Mesenteric Venous Thrombosis in a Referral Hospital in East Africa: A Retrospective Study of Four Cases

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Introduction: Acute mesenteric venous thrombosis is a rare condition with the most common site of thrombosis development being the superior mesenteric vein. Patients predisposed to this condition tend to develop a disruption to Virchow’s triad of endothelial injury, stasis and hypercoagulability. In the acute form the presentation is with bowel ischaemia and so a diagnosis before bowel gangrene develops remains a challenge. The limited experience with this condition in the East African region shows that a delayed diagnosis due to limited investigative capacity results in patients’ experiencing acute renal failure and a high mortality. This review describes the aetiology, clinical features and management of acute mesenteric venous ischaemia.

Methods: A descriptive retrospective review of four patients over an 18-month period. Demographic and clinical data was extracted from the patients’ clinical files and manual analysis using a spreadsheet was performed.

Results: Over an 18-month period, four patients were reported. All patients had a delay in diagnosis with acute symptoms persisting for 5 days up to 21 days. Two patients died within 30-days post-operatively of complications which included short bowel syndrome and acute kidney failure. Two patients survived developing complications from short bowel syndrome and another the complications of acute kidney injury requiring haemodialysis.
Conclusions: A delay in diagnosis of acute MVT characterises this short case series. This resulted in all cases presenting with gangrenous bowel and hence the high mortality. Venous clot propagation is prevented with anticoagulation which is associated with decreased mortality and recurrence. Thrombolysis and thrombectomy should be considered in certain circumstances to prevent bowel of questionable viability. In the last four decades the mortality from MVT has decreased and currently stands at 10-20% however there is no sufficient literature in East Africa to make this judgement.

Keywords: MVT: mesenteric vein thrombosis; AMI: acute mesenteric ischaemia; short case series; blood coagulation disorders; thrombectomy; thrombolysis; East Africa.

1. INTRODUCTION

In the Western world, mesenteric venous thrombosis is now diagnosed more easily and at an early stage because of access to highly specific and sensitive diagnostic imaging modalities. Routine testing for hypercoagulable conditions has resulted in a fall in the proportion of cases in which the aetiology remains unexplained [1] Due to early diagnosis before the development of intestinal infarction, use of anticoagulation therapy and prompt surgical intervention the mortality associated with acute mesenteric venous thrombosis has decreased. Mesenteric venous thrombosis tends to present in acute, subacute and chronic subtypes. New onset symptomatic MVT is the result of Virchow’s triad (stasis of blood flow, endothelial injury and hypercoagulability) [1,2]. It is easy to diagnose on imaging however this condition is associated with a therapeutic dilemma as both operative and conservative means have significant risks.

New onset symptomatic thrombosis of the superior mesenteric vein and its branches without any evidence of collateralization is the presentation of acute MVT [3]. A typical patient presents with abdominal pain and unless diagnosed and treated promptly will lead to bowel infarction. Chronic and subacute MVT tends to be asymptomatic and some patients may present with bleeding due to portal hypertension.

The ischaemia due to mesenteric venous thrombosis may result in bowel infarction having a mortality up to 34% following bowel resection [4]. In the East African context, sparse literature is available about the presentation and management of this condition. This paper therefore describes the presentation and management of four patients with mesenteric venous thrombosis in a Referral Hospital in East Africa, followed by a review on the aetiology, clinical features and management of this condition.

2. METHODS

A retrospective descriptive review at a Referral Hospital in East Africa of four mesenteric venous thrombosis patients diagnosed at laparotomy over a period of 18 months was performed. The patients’ clinical files were used to extract and review data on demographics (age, sex), co-morbidities, risk factors, clinical presentation, management and outcomes.

3. RESULTS

Four patients were reported over an 18-month period. Table 1 and Table 2 summarise the demographics, risk factors, clinical features and management of the four cases reported with acute mesenteric venous thrombosis.

One patient developed short bowel syndrome resulting in malnutrition due to frequent bowel motions and eventually weight loss. Two patients developed acute and chronic renal failure secondary to dehydration due to diarrhoea post-operatively with one death. The fourth patient developed hepatorenal syndrome and eventually died 13 weeks post-operatively.

4. DISCUSSION

4.1 Aetiology and Risk Factors

Between 28% to 49% of cases tend to be idiopathic cases however one risk factor is normally recognised to be the predisposing factor in patients presenting with mesenteric venous thrombosis. The risk factors may be categorised into hypercoagulable states (due to malignancy and nephrotic syndrome), acquired and heritable coagulable thrombophilias (e.g: prothrombin G20210 mutation) and intra-abdominal processes (diverticulitis, trauma, splenectomy).
### Table 1. A summary of the four case series of patients presenting with mesenteric venous thrombosis

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Co-morbidities</th>
<th>Preliminary diagnosis</th>
<th>Duration of symptoms</th>
<th>Clinical features</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>F</td>
<td>Hypercoagulability, History of recurrent DVT; HIV negative</td>
<td>Intestinal perforation</td>
<td>5 days</td>
<td>Persistent and progressive abdominal pain radiating to the back</td>
<td>Exploratory laparotomy showed evidence of infarcted jejunal loop ~150cm in length. Proximal part of SMV was occluded with thrombus. A jejunojejunal end-to-end anastomosis was performed.</td>
</tr>
<tr>
<td>62</td>
<td>M</td>
<td>Peptic ulcer disease; HIV negative</td>
<td>Gastritis</td>
<td>21 days with 2 days of severe mid-abdominal pain</td>
<td>Epigastric pain which became generalised abdominal pain</td>
<td>Exploratory laparotomy showed evidence of extensive gangrene of the small bowel. Only ~40cm of bowel was left. An end-to-end jejunooileal anastomosis was performed. Proximal part of SMV occluded.</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>Recurrent history of DVT; HIV negative</td>
<td>Diverticular disease secondary to PR bleeding</td>
<td>6 days of generalised abdominal pain</td>
<td>Haemodynamically unstable (hypotensive and tachycardic)</td>
<td>Exploratory laparotomy showed evidence of extensive gangrene of jejunum and ileum and ~10cm of viable ileum left. An end-to-end jejunoileal anastomosis was carried out. Proximal part of SMV occluded.</td>
</tr>
<tr>
<td>27</td>
<td>M</td>
<td>Nile of note; HIV negative</td>
<td>Intussusception</td>
<td>7 days of colicky abdominal pain</td>
<td>Generalised colicky abdominal pain with pr bleeding</td>
<td>Exploratory laparotomy showed evidence of 3m of gangrenous small bowel. An end-to-end jejunoileal anastomosis was carried out. Proximal part of SMV occluded.</td>
</tr>
</tbody>
</table>
Table 2. Summary of Morbidity and Mortality for the four patients presenting with mesenteric venous thrombosis

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>F</td>
<td>Short bowel syndrome resulting in weight loss and frequent motions of stool (malnutrition). No evidence of anastomotic leakage post-operatively.</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>Weight loss and chronic renal failure due to frequent motions of watery diarrhoea (~15x/day); No evidence of anatomic leakage post-operatively. Death at 11 weeks.</td>
</tr>
<tr>
<td>27</td>
<td>M</td>
<td>Hepatorenal syndrome; No evidence of anastomotic leakage post-operatively. Death at 13 weeks</td>
</tr>
</tbody>
</table>

In a patient with a history of DVT, there should be a high suspicion for mesenteric venous thrombosis [5,6]. In 1965, Egeberg, coined the term ‘thrombophilia’ and this was used to describe a family having antithrombin deficiency and presenting with recurrent episodes of venous thromboembolism [7]. Recurrent thromboembolism has been associated with deficiencies in protein C, protein S, antithrombin, factor V Leiden, hyperhomocystinaemia and elevated levels of VIII, IX, XI and fibrinogen [8]. It is unclear whether heritable thrombophilias are uniquely associated with superior mesenteric vein thrombosis compared to splenic or portal vein thrombosis [9,10].

In 4-16% of patients presenting with acute mesenteric venous thrombosis, malignancy is a hypercoagulable risk factor [5,11-15]. As a systemic risk factor as well as a local risk factor, intra-abdominal tumours have a high risk of thrombosis even when the wall of the vein is not invaded by tumour. Studies have not compared the incidence of MVT in patients with blood malignancies, solid extra-abdominal tumours and intra-abdominal tumours. Inflammatory bowel disease is not associated with an increased risk of thrombophilia [16]. Inflammatory bowel disease is associated with inflammation and coagulation leading to a higher rate of extraintestinal and intraintestinal thrombosis [17,18]. In patients who have undergone colectomy for inflammatory bowel disease, there has been a 5% rate of acute mesenteric thrombosis. This increased risk of acute superior mesenteric vein thrombosis is due to the additive effects of surgical manipulation, systemic hypercoagulability and local inflammation [19].

An increased rate of both arterial and venous thrombosis is associated with myeloproliferative disorders. Acute and chronic MVT has resulted from myeloproliferative disorders in 8-18% of patients. Fiorini et al, showed that the JAK2 V617F genetic mutation predisposes to splanchnic vein thrombosis in 34% of patients with myeloproliferative diseases [10]. In more common anatomic sites such as the lungs and lower extremities, the JAK2 V617F gene mutation was only present in 1% of patients [10]. In paroxysmal nocturnal haemoglobinuria (PNH), portal and hepatic vein thrombosis is more common than mesenteric vein thrombosis [20].

In splanchic vein thrombosis, two or more risk factors whether acquired or inherited have been identified in patients. Orr et al., noted that in 17% of patients with chronic MVT, more than one procoagulant risk factor has been identified [21]. Therefore in some cases the understanding of a ‘two-hit’ hypothesis is needed [21]. Patients with intra-abdominal infection or with pancreatitis are more commonly predisposed to mesenteric venous thrombosis.

For the small number of patients in this case series, hypercoagulability was noted in one patient and a history of recurrent DVT in another patient. The 27 year old and the 50 year old patients had hypercoagulability due to a history of recurrent DVT but the exact aetiology was never established. For the other two male patients no other risk factors were identified.

4.2 Clinical Presentation

Mesenteric venous thrombosis presents in three forms: acute, subacute and chronic presentations [22]. The clinical features are determined by the timing and location of thrombus formation within the splanchnic vessels. Severe colicky mid-abdominal pain lasting a few hours and being out of proportion to the abdominal examination findings mimicking acute pancreatitis [23]. An insidious onset of symptoms with vague abdominal discomfort is evident and typically develops over 7-10 days. The patients presenting in this short case series tend to be
consistent with this duration. At least 2 days of abdominal pain are reported in over 75% of patients with MVT. Some authors limit the definition of acute MVT with less than 4 weeks’ duration of abdominal pain however patients may report abdominal pain persisting for more than one month \([5,24]\). Between 15%-70% of patients present with signs of peritonism which suggests intestinal infarction thus mandating laparotomy. For early diagnosis, a high index of suspicion is necessary as no symptoms or sign is specific for acute MVT \([1]\).

In this series, all four patients presented as an emergency with an acute abdomen and needed laparotomy. At laparotomy, all had extensive bowel gangrene and presented with late symptoms and signs. In our environment a challenge to establish early diagnosis is evident before gangrenous bowel develops due to occasional lack of imaging facilities. The recurrent history of DVT in two patients presented made acute mesenteric ischaemia likely on clinical grounds however the patients with bleeding per rectum made intussusception a more likely cause in our environment. All of the patients presented in this short case series had bowel resection and an end-to-end anastomosis of healthy bowel. None of the patients developed clinical signs or symptoms of bowel anastomotic leakage post-operatively. The main cause of mortality in the two patients that died was due to renal failure following short bowel syndrome in one patient and in the other patient due to hepatorenal syndrome.

The colon is less commonly involved than the small bowel due to collateralization into the systemic circulation via the inferior hemiazygous system, splenic vein and left renal vein \([13]\). The frequent anatomic sites for MVT include the ileum (64-83%), jejunum (50-81%) followed by the colon in 14% of patients. The duodenum is involved in only up to 4-8% of patients \([5,11]\).

4.3 Diagnosis

A prompt diagnosis is essential if any intervention is to be lifesaving. A high index of suspicion is required due to the nonspecific presentation of MVT. Unfortunately, laboratory testing and plain abdominal X-rays lack specificity and sensitivity to reliably confirm or exclude the diagnosis of MVT. When bowel gangrene sets in, thumb-printing or pneumatosis can be seen on the plain films and lactic acidosis may occur, however at this point the mortality is over 75%. Therefore intervention is required when the plain abdominal films are normal \([25]\).

The most reliable modality which is highly sensitive and specific to diagnose MVT is a portal venous phase contrast enhanced CT scan of the abdomen. A contrast enhancing vascular vasorum in the vessel wall and central low attenuation which represents the venous thrombus are the CT findings of MVT \([15]\). The reported accuracy of these CT findings in MVT is greater than 90\% \([5,15,26-28]\).

Abnormal bowel enhancement patterns, thickened/hazy mesentry, bowel wall thickening >3mm, indistinct bowel wall margins, distended luminal diameter of the bowel and ascites are the CT findings of intestinal ischaemia secondary to MVT. In the CT images, a layered pattern of bowel enhancement is visualised with hyperaemia of the mucosa and submucosa being represented by increased density. With increased and persistent venous obstruction, arterial vasospasm and bowel wall tension develops which results in bowel infarction. This may be visualised as an enhancement pattern which is homogenous with decreased density compared to the normal bowel wall. This represents transmural infarction with a sensitivity of 90\% \([29]\). Splanchnic angiography is the gold standard invasive investigation which distinguishes venous from arterial forms of AMI.

Angiography may also allow for intra-arterial therapy with vasodilators \([6]\). On angiography the findings include failure of emptying of arterial arcades, arterial spasm, reflux of blood back into arterial arcades, prolonged vascular blush, late fillings with thrombus of SMV \([30]\). If the patient is a candidate for intra-arterial therapy or if the patient with thrombophilia has new onset abdominal symptoms however and equivocal CT scan then angiography should be considered in the diagnosis of acute MVT. A 100\% sensitivity and specificity for the diagnosis of chronic or acute MVT is obtained with magnetic resonance angiography (MRA) \([31-33]\). A noninvasive investigation which is non-invasive and rapidly performed is Doppler ultrasound and this investigation is not capable of detecting thrombus in small mesenteric vessels. It has poor sensitivity (70-90\%) but good specificity (100\%) at detecting mesenteric venous thrombosis \([31-34]\).

In older case series, laparotomy was the diagnostic modality of choice to diagnose MVT.
However, recently after CT scanning detects or is suspicious for infarcted bowel then diagnostic laparoscopy is performed. However, despite mucosal and submucosal ischaemia, the serosa of the intestine may look normal because of shunting of blood from the mucosa and submucosa to the serosa due to increased intra-abdominal pressure [35]. If the intra-abdominal pressure exceeds 20 mmHg during laparoscopy, the SMA blood flow decreases and bowel ischaemia may be worsened [35]. After the diagnosis and treatment of mesenteric venous thrombosis, patients should be treated for thrombophilies to help in determining the duration of anticoagulation.

The initial diagnostic investigation of choice for MVT is abdominal CT with adequate venous contrast or magnetic resonance angiography which offer excellent diagnostic capabilities for patients with MVT. Angiography is only reserved when there is reasonable suspicion for MVT however the findings on CT are nonspecific. These diagnostic modalities are only available in well-resourced settings. Despite these diagnostic modalities the diagnosis of MVA is often made during laparotomy or at autopsy.

### 4.4 Management

The management of MVT depends on (i) diagnosing hypercoagulable conditions in patients and treating them with long-term anticoagulation and (ii) minimizing the extent of bowel resection in acute MVT and preventing bowel infarction.

Phlebotomy should be carried out in patients presenting with polycythaemia whilst anticoagulation with low molecular weight heparin should be given to patients with clotting abnormalities, even in those patients presenting with bleeding due to MVT-induced ischaemia. After bowel resection, heparin prevents recurrence of thrombosis (0% versus 19% in one study) [36]. When recurrence occurs, it is associated with a lower mortality (22% versus 59%) [13]. In patients not undergoing surgery, anticoagulation will completely recanalize thrombosed veins over time. A study showed vascular recanalization of 80% of patients being anticoagulated for mesenteric vein/portal vein thrombosis compared to only <10% of non-anticoagulated patients over 5 months [37]. After achieving appropriate anticoagulation, patients presenting with acute MVT and having a temporary risk factor should receive anticoagulation with warfarin for 3-6 months with regular follow up with INR measurements. The 50 year old gentleman reported in this paper was followed up in a haematology clinic and placed on long term anticoagulants. In patients with idiopathic MVT or with an underlying thrombophilia then lifelong warfarin is advised.

In some cases, lytic therapy with streptokinase, urokinase or tissue plasminogen activator is beneficial [38,39]. Mechanical thrombectomy is a useful option when acute large vessel thrombosis is identified [6,12]. This will lead to long term patency without the need for thrombolytic therapy. Transvenous thrombolysis and thrombectomy may be performed via transfemoral, transjugular and transhepatic approaches [3,40-45]. In the setting of ascites, the transjugular approach is preferred. A poorer outcome has been experienced when thrombolytic treatment is started more than 24 hours after presentation [46].

As an adjunct to anticoagulation, aggressive intravascular thrombolysis should be considered for patients with MVT without bowel infarction. In those patients that are not candidates for anticoagulation then surgery should be considered.

### 4.5 Surgery

Patients presenting with MVT should have nasogastric decompression, intravenous fluid resuscitation to correct hydration and acid base abnormalities and bowel rest initially preoperatively. Anticoagulation should continue intra-operatively with intravenous heparin. With acute MVT, the indications for surgery include haemodynamic instability and signs of peritonitis with bowel infarction. Bowel resection and anastomosis is most commonly performed. At least 4 units of packed red blood cells preoperatively are needed due to massive blood loss to the bowel. Preoperatively broad spectrum antibiotics should be given. When the viability of long ischaemic segments of bowel is questioned there are methods which have been developed to avoid resection of viable bowel. Resection of short non-viable segments of bowel should be carried out. Surgeons should not resect with wider margins than the grossly infarcted bowel in extensive resections.

In order to prevent extension of the bowel infarction, thrombolytic agents via catheters and intra-arterial papaverine which reduces arterial
spasm have been used [35,47,48]. Bowel segments of questionable viability should be reassessed during the first 12-48 hours post-operatively by performing a ‘second-look’ laparotomy. This approach limits the extent of bowel resection during the first laparotomy [5,35,49,50]. A study by Rhee RY et al., found that after initial bowel resection on 31 patients with MV, ‘second-look’ laparotomy in 14 patients revealed gangrene requiring bowel resection in all cases [5].

Therefore when bowel resection is performed for MVT, a second-look laparotomy should be considered in all cases. An intravenous infusion of one gram of fluorescein followed by bowel examination under Wood lamp illumination may detect poor perfusion of the bowel. Intraoperative Doppler ultrasound has also been shown to aid in the assessment of bowel viability [5,35]. Intravenous fluorescein was found to be superior to clinical judgement and to Doppler ultrasound in determining bowel viability [51].

4.6 Prognosis

Mesenteric venous thrombosis carries the best prognosis of all the aetiologies of mesenteric ischaemia. The presence or absence of bowel infarction determines the mortality rate in acute MVT. In a systematic review carried out between 1966 and 2002, the mortality rate with MVT was 44%. This is lower than the mortality associated with arterial ischaemia which ranges from 66-89% [52]. In developed countries, aggressive treatment of thrombosis and an improvement in early diagnosis have resulted in lower mortality rates. In 1994, Rhee et al reported a 27% 30-day mortality rate whilst in the current century the mortality rate stands at 10-20%. Therefore in the last four decades there has been a decrease in the mortality rate from MVT [52,12,14] however there is no sufficient literature in East Africa to make this judgement [53].

Patients that do survive have challenges associated with short bowel syndrome and malnutrition [3]. Therefore codeine, vitamin supplements and a change in diet is used to reduce the frequency of bowel motions associated with short bowel syndrome.

5. CONCLUSIONS

A high index of suspicion is required for an accurate diagnosis to be made of MVT due to the nonspecific symptoms, signs and laboratory tests. Only 3-15% of cases of acute mesenteric ischaemia are due to acute mesenteric thrombosis. In developed countries systematic testing for thrombophilia has become standard and therefore the proportion of idiopathic cases of MVT is likely to decrease. Contrast-enhanced abdominal CT detects MVT before bowel infarction occurs and is the diagnostic investigation of choice for MVT. Emergency laparotomy and aggressive intravascular therapy is needed when there is evidence of bowel infarction. Long-term anticoagulation shall be administered in patients with thrombophilia.

The short term mortality depends on an early diagnosis with aggressive treatment and whether bowel infarction is present. In the East African environment, early diagnosis of MVT remains a challenge due to the occasional lack of CT imaging facilities. When the diagnosis is not clear cut, then surgeons should always consider MVT especially if there is a history of hypercoagulability. Mesenteric venous thrombosis should also be considered as a possibility in patients presenting with rectal bleeding and although a late sign, if MVT is suspected in our East African environment, then early conservative measures in the form of anticoagulation and early operative management may lead to a decrease in mortality.

CONSENT

The author declares that written and informed consent was obtained from the patients for publication of this case series.

ETHICAL APPROVAL

As per international standard or university standard, ethical approval has been collected and preserved by the author.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES


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