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Ischemic colitis with non-gangrenous, stenotic evolution following hemorrhagic shock

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Ischemic colitis with non-gangrenous, stenotic evolution following hemorrhagic shock. A case report and review of the literature.

INTRODUCTION: *Ischemic colitis (IC) accounts for more of the half of total diagnosis of gastrointestinal ischemia. It is a challenging condition due to non-specificity of the symptoms at onset, inconstant behaviour and a wide range of clinical gravity with a different therapeutic approach. A classification of IC into gangrenous, stricturing and transient forms can be considered.*
CASE REPORT: *In the presented case, due to hypovolemic hemorrhagic shock, the patient developed a progressive IC without gangrene but slowly evolving in multiple colonic strictures with general serious clinical condition. Endoscopy was used to confirm diagnosis and to tempt a pneumatic stricture dilation which resulted ineffective. A diverting stoma was required and an elective subtotal colectomy was carried out after resolution of the acute phase.*
CONCLUSIONS: *IC may present with a large spectrum of clinical conditions. In acute shocked patients it must be always considered when a complicated abdominal picture is present. Immediate surgery is not always required considering the spontaneous resolutions of the milder forms. Strictures are the most frequent evolution following the intermediate non-gangrenous presentation and initially they can be treated conservatively with postponed tailored resection after the healing of the diffuse mucosal injuries.*

KEY WORDS: Ischemic, colitis, Shock, Stricture

Introduction

Ischemic colitis (IC) is the most common form of gastrointestinal ischemia. Patients present with either occlusive or non-occlusive vascular disease. Among cases of non-occlusive IC, shock of cardiogenic, hypovolemic, traumatic, hemorrhagic and septic origin is the more relevant cause followed by mechanical conditions or collateral effects of medications [1-2].

In critical patients the associated hypovolemia may induce different grade of IC, but the complexity of the clinical scenario in such cases might induce delay and pitfalls in the diagnostic process [2-3]. This is due to a spectrum of clinical presentation, characterizing IC, that ranges from a mild or a transient ischemia to an acute fulminant colitis with gangrene. The latter requires urgent surgery with colonic resection when possible, the reversible form with a mild clinical picture can be usually managed conservatively unless the development of complications such as strictures. The impact of the clinical onset and of the presentation varies, depending on the severity and the extent of the colonic disease [2,4]. On these clinical bases a classification of IC into gangrenous, stricturing, and transient forms was proposed [5]. We report a case of non-gangrenous IC following a severe hemorrhagic shock, complicated by strictures formation and based on this experience we analyse the criteria of

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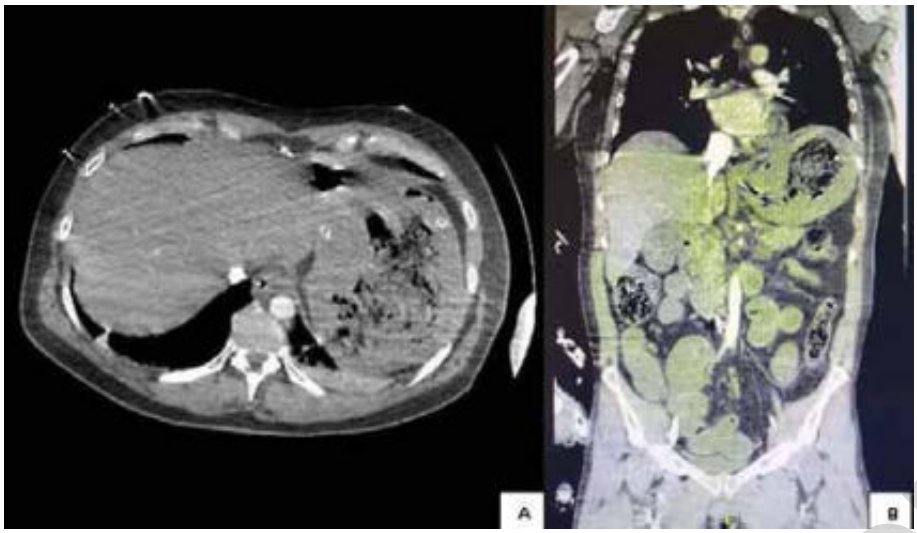

Fig. 1: Rectos igure 1. CT showing gastric dilation with haematic content without contrast medium extravasation (A-B).

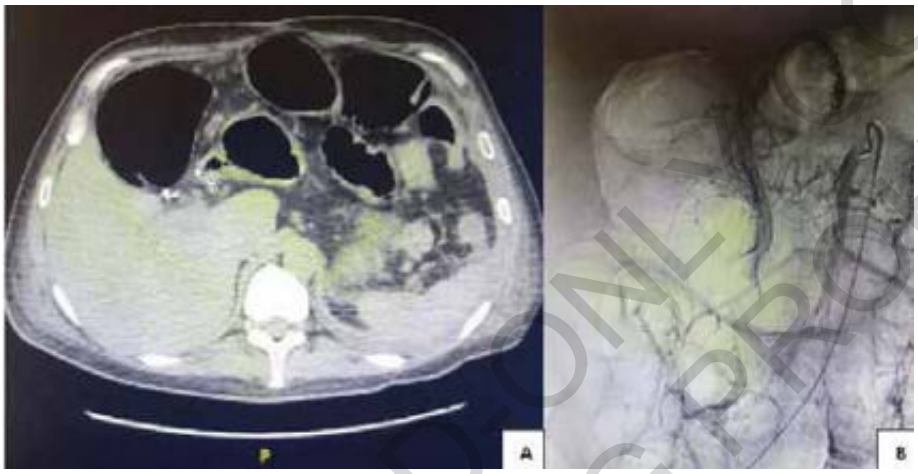

Fig. 2: CT showing large and small bowel dilation without obstruction and a pancreatic artery ectasia (A). Arteriography showing normal vascular anomaly without active bleeding (B).

differential diagnosis and the timing and features of the treatment in this clinical setting.

A 47-years-old man was admitted overnight to the emergency department with an hemorrhagic shock due to a severe hematemesis. Four weeks earlier the patients had been admitted to our medical department due to a gastrointestinal bleeding and had been investigated by esophagogastroduodenoscopy which had revealed a gastric ulcer with active bleeding. He had been treated by endoscopic clips application and after recovery he was discharged. At home during this further hemorrhagic event, he presented massive hematemesis with following cardiac arrest. A successful resuscitation with oro-tracheal intubation was carried out by the emergency team promptly intervened and a valid cardiac activity was finally restored. At hospital admission he presented intubated with critical hemodynamic (80/40 mmHg, heart rate 120 beats/min, SO2 84%), sustained with continuous infusion of catecholamines and with a severe anaemia (hemoglobin value of 4 gr/dl) and he was promptly treated with blood transfusion and intensive care. The gastric tube showed continuous haematic drainage. An esophagogastroduodenoscopy was carried out in the shock room of the emergency department and showed in the gastric body and fundus a large amount of blood and clots. Despite lavages and aspiration, endoscopy could not completely aspirate the gastric haematic content offering limited exploration, whereas stable healing of the known bulbar ulcer and no signs of duodenal recent bleeding were observed. The patient therefore underwent contrast CT which showed gastric dilation with haematic content but no contrast medium extravasation (Figs. 1 A-B). The interventional radiologist gave no indication to angiography. The patient despite intensive care and vasoactive treatment showed life-threatening unstable hemodynamic and therefore laparotomy as savage procedure was decided on. An emergency laparotomy with anterior gastrotomy was carried out and all the gastric content was aspirated allowing, by a laparoscope, a complete gastric exploration with no signs of ulcers or active bleeding. Soon after surgery the patients was admitted in the intensive care unit and recovered in few days with no vasoactive sustained stable hemodynamic. Wide spectrum antibiotic treatment, artificial feeding and proton-pump-inhibitors were administered. Despite transanal and gastric tubes

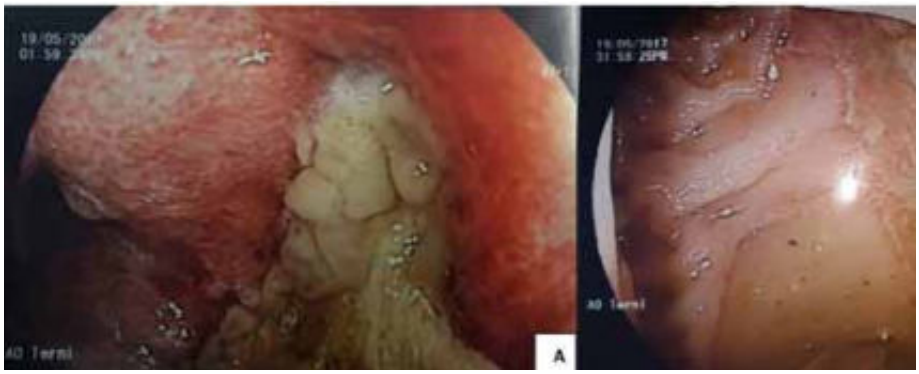

Fig. 3: Imoidoscopy showing hyperaemia, edema, fibrin deposits (A) and wide ulcers (B).

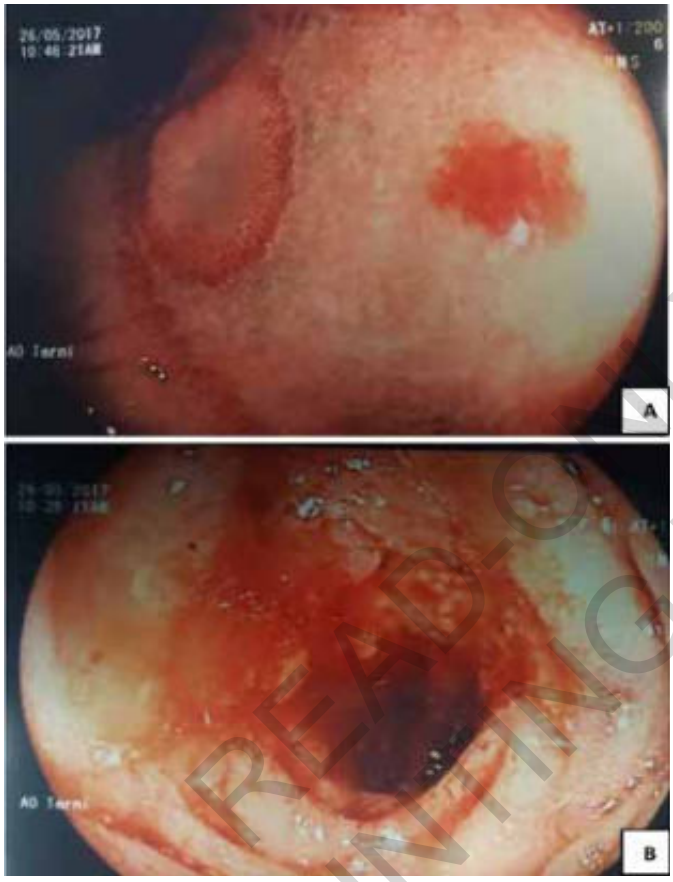

Fig. 4: Control colonoscopy showing partial healing of the ulcers (A). Aspect of the serrated stricture of the left colon after pneumatic dilation (B).

Fig. 5: Trans-stomal gastrografin enema showing multiple stenosis involving the right, transverse and left colon.

drainage a progressive abdominal distension and systemic inflammatory response occurred. CT confirmed large and small bowel dilation without obstruction (Fig. 2A) and a pancreatic artery ectasia further investigated by arteriography which excluded vascular anomalies and any active bleeding (Fig. 2B). Since progressive complication of the above clinical picture with persistent low level of hemoglobin the patient underwent gastroscopy which showed normal mucosal picture, with healing of the gastrotomy and of the former bulbar ulcer and no bleeding lesions. Rectosigmoidoscopy instead revealed hyperaemia, oedema, fibrin deposits (Fig. 3A) and wide ulcers (Fig. 3B). Histologic on colonic biopsy excluded active form of specific colitis but features referable to IC. No Clostridium difficilis was detected. Mesalazine, parenteral nutrition and antibiotic were administered. Control endoscopy one week after showed partial improvement of the above described ulcers (Fig. 4A) and revealed a serrated stricture of the left colon. A pneumatic dilation by Hercules® 3 Stage Wire Guided Balloon (Cook Medical, Bloomington, Indiana 47402-0489, United States) at two Atm was carried out (Fig. 4B). Nevertheless no significant benefit was observed in the following clinical course and still severe abdominal distension was evident. The persistence of the colonic stric-

ture, the impossibility of excluding further segmental stenosis in the proximal colon and the still active lesions in the sigmoid and rectum guided the decision not to perform immediately a subtotal/total colectomy. Therefore we preferred to carry out a decompressive cecostomy as first approach. After surgery local and general conditions promptly improved, inflammation indexes normalized, the patient started oral feeding and he was finally discharged. Eight weeks after the complete recovery the patient was admitted to our unit and underwent trans-stomal gastrografin enema (Fig. 5) which showed multiple stenosis involving the right, transverse and left colon. Control endoscopy demonstrated complete healing of the post-stenotic left colonic mucosa. A subtotal colectomy was therefore carried out with gross specimen showing five segmental stenosis, the longest of 120 mm, respectively at 10, 125, 320, 390 and 450 mm from the distal resection margin. Final histology showed superficial erosion, atrophy, glandular distortions and inflammatory infiltrates, hemosiderin and mucus, all features referable to IC. The patients was discharged in 6th post-operative day without perioperative complication. At the current follow up the patient is doing well.

Discussion

IC accounts for more of the half of total cases admitted to hospital with diagnosis of gastrointestinal ischemia. It remains a challenging clinical condition due to non-specificity of the symptoms at onset and inconstant behaviour [4]. Although linked to the common cause of impaired blood supply to the colon, the different clinical presentations of IC, with variable prognosis, differ for the occlusive and non-occlusive origin, for the size of the vessels involved and the available collateral circulation, for the extension of the ischemia and mainly for the mucosal or full-thickness bowel wall involvement [4]. Based on these variables it is possible to define three groups of IC as previously systematically described by Marston et al. [5] in 1966: acute gangrene, mild colitis with ischemic stricture without gangrene and transient ischemia. The management of these three types of ischemic events is rather different. Gangrene is the most dramatic event and represent a life threatening condition especially in the elderly. It is characterized by large vessel involvement, insufficient collateral circulation, hypotension and pathogenic bacterial growth following necrosis. It was previously defined as ischemic infarction[6], infarction of colon [7], necrotizing colitis [8]. In this form the ischemia is associated to a full thickness necrosis and represents an emergency condition initially treated by replacement of blood volume and antibiotics to stabilize the patient. Emergency surgery is almost always required with colectomy tailored on the extension of gangrene, usually with end colostomy. In the elderly it could be a salvage procedure due to patient's critical general condition at hospital admission. This picture is generally associated to high mortality rate. Other patients present with intermediate gravity, sometimes in these cases the ischemia is secondary to other primary events such as hypovolemia in hemorrhagic shock and trauma. Ischemia usually is not trans-mural and shows segmental distribution. Diagnosis could be less immediate due to the concomitant abdominal picture such as in septic, shocked patients [5]. This form is strictly related, given the absence of gangrene, to the mucosal manifestations as ulcers and fibrin deposition and to the chronic fibrotic evolution with strictures formation. This group with ischemic strictures was originally described as regional colitis[9], stenosis [10], benign stricture [11], acute segmental colitis[11] and fibrosis and stenosis [12]. Postponed surgery is the treatment of choice and one-stage resection and anastomosis the most used procedure. Due to the severity of the clinical status or the gravity of the general conditions, a two stage approach is alternatively used especially if patients are admitted to hospital in emergency [5]. In the above two categories the ischemia of the bowel results in intestinal barrier changes and consequent immediate bacterial invasion. When a minimal amount of blood is supplied to the intestine as in the subacute form, it is enough to prevent a complete death, but it could not be sufficient to support a complete vitality and function of the mucosa. This may result damaged with altered membrane function and consequent bacterial translocation with infection and risk of septic evolution, mainly due to the selection of aggressive anaerobic pathogens. The mechanism of the ischemia reperfusion setting was previously shown, in animal and human model, with clear description of cytokines cascade and pro-inflammatory mediators involved [13-14]. After ischemia or other similar damaging injury, when the rate at which surviving epithelial cells killed, exceeds the maximum rate at which new cells are replaced the injury is more evident. The deeper the lesion is, the slower the re-epithelization with loss of barrier function since the main damage is to the epithelial stem cells at the basement membrane zone[15]. The latter group of patients presents a picture of transient ischemia with milder symptoms and not critical clinical status with less extensive and less severe pathological injury to the bowel although sometimes not occluding stenosis can be observed. The etiopathology is based on small vessel occlusion but good collateral circulation, transient hypotension and only commensal, not pathogenic bowel flora growth are present. The picture was originally described as reversible vascular occlusion [16], as segmental infarction [17] and as partial occlusion [18]. This group requires no special treatment because the bowel damage generally presents complete spontaneous recovery with stricture and mucosal injuries resolution. Thus only medical treatment and repeated radiological and endoscopic controls are required. According to a more recent and detailed classification by Brandt and Boley six types of IC are

described: reversible ischemic colonopathy, transient, chronic ulcerative, ischemic colonic stricture, colonic gangrene and fulminant [19]. On a diagnostic point of view blood text although not specific, have been shown to have some utility in the acute severe forms of IC [20]. Standard radiological examination as plain abdominal radiography is not specific for the diagnosis of IC but can immediately show signs of complications such as free intra-abdominal air. Gastrografin® enema may suggest colonic ischemia based on unspecific features as thumbprinting, ulcers, ridges, edema and in the chronic evolution even strictures. Nevertheless when IC is suspected, the mandatory examination is computed tomography (CT) which is usually the second level imaging carried out when a severe abdominal picture is evaluated in the emergency department or in hospitalized patients. CT provides information of the bowel features including all the above revealed not specifically by enema. CT furthermore assess the extension of the modifications through the bowel wall, confirms the pneumatosis and pneumobilia and mainly provides accurate details of the vascular supply in the contrast enhanced arterial and venous phases. Non occlusive megacolon is also clearly shown as well as segmental stenosis. In recent years, colonoscopy has replaced barium enema as the most common diagnostic method and it is the gold standard for confirmation of IC. The endoscopic features and the related histopatology after biopsy of the three different forms of IC are fundamental in suggesting a proper diagnosis although they cannot be specific. The gangrenous colitis presents with cyanotic mucosa and pseudopolyps. Clinicopathologic characteristics of the different grades of IC were previously described [21]. In the presented case due to hypovolemic hemorrhagic shock the patient developed a progressive IC without gangrene but slowly evolving in multiple colonic strictures. According to the above classification the IC observed in our report can be referred to the intermediate group with stenotic evolution since not spontaneous remission of the strictures was obtained despite the defunctioning stoma and the specific therapy. The seriated CT controls showed unclear picture of colonic distension without typical signs of acute colonic gangrene. Colonoscopy described a typical picture of mucosal injury without necrotic lesions. In case of symptomatic strictures resection is always adequate while endoscopic dilation has been proposed as an alternative to surgery especially in critical ill patients as described in the present paper [22-23]. Since the presence of ischemic lesions in the descending and sigmoid colon and the possibility of partial recovery of the occlusion, a postponed resection was considered. In the acute setting in fact the extent of the affected bowel is uncertain and the suture line may lie in an ischemic area because the external appearance of the bowel may be normal during laparotomy since the serosa may be unaffected, despite extensive mucosal damage. Therefore it is recommended that the extent of resection should be tailored by the distribution of the ischemia diagnosed preoperatively. Our clinical choice was also based on the evidence that the non-gangrenous form, accounting for 80%-85% of cases, are reversible in about 50% of cases [20]. Proximal colonic decompression with cecostomy was therefore carried out to obtain defunctionalisation of the bowel and availability of the proximal colonic study by enema which was diagnostic for multiple irreversible segmental stenosis before definitive surgery. This approach, possible for the improved clinical condition after decompression, allowed elective tailored resection of the affected colon with endoscopically verified healing of the remaining descending portion, with direct anastomosis secured by optimal patient condition after the acute critical phase. The differential diagnosis from inflammatory bowel disease and Clostridium difficilis colitis is demanding due to the fact that inflammatory and infectious colitis manifest similarly in the acute critical patients, thus the real incidence of IC is probably underestimated. Testing for Clostridium is recommended in case of uncertain diagnosis of IC especially in patients treated with large spectrum antibiotics [24-26]. The treatment of IC ranges from supportive therapy in moderate, transient forms which usually resolve spontaneously, to emergency surgery in the gangrenous form with acute peritonitis and sepsis. Nil by mouth or liquid diet, close observation and antibiotics represent the basic approach. Antibiotic use is justified also in the milder presentation for a certain risk of bacterial transmigration[27]. According to the severity of the clinical status, if prolonged starving is needed, support with intravenous fluids or parenteral nutrition becomes mandatory. If ileus is present the use of a nasogastric and colonic decompression by use of a rectal tube may be useful. Some critical aspects can be raised in the clinical management of the presented case. First surgery carried out was actually unnecessary. Despite the setting of this clinical scenario was a tertiary university hospital, offering 24/hours emergency specialty facilities and services on call, the first endoscopic evaluation was not complete. The use of large channel aspiration endoscope is supposed to allow an adequate mucosal exploration and treatment [28] but in the present case something didn't work properly. Contrast enhanced CT scan was negative for active bleeding, thus not indicating emergency arteriography for embolization according to current guidelines [29]. It would be indicated in a theoretical flowchart to refer a stable patient to a further endoscopic control. Maybe emergency arteriography could be forced but there is little evidence to support the use of angiographic embolization as an alternative to surgery after endoscopic treatment has failed [30]. Angiographic localization of the site of bleeding without contrast medium extravasation at CT is improbable. Furthermore the activation of emergency arteriography would have required a not available "time door to balloon" considering the clinical condition and therefore it was excluded. Theoretically the radi-

ological picture should have been sufficient for excluding the necessity of a surgical exploration but the patient's critical condition with weak hemodynamic balance despite maximal medical therapy, together with the young age forced the indication to emergency laparotomy when critical hemodynamic became life-threatening. As a matter of fact the cause of bleeding was not identified. Surgery was just effective in completing gastric exploration to exclude active bleeding. The role of surgery has in fact decreased over the last decades due to the efficacy of the medical treatment and the advances in endoscopy and endovascular techniques. Surgery should be reserved when endoscopic and/or endovascular approaches have failed or when complication or malignancy are present [30]. Because of other confounding factors and mild abdominal picture the diagnosis of IC was delayed and confirmed only after endoscopic biopsies. Since poor general condition we preferred to postpone colonic resection after the stabilization of the clinical picture and we proceeded to a diverting stoma in order to exclude stools transit through the colon, to allow better diagnostic of the evident stricture and to attempt their physiological spontaneous resolution or improvement according to what sometimes observed in the non-gangrenous IC.
The strictures remained stable, but improved general conditions allowed tailored colonic resection for adequate left colonic residual with sufficient function and adequate continence. This result was possible because the postponement of the definitive surgery favoured the healing of the ischemic lesions occurred in the descending colon and sigmoid which could be preserved.

Conclusions

IC may present with a large spectrum of clinical condition. In acute shocked patients it must be always considered when a complicated abdominal picture is present. Immediate surgery is not always required considering the spontaneous resolutions in the milder forms. Strictures are the most frequent evolution following the intermediate non-gangrenous presentation and initially they can be treated conservatively with postponed tailored resection after resolution of the diffuse mucosal injuries.

Riassunto

La colite ischemica rappresenta più della metà dei casi di ischemia gastrointestinale. E' una condizione di complesso inquadramento tenuto conto della non specificità dei sintomi di esordio e dell'andamento clinico incostante associato ad un ampio spettro di gravità. L'approccio terapeutico risulta pertanto diverso in relazione alla tipologia di presentazione clinica. Presentiamo il caso di un paziente che, giunto alla nostra osservazione in emergenza per ematemesi massiva con conseguente shock emorragico, ha sviluppato nel successivo decorso clinico un quadro latente di ischemia colica senza gangrena, caratterizzato dal progressivo instaurarsi di multiple stenosi del colon con aggravamento delle condizioni generali. Il paziente è stato sottoposto a rettosigmoidocolonscopia che ha confermato il reperto TC di dilatazione colica e di stenosi del colon discendente. Un tentativo di dilatazione pneumatica della stenosi è risultato inefficace e pertanto in relazione alla precarietà delle condizioni cliniche e alla tipologia dell'ischemia colica si è ritenuto opportuno eseguire inizialmente esclusivamente una ciecostomia decompressiva con l'obiettivo di derivare il transito fecale e di favorire la risoluzione o la stabilizzazione delle lesioni ischemiche. Il differimento della colectomia ad una fase successiva ha permesso una migliore definizione dell'estensione della resezione colica richiesta. La colite ischemia si presenta con uno spettro di manifestazioni cliniche molto ampio.
Come descritto nel presente lavoro, nella valutazione del paziente con shock che presenta un quadro addominale complesso, è raccomandabile tenere sempre in considerazione la possibilità che si sia instaurata una condizione di ischemia colica, anche in forma subacuta senza gangrena e che in questo contesto spesso lo sviluppo di stenosi ne rappresenta l'evoluzione più frequente. La resezione colica immediata non è sempre necessaria in considerazione di un certo grado di remissione spontanea del quadro clinico. Conseguentemente un approccio inizialmente conservativo, con differimento della resezione colica ad una successiva fase di stabilizzazione della stenosi e di miglioramento delle condizioni cliniche generali, risulta raccomandabile anche nell'ottica di limitare l'estensione della resezione colica richiesta.

References

1. Sun MY, Maykel JA: I*schemic colitis*. Clin Colon Rectal Surg, 2007;20:5-12.

2. Ashour M: *Chest injury complicated by shock induced necrosis of the colon*. Thorax, 1985;40:556-57.

3. Picardi N, Masella A:In *tema di coliti ischemiche: la forma "da emostorno" senza ostruzioni vascolari [Ischemic colitis: the "blood diversion" form without vascular obstruction*]. Ann Ital Chir, 1981;53(2):137-48.

4. Battisti G, Porcelli C, Scaldaferri T, et al: *Ischemic colitis with chronic stenotic evolution*. Ann Ital Chir, 1999;70(1):115-21.

5. Marston A, Pheils MT, Thomas ML, Morson BC: *Ischaemic colitis. Gut, 1966;7:1-15.*

6. THOMSON FB: Ischaemic infarction of the left colon. Canad Med Ass J, 1948; 5: 183-85

7. Engelhardt JE, Jacobson G: *Infarction of the colon, demonstrated by barium enema*. Radiology, 1956;67:573-75.

8. Killingback M J, Williams K L: *Necrotizing colitis. Brit J Surg, 1961; 49: 175-85*

9. Brownlee T J*: Regional colitis as an acute abdominal emergency*. Brit J Surg 1951;38:507-13.

10. Corbett R: St*enosed segment of descending colon associated with traum*a. Proc Roy Soc Med, 1957;50:271-72.

11. Kellock TD: *Acute segmental ulcerative colitis*. Lancet, 1957;2:660-63.

12. Hannan JR, Jackson BF, Pipik P: *Fibrosis and stenosis of the descending colon and sigmoid following occlusions of the inferior mesenteric artery*. Amer J Roentgenol, 1964;91:826-32.

13. Riaz AA, Wan MX, Schaefer T, Schramm R, Ekberg H, Menger MD, et al.: *Fundamental and distinct roles of P-selectin and LFA-1 in ischemia/reperfusion-induced leukocyte-endothelium interactions in the mouse colon*. Ann Surg, 2002;236:777-84

14. Hundscheid IH, Grootjans J, Lenaerts K, Schellekens DH, Derikx JP, Boonen BT, et al.: *The human colon is more resistant to ischemia-reperfusion-induced tissue damage than the small intestine: an observational study*. Ann Surg, 2015;262(2):304-11.

15. Polistena A, Johnson LB, Röme A, Wittgren L, Bäck S, Osman N, et al.: *Matrilysin expression related to radiation and microflora changes in murine bowe*l. J Surg Res, 2011;167:e137-43

16. Boley SJ, Schwartz S, Lash J, Sternhill V: *Reversible vascular occlusion of the colon.* Surg Gynecol Obstet, 1963; 116:53-60.

Marshak RH, Maklansky D, Calem SH: *Segmental infarction of the colon.* Dis, 1965; 10:86-92.

Irwin A: *Partial infarction of the colon due to reversible vascular occlusion*. Clin Radiol, 1965; 16:261-63.

Brandt LJ, Boley SJ: *Colonic ischemia.* Surg Clin North Am, 1992; 72: 203-29.

Theodoropoulou A, Koutroubakis IE: *Ischemic colitis: Clinical practice in diagnosis and treatment*. World J Gastroenterol, 2008; 14: 7302-08 .

Zou X, Cao J, Yao Y, Liu W, Chen L: *Endoscopic findings and clinicopathologic characteristics of ischemic colitis: a report of 85 cases*. Dig Dis Sci, 2009; 54:2009-15.

Adler DG: *Colonic strictures: Dilation and stents.* Gastrointest Endosc Clin N Am, 2015;25:359-71.

Misiakos EP, Tsapralis D, Karatzas T, Lidoriki I, Schizas D, Sfyroeras GS, et al.: *Advents in the diagnosis and management of ischemic colitis.* Front Surg, 2017; 4:47.

Guerri S, Danti G, Frezzetti G, Lucarelli E, Pradella S, Miele V: *Clostridium difficile colitis: CT findings and differential diagnosis.* Radiol Med, 2019; 124:1185-198.

Wiland HO 4TH, Procop GW, Goldblum JR, TuohY M, Rybicki L, Patil DT: *Interobserver variability and feasibility of polymerase chain reaction-based assay in distinguishing ischemic colitis from Clostridium difficile colitis in endoscopic mucosal biopsies.* Am J Clin Pathol, 2013; 139:730-35.

Higashihara T, Okada A, Kishida Y, Maruno S, Matsumura M, Tamura K, et al.: *Atypical cause of intractable diarrhea in a hemodialysis patient, masked by Clostridium difficile-associated diarrhea and ischemic colitis: A case report*. BMC Nephrol, 2018; 19:303.

Luo CC, Shih HH, Chiu CH, Lin JN: *Translocation of coagulase-negative bacterial staphylococci in rats following*. Biol Neonate, 2004; 85:151-54.

GralneK IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, KURIEN M et al.: *Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline.* Endoscopy, 2015; 47:a1-46

Sung JJ, Chiu PW, Chan FKL, Lau JY, Goh KL, Ho LH, et al.: *Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018*. Gut, 2018; 67:1757-768.

Samuel R, Bilal M, Tayyem O, Guturu P: *Evaluation and management of non-variceal upper gastrointestinal bleeding*. Dis Mon, 2018; 64:333-43.