal or mesenteric venous system, thrombosis, liver/splenic infarcts, and focal thickening of bowel with lack of post-contrast enhancement are highly specific. Other features are ascites, free air in the peritoneum, solid organ infarction, mesenteric edema, engorged mesenteric veins, presence of collaterals, and features of intestinal obstruction. In comparison to conventional CT, multi-detector helical CT with CT angiography and MRI with gadolinium-enhanced MR angiography are almost 100% sensitive. Mesenteric angiography is valuable for better delineation of thrombosis in smaller vessels and for definitive preoperative diagnosis.

In MVT, 95% of cases have segmental involvement of jejunum, ileum or both, and 5% have involvement of terminal ileum and right colon. Inferior mesenteric vein involvement is seen in less than 6%. In addition to SMV, 32%-56% of cases have involvement of portal or splenic vein.

The division into acute, subacute and chronic MVT seems to be helpful in management. Cases with acute MVT are at maximum risk for development of bowel infarction, which is seen in up to 66% of cases. Subacute cases may rarely progress to intestinal infarction because of new thrombosis. Subacute MVT can be due to extension of thrombosis at a rate that is rapid enough to cause pain but that permits collaterals to develop.

In acute MVT, presence of peritonitis mandates laparotomy with resection of infarcted bowel with the aim of conserving as much bowel as possible, and institution of anticoagulant therapy to prevent recurrence and progression of thrombosis. The role of thrombolysis and thrombectomy is limited to patients with fresh thrombosis of large mesenteric veins. In patients without signs of peritonitis in acute or subacute MVT, immediate heparinization is advocated; oral anticoagulation is instituted once there is no evidence of ongoing ischemia. In chronic MVT, control of GI bleeding with endoscopic or pharmacological interventions and long-term anticoagulation are the mainstay of treatment.

Anticoagulation in all and surgical treatment as indicated remain the mainstay of treatment; with such a strategy mortality rates are now below 15%. Almost 50% of operated cases have in-hospital complications like short-bowel syndrome, wound infection or sepsis. Around 38% of cases have relentlessly progressive disease. Recurrence rates have decreased to less than 15% with prompt anticoagulation, and the site of recurrence in 60% of patients is the site of previous thrombosis or at the site of anastomosis.

In conclusion, mesenteric venous thrombosis must be kept in mind as a possible diagnosis in patients with abdominal pain out of proportion to physical findings. Early imaging allows for immediate anticoagulation and seems to improve outcome. Surgical treatment becomes mandatory in presence of signs of peritonitis or perforation. Long-term follow up of these patients is needed to monitor for development of recurrence, portal hypertension and/or bowel stricture.

References


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