

Intestinal thromboangiitis obliterans: Consequence of a delay in diagnosis

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Case report

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Abstract

Background: Thromboangiitis obliterans (TAO) or Buerger's disease is a form of peripheral vascular disease in young male smokers. The involvement of the intestine occurs only about 2% of the cases. Symptoms of peripheral vascular disease usually precede intestinal manifestations, although the latter can sometimes be the index presentation. The cessation of smoking usually, though not necessarily, prevents the progression of the disease and visceral involvement.

Case presentation: Our patient presented with diffuse abdominal pain along with bouts of vomiting and loose motions. He was a known smoker with a prior history of amputation of the right foot, four years before. Physical examination revealed abdominal distension and diffuse tenderness and guarding. An omental band attached to the tip of the appendix was discovered at the initial exploration along with dilated proximal bowel loops, for which a release of the omental band along with appendectomy was done. He developed an enterocutaneous fistula on the sixth postoperative day for which the abdomen was re-explored which revealed multiple segmental perforation in the jejunum and two subcentimetric perforation adjacent to each other in the distal ileum. Resection of the affected jejunal segment was performed followed by Roux-en-Y gastrojejunostomy and distal ileostomy. A feeding jejunostomy was also performed. The bleeding from the cut ends was unsatisfactory. The patient however had persistent feculent discharge from the wound for which a third exploration was done which revealed a leak from the gastrojejunostomy and feeding jejunostomy sites, both of which were repaired primarily. However, the patient developed septicemia with persistently elevated serum lactate levels which progressed to refractory septic shock and ultimately succumbed to the illness on 23rd postoperative day of the index surgery.

Conclusion: Acute abdomen in a young man, who is a chronic smoker and having an antecedent history of amputation of some part of an extremity for a nontraumatic cause should raise the suspicion of Buerger's disease of the intestine. Although it is a progressive disease and things are already late by the time intestinal symptoms manifest, early detection may give some scope of salvage and decreasing morbidity and mortality.

Background

Acute mesenteric ischemia is one of the many causes of acute abdomen, which may be missed unless there is a high index of clinical suspicion, which is imperative for early diagnosis and management. Impaired circulation, secondary to chronic narrowing of the mesenteric vasculature, manifests with postprandial abdominal pain and weight loss. Acute onset of ischemia, on the other hand, manifests as severe abdominal pain, with vomiting and blood mixed stool, eventually progressing to features of peritonitis. ⁽¹⁾ Early exploration is indispensable not only for resection of any necrotic bowel segment but also to rule out any focus of thrombus or emboli. CT angiography (CTA) is a useful initial investigation to demonstrate the narrowing of the vessels and ischemic changes in the gastrointestinal (GI) tract. A prior history of smoking and amputation in a case with clinical features of mesenteric ischemia is pertinent for

a probable etiology of Buerger's disease. However, histopathological characterization of the vessels in the resected bowel is diagnostic. The awareness of the histopathologists and exclusion of atherosclerosis and other vasculitic disorders are important for the diagnosis of this rare entity.

Case Presentation

A 45-year-old non-hypertensive and non-diabetic gentleman presented to the casualty with pain in the abdomen for ten days, along with vomiting and loose stools for five days. The pain was constant, diffuse, and severe, with an increase in its intensity for the last three days. This pain was associated with a non-bilious type of vomiting and loose stools. Besides, there was associated history of blood in stool for the last three days. The patient had a significant history of smoking with the amputation of right mid-foot years prior to this admission, detail records of which were not available. The patient claimed to have stopped smoking since the amputation. There was no history of alcohol consumption or any other co-morbidity. There was no family history of any similar illness.

On examination, the patient was afebrile, normotensive, conscious, alert, and cooperative. The pulse rate was 110 per minute. The abdomen was slightly distended with the presence of diffuse tenderness and guarding. The liver dullness was not obliterated, and the bowel sounds were sluggish. On the digital rectal examination, the rectum contained blood-stained fecal matter. Appendicular perforation peritonitis or an ischemic bowel pathology were kept as differentials (the possibility of Buerger's disease of intestine was never suspected). The ultrasonography of the abdomen showed dilated small bowel loops. His complete blood count, liver and renal function tests were within normal limits. Serum antinuclear antibody (ANA) and anti-neutrophil cytoplasmic antibody (ANCA) were negative.

On exploratory laparotomy, an omental band was found adherent to the tip of the appendix (Fig 1). This appeared to be causing an intestinal obstruction as proximal bowel loops were dilated. Hence, an appendectomy along with the release of the appendico-omental band was done. The patient clinically improved initially for a couple of days postoperatively, when oral liquids were started. However, symptoms of vomiting and blood mixed stool recurred, and the abdomen was tender. He started discharging pus from the midline abdominal wound from the second postoperative day, for which the wound was laid open. On the 6th postoperative day, there was feculent discharge from the wound for which he was re-explored, which revealed multiple patchy areas of gangrene in the jejunum starting 5 cm distal to the duodenojejunal (DJ) flexure up to 60 cm distally. There were multiple jejunal perforations in this involved segment of the jejunum. In addition, there were two small perforations adjacent to each other approximately 10 cm proximal to the ileocecal junction (Fig 2). The two feet of the affected jejunum was resected, but remarkably, the cut ends of the bowel showed minimal bleeding. A Roux-en-Y gastrojejunostomy and distal loop ileostomy were performed along with a feeding jejunostomy. The patient again developed feculent discharge from the wound site on a post-operative day 3 of the second surgery, for which another laparotomy was undertaken. The feeding jejunostomy and the gastrojejunostomy site was found to be leaking (Fig 3). A primary repair of the feeding jejunostomy and a falciparum ligament patch repair of the gastrojejunostomy leak sites were performed. However, the

patient developed septicemia with persistently elevated serum lactate levels which progressed to refractory septic shock and ultimately succumbed to the illness on day 23 of the first surgery.

The appendectomy and the jejunal resection specimens from the first two laparotomies were sent to for histopathology examination. The jejunal segment measured 70 cm in length. It contained multiple patchy gangrenous areas along with perforation approximately at distances of 3 cm, 5 cm, 15 cm, 37 cm, 42 cm, 50 cm, and 66 cm from one resection end. The corresponding mucosal surfaces showed transverse ulcers with bile staining and multiple transverse perforations at places. The largest ulcer measured 5 cm in length, whereas the smallest one measured 0.5 cm. The jejunal wall was paper-thin at the gangrenous patches, and the serosa showed the presence of fibrinous exudates. The intervening mucosa was oedematous and erythematous. The cut surfaces of the mesenteric vessels did not show any thrombi.

Microscopy from different areas showed multiple intestinal ulcers that were superficial mucosal, deep, and transmural (Figure 4a). The submucosa was fibrotic and contained mixed inflammation. Notably, vascular pathology was demonstrated in both arteries and veins of small and medium caliber at the ulcer base as well as in the submucosal vessels underneath the non-ulcerated mucosa (Figure 4b). The small and medium-sized arteries showed near-total to complete obliteration by intimal proliferation that showed peculiar fibro cellular hyperplasia in a myxoid stroma. The proliferated intima contained refractile red degenerated elastic material in a few arteries. The corresponding internal elastic laminae of these arteries were extremely hypertrophic, markedly tortuous, and at places crumpled (Figure 4c). Nevertheless, in a few arteries, the internal elastic lamina showed abrupt discontinuity at places. The arteries did not show any inflammatory infiltrate except for a few where infiltration of the media by a few histiocytes and lymphocytes was noted. The submucosal veins showed a spectrum of changes from containing fresh fibrin thrombi (Figure 4d) to old occlusive thrombi completely/ near-completely obliterating their lumina. The fresh fibrin thrombi were partially occlusive with a cellular inflammatory infiltrate traversing the vessel wall and beyond. Organization and recanalization of these thrombi were also noted. Both the arteries and the veins showed mild adventitial fibrosis. No cholesterol cleft, atheromatous plaque, calcification, or fibrinoid necrosis was noted in any of the vessels to suggest atherosclerosis or other forms of vasculitis. Similar changes were also observed in the resected specimen of the appendix. A diagnosis of thromboangiitis obliterans involving the gastrointestinal tract was rendered.

Discussion And Conclusion

Thromboangiitis obliterans (TAO) is a non-atherosclerotic, vasocclusive disease of young smokers involving small and medium-sized arteries and vein, although about 5% non-smokers tend to develop the disease. ⁽²⁾ The exclusive male status is also partially offset by a recent rise in its prevalence among the women as a result of increased smoking activity in the women. ⁽²⁾ The disease typically affects the upper and lower limbs and is one of the common global causes of peripheral vascular disease. The disease is also called “Buerger’s disease” or “Morbus Winiwarer-Buerger” to commemorate Dr. Leo Buerger, and Dr. Felix von Winiwarer, the American and Austrian surgeons who are credited with the first descriptions of the disease. ⁽³⁾

The involvement of the gastrointestinal tract is fairly uncommon and that causing mesenteric ischemia is a rarity. The spectrum of clinical manifestation of Buerger's disease of the GI tract may range anything from chronic intermittent pain abdomen, weight loss, chronic diarrhea, to sometimes acute abdomen. The small intestine is the most commonly affected, which is usually segmental. Isolated involvement of colon and simultaneous involvement of small and large intestine have also been reported. ⁽³⁾ In most cases, an antecedent history of amputation of some part of one or more extremities was consistent. However, out of 50 cases of Buerger's disease involving the GI tract that has been reported, 12 cases have intestinal involvement as an inaugural presentation. ⁽⁴⁾

Cessation of smoking has high preventive value. Only 5% of ex-smokers progress to develop the disease in another site following abstinence from smoking in contrast to 100% progression rate in the patients who continue to smoke. ⁽⁵⁾ The case being reported was a known smoker for 20 years, which he quit after he underwent a right midfoot amputation for Buerger's disease, four years before. Despite this, he landed up in acute mesenteric ischemia and developed segmental patchy gangrene and perforation of the small intestine, which makes this case unique. A similar phenomenon was previously reported by Kamiya et al, where the patient had a right below-knee amputation. ⁽⁶⁾

Acute mesenteric ischemia evolves through 4 stages, as proposed by Haglund et al. ⁽¹⁾ The first one is the hyperactive stage which is characterized by intermittent severe abdominal pain, vomiting, and loose stools often associated with blood. The bowel sounds are usually exaggerated in this phase. This is followed by a paralytic stage in which the patient experiences continuous diffuse abdominal pain, abdominal distention, and absent bowel sounds. The stage of deranged fluid balances follows, which leads to leakage of intestinal content into the peritoneal cavity when the patients develop frank peritonitis. If not detected and managed early, these cases progress into a stage of irreversible shock. Hence the index of suspicion needs to be high in patients presenting with an acute abdomen especially when there is an antecedent history of chronic smoking and amputation involving the extremities. Severe abdominal pain out of proportion to physical findings should be assumed to be in lines of acute mesenteric ischemia unless proven otherwise, which is a Level 1b recommendation of the World Society of Emergency Surgery. ⁽⁷⁾ In our case, the patient presented with non-bilious vomiting and loose stools, which persisted even in the postoperative period after the index laparotomy, which we overlooked. The patient continued to pass blood mixed stool during the post-operative period, which was a useful clue to suspect mesenteric ischemia, which was again missed, which proved costly. Eventually, the patient developed fecal discharge from the wound for which he needed to be re-explored. By this time, he had multiple segmental necrotic patches in the jejunum along with two perforations in the ileum, which triggered the possibility of a segmental mesenteric inflammatory/ischemic etiology.

As per the World Society of Emergency Surgery guidelines, CT angiography (CTA) is an investigation modality of choice and should be performed in all high suspicious cases without delay. It suggests that even deranged renal parameters should not be considered as a contraindication for performing a CT angiography. CTA of the small intestine has a similar appearance as that seen in the extremities.

However, the degree of corkscrew appearance is less evident, and characteristically there is the involvement of the branches instead of the main trunk. ⁽⁸⁾ CTA may also demonstrate intestinal dilation, lack of vascularity, pneumatosis intestinalis, and gas in the portal vein. ⁽⁷⁾ According to a study by Nuzzo et al, bowel loop dilatation is the strongest predictor of intestinal necrosis. ⁽⁹⁾ However, the index patient did not undergo CTA as Buerger's disease of the intestine was never suspected. Intraoperative Doppler study can be useful in assessing the vascularity of the bowel segment whenever there is a suspicion irrespective of the color of the bowel (healthy or dusky). Intraoperative palpation of the superior mesenteric artery can be beneficial to rule out thrombosis. ⁽⁷⁾

Elevated serum lactate > 2 mmol/L is an important predictor of intestinal necrosis (Nuzzo et al) and levels greater than 2.7 mmol/L is a predictor of ICU death (Leone et al). ⁽⁹⁾⁽¹⁰⁾ The presence of elevated lactate, organ failure, and bowel dilatation should prompt immediate exploration. ⁽⁹⁾ Serum D-dimer is not predictive of acute mesenteric ischemia. ⁽¹¹⁾ In this patient, lactate levels were persistently elevated even after multiple explorations, and ultimately patient developed high anion gap metabolic acidosis.

Intravenous fluids should be administered to improve end-organ perfusion, crystalloids being the fluid of choice. ⁽¹²⁾ Goal-directed fluid therapy should be carried out with continuous monitoring of hemodynamic parameters and urine output. Supplemental oxygen should be administered immediately to improve oxygen supply to the ischemic bowel loops. ⁽¹³⁾ Vasopressors should be avoided as it further reduces the splanchnic blood flow, although vasopressors such as dobutamine and a low dose of dopamine and milrinone can be considered which have minimal effect on splanchnic blood flow. Although some studies have advocated the use of heparin in cases of mesenteric ischemia (Bodabilli et al), other studies have reported against it (Abdullah et al). ⁽¹⁴⁾⁽¹⁵⁾ ESTES guidelines recommend the use of heparin mostly for mesenteric venous thrombosis and mesenteric arterial embolism. Intestinal mucosal ischemia can lead to translocation of gut bacteria and endotoxins. Therefore broad-spectrum antibiotics should be initiated although any fixed regimen of choice has not been established. ⁽¹⁶⁾

Damage control surgery should be performed if there is a suspicion of mesenteric ischemia, as the viability of suspicious-looking bowel loops can be assessed later, and the status of the anastomotic site can be inspected postoperatively. In our case, the bowel during the first laparotomy was grossly pink and normal looking. An appendectomy, to which the omentum was adherent, was done before closing the abdomen. However, in the second laparotomy, there were multiple segmental necrotic patches in the jejunum, starting from 5 cm from the DJ flexure, through a length of 60 cm of the jejunum. There were two other perforations in the distal ileum adjacent to each other, 10 cm proximal to the ileocecal junction. The necrotic jejunal segment was resected and Roux-en-Y side to side gastrojejunostomy with a hand-sewn side to side jejuno-jejunostomy was performed. The ileal perforations were brought out as a loop ileostomy after sending the perforation margins for biopsy. A feeding jejunostomy (FJ) was also performed. The laparotomy wound was again closed with the placement of the abdominal drain, as the possibility of a Buerger's disease of the small bowel was yet to be figured in our differentials. In hindsight, a temporary abdominal closure with Bogota bag or vacuum-assisted closure would have been a better

alternative. Vacuum-assisted closure helps in wound healing and also renders an option for a scheduled second-look laparotomy within 48 hours of exploration. ⁽¹²⁾

A stoma is always preferable over an anastomosis, particularly when vascularity of the bowel loop is in jeopardy. But the proximity of the proximal resection margin being very close to the DJ flexure and the concurrent terminal ileal perforation, precluded the possibility of a proximal stoma, for which we were forced to consider a Roux-en-Y gastrojejunostomy with a jejunojunction along with a distal loop ileostomy. Some cases requiring repeated resection of the intestine have been reported in the literature. ⁽¹⁷⁾ Even in our case, a third exploration was required due to leakage from the GJ and FJ sites, which again necessitated fixing the leakage sites, although the mission was not successful.

Histologically, small and medium-caliber arteries and veins are both affected with thrombotic manifestations at variable stages of the organization. The acute stage arteriovenous changes are considered pathognomonic with intravascular fibrin thrombi having a centrifugal pattern of inflammatory infiltrate. The subacute changes show the organization of the thrombi with microabscess and/ or granuloma and giant cells, a tell-tale feature of Buerger's disease. The chronic features include recanalization and/ or intimal fibroplasia and luminal obliteration. ⁽³⁾ The index case showed a spectrum of arteriovenous changes ranging from acute (fibrin thrombi in the veins with inflammation spreading to the periphery) to subacute (organizing thrombi with inflammation of the arteriovenous wall) to chronic (arterial intimal fibroplasia and luminal obliteration with hypertrophic internal elastic lamina and adventitial fibrosis and recanalizing thrombi in the veins) suggesting a chronic ischemic process with superimposed acute insult.

The role of histopathology in such cases is manifold. First of all, the vasculopathy is characteristic, although often missed by the histopathologists due to its rarity. Also, the history of amputation or Buerger's disease may be unavailable to the pathologists if the clinical suspicion of intestinal Buerger's disease is lacking. Secondly, the pathologists play a pivotal role in identifying the stage of vasculopathy, thereby documenting disease pathogenesis. Lastly, the exclusion of relevant vascular diseases, especially atherosclerosis and vasculitis especially polyarteritis nodosa can be made by histopathological examination.

A high index of clinical suspicion is crucial for embarking upon early supportive measures. The clinical course can often be deceptive and get further complicated when they land up in septicemia auguring a fatal outcome. CT Angiography should be done early at the slightest suspicion and especially so in a smoker with a prior history of amputation. Exploratory laparotomy and resection of the infarcted/ perforated/ strictured bowel remain the mainstay of therapy, although single surgery often does not suffice due to the patchy nature of the disease. Despite adequate treatment, a mortality rate of 30% has been reported. ⁽³⁾The histopathology of the vessels in the resected intestine is typical of this disease.

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

Consent was taken.

Availability of data and materials:

Not applicable.

Competing interests:

The authors do not have any conflict of interest.

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Authors' contributions:

SSM, TM, PK contributed to the clinical and surgical aspects of the case report. SM contributed to the histopathological aspect of the case report.

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Abbreviations

TAO: Thromboangiitis obliterans

CTA: CT Angiography

ANA: Antinuclear antibody

ANCA: Antineutrophil cytoplasmic antibody

ESTES: European Society of Trauma and Emergency Surgery

DJ: Duodenojejunal

GJ: Gastrojejunostomy

FJ: Feeding jejunostomy

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Figures

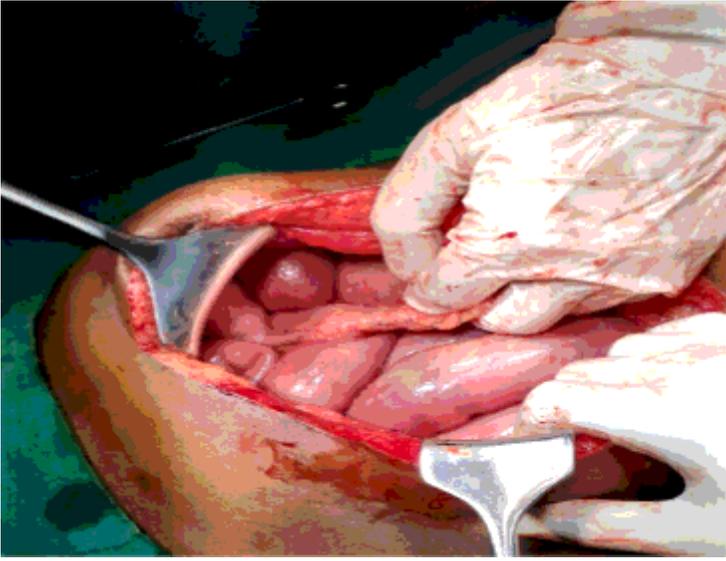


Figure 1

1st exploration-band adherent to appendix.

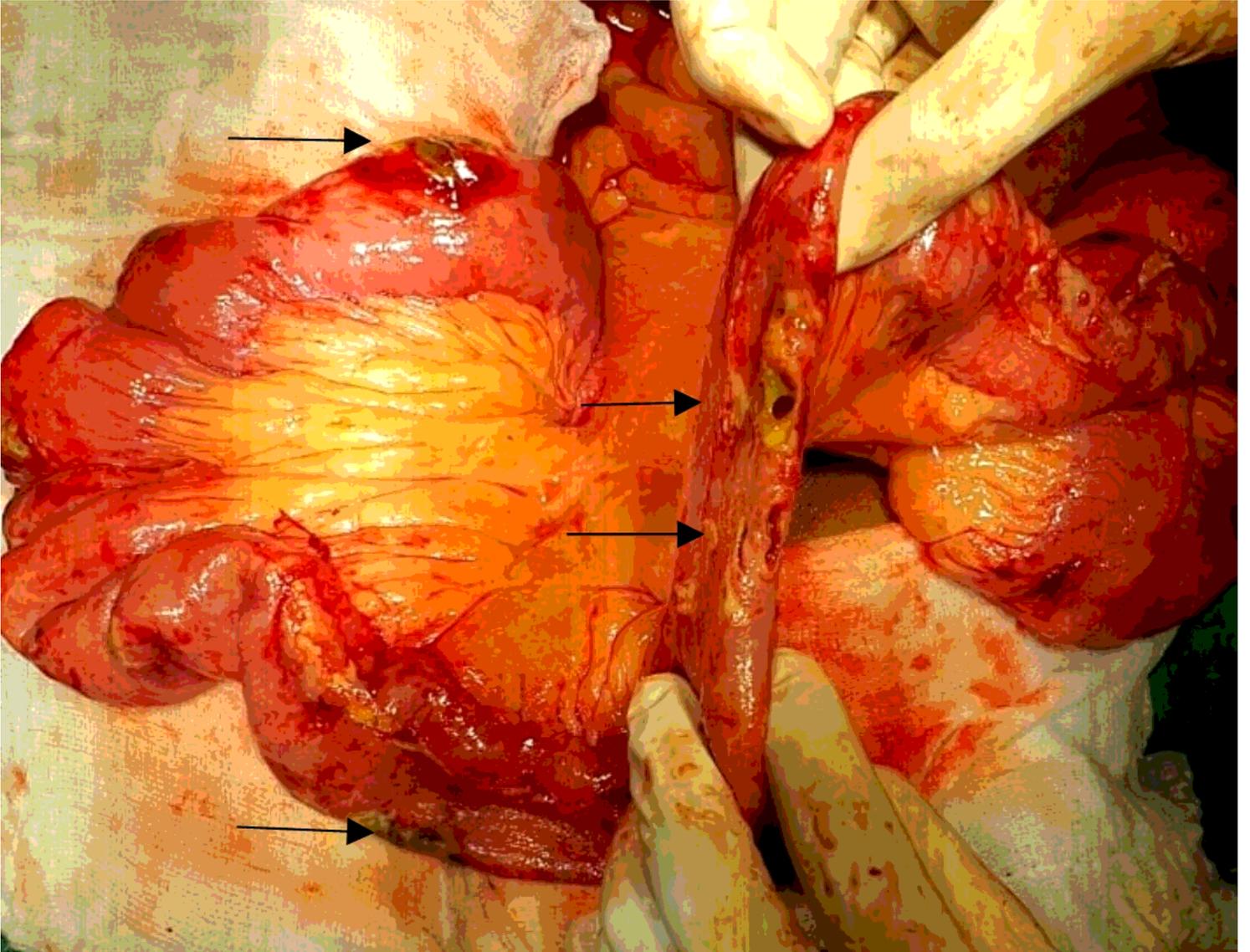


Figure 2

Black arrow showing multiple areas of perforation in 2nd exploration.

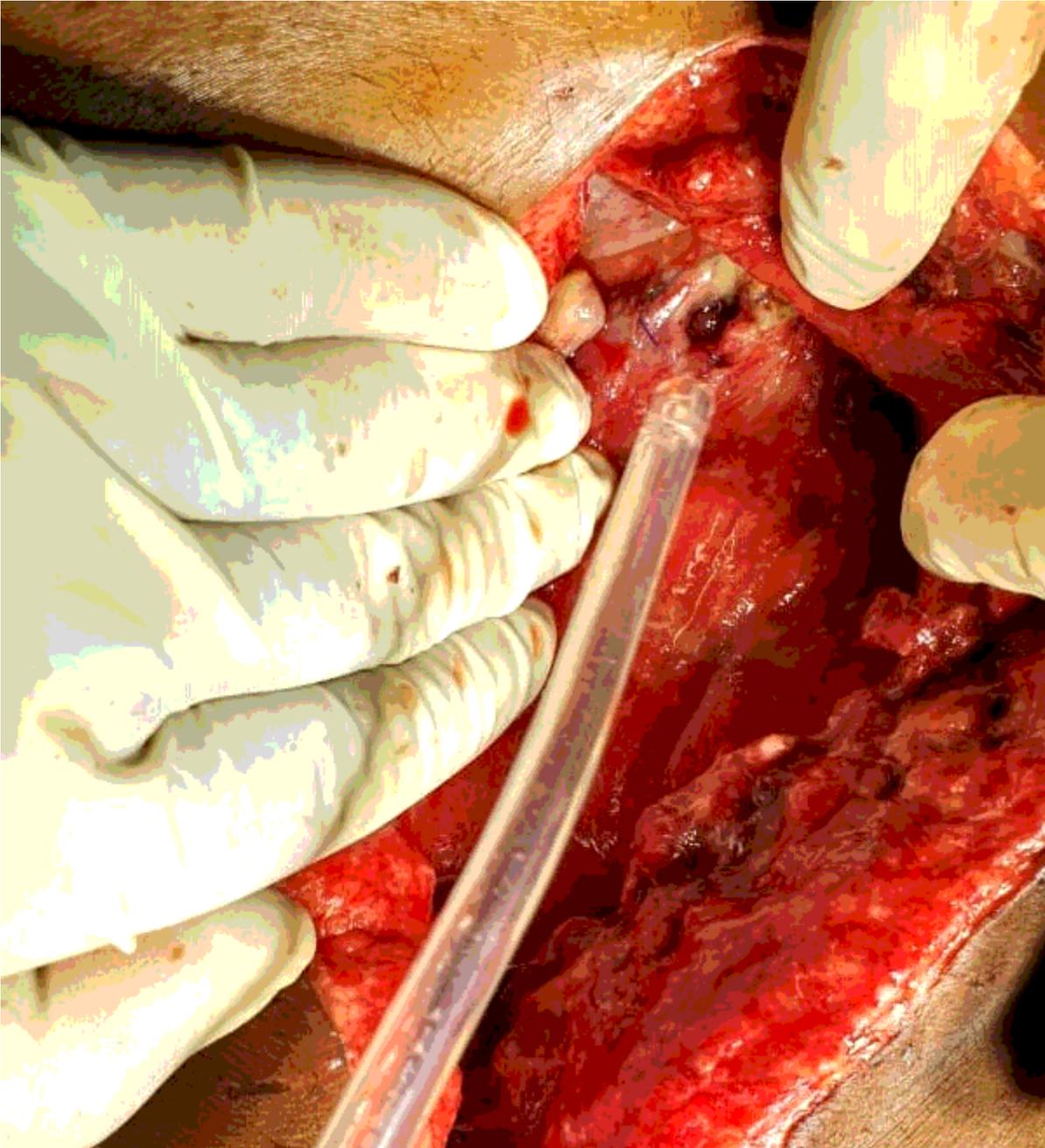


Figure 3

Leak from GJ site in 3rd exploration.

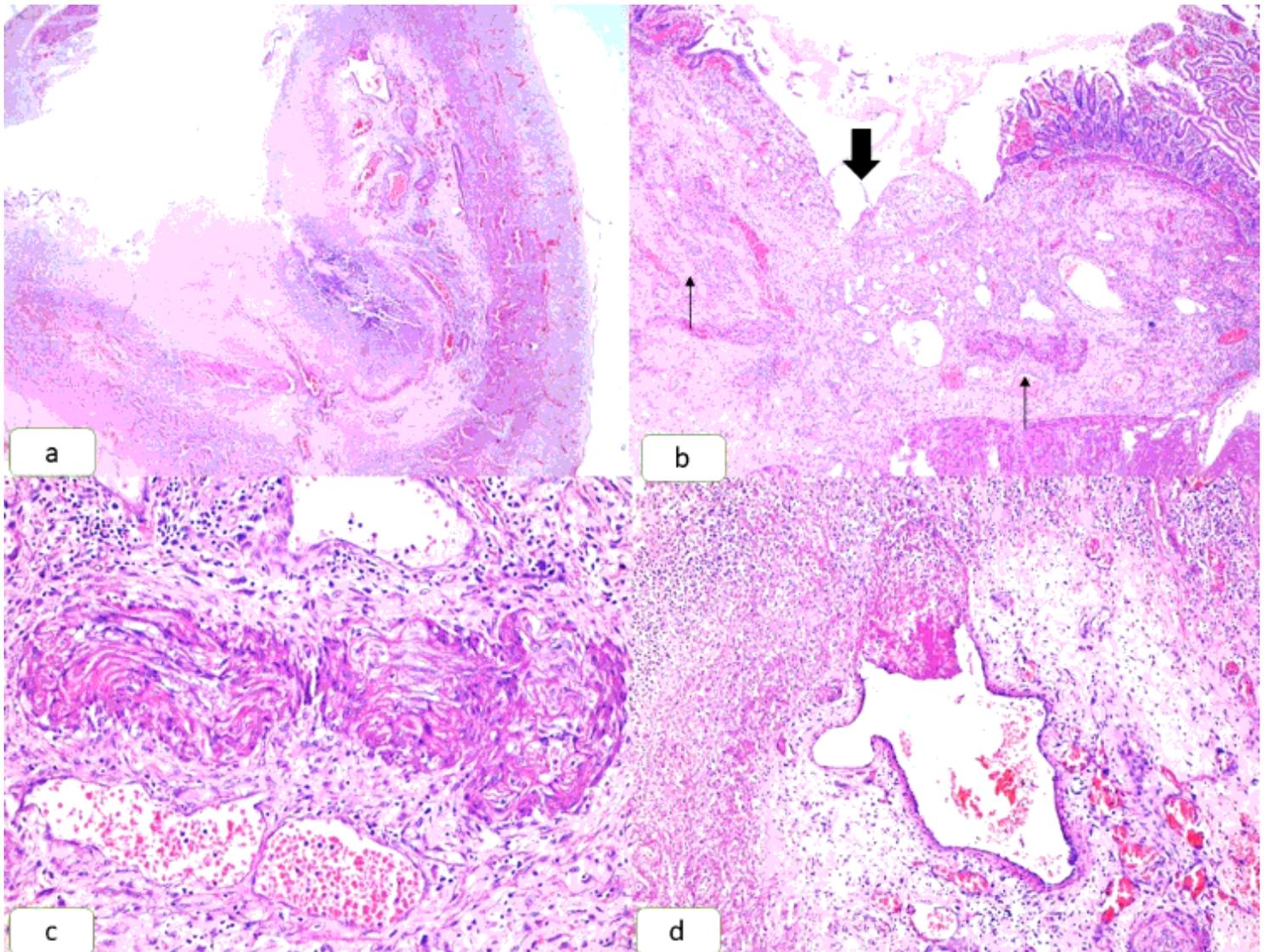


Figure 4

a: Low magnification showing an intestinal ulcer (Hematoxylin and Eosin, 20x) b: The changes in the blood vessels (thin black arrows) highlighted at the base of an ulcer (thick black arrow) (Hematoxylin and Eosin, 40x) c: The arteries showing typical changes with luminal occlusion, myxoid subintimal matrix and hypertortuous eosinophilic internal elastic lamina (Hematoxylin and Eosin, 200x) d; One of the veins showing occlusive fibrin-rich thrombus (Hematoxylin and Eosin, 100x)