ELMER PRESS

Case Report

Gastroenterol Res. 2022;15(2):100-105

Extensive Aortic Thrombosis and Renal Infarction in Association With an Active Flare-Up of Crohn's Disease

Eltaib Saad[a, c], Abdalaziz Awadelkarim[b], Mohamed Agab[a], Akram Babkir[a]

Abstract

Venous thromboembolism (VTE) is a recognized extraintestinal manifestation of inflammatory bowel disease (IBD), with deep venous thrombosis (DVT) and pulmonary embolism being reported as the most frequent vascular complications in IBD patients. Much less frequently, arterial thromboembolic events may also be associated with greater morbidity and mortality. Aortic mural thrombosis is a rare phenomenon described in patients with IBD that often results in serious consequences such as visceral infarction and acute ischemia of the lower extremities. We described an unusual case of a female patient with Crohn's disease (CD) who presented with generalized abdominal pain and vomiting. Imaging showed an active flare-up of intestinal CD as well as two mural thrombi in the distal descending thoracic aorta and the abdominal aorta at the level of the left renal artery, respectively, with a left renal infarction. The mesenteric angiogram revealed a patent celiac axis and mesenteric arteries. The patient was therapeutically anticoagulated, and she underwent a right hemicolectomy for the perforated ileal disease. A comprehensive diagnostic workup for hypercoagulability and thrombophilia was negative for an underlying etiology, and the active CD flare-up was considered the main culprit triggering the aortic thrombosis in this reported patient. Our case highlighted the occurrence of aortic thrombosis in a patient with IBD and that entails careful attention. Early recognition and timely management with a multidisciplinary team is the key to improving the outcome of aortic events that coincide with the active flare-up of IBD.

Keywords: Aortic mural thrombosis; Aortic disease; Crohn's disease; Hypercoagulability

Introduction

Patients with inflammatory bowel disease (IBD) are at substantial risk of thromboembolic events [1, 2], with venous diseases accounting for the vast majority (about 85%) of thromboembolism, which usually manifested as deep venous thrombosis (DVT) and pulmonary embolism [1, 2]. Arterial events are very much less frequently encountered with IBD, but they are associated with significantly worse outcomes [1-3]. Aortic mural thrombosis is an exceedingly rare phenomenon being reported among a small series of patients with IBD in the lack of underlying aortic pathologies that usually predispose to thrombosis (such as ulcerated atherosclerotic plaques, aneurysm, and dissection) [1, 3-9]. These aortic thrombi carry an inherently high risk of embolization that may result in serious consequences such as mesenteric infarction and acute ischemia of the lower extremities [1-4]. Herein, we report an unusual case of a female patient with Crohn's disease (CD) who presented with acute abdomen and was found to have active Crohn's ileal disease and an extensive mural thrombosis of the aorta that was complicated by a left renal infarction. A comprehensive hematological workup was unrevealing for an underlying cause for aortic lesions, and the aortic mural thrombosis was attributed to the active flare-up of intestinal CD.

Case Report

A 61-year-old female patient was brought to the emergency department (ED) with a sudden onset of abdominal pain and bilious vomiting that started 3 days prior to presentation. The pain was associated with left flank pain and dysuria for 1 day. She denied fevers or rigors, diarrhea, and rectal bleeding. The review of systems was negative for other pertinent symptoms. She was diagnosed with CD with stenosing ileal disease, and her regular medications included mesalamine 800 mg twice daily, methotrexate 15 mg weekly, and infliximab 5 mg/kg injection every 8 weeks, but she stopped taking her regular medications due to complex psycho-social issues. Notably, the patient had previously declined elective laparoscopic surgery for the ileal disease. Her past medical history also included bipolar disorders and fibromyalgia. The patient was an active smoker, and she never used oral contraceptives or hormonal replacement therapy.

The patient was confused, febrile to 104 °F, hypotensive to 90/55 mm Hg, and tachycardiac to 140 beats per minute. Abdominal examination revealed right lower quadrant tenderness with focal guarding as well as tenderness over the left costophrenic

Manuscript submitted January 29, 2022, accepted February 23, 2022
Published online March 12, 2022

[a]Department of Internal Medicine, Saint Francis Presence Hospital, Evanston, IL, USA
[b]Department of Internal Medicine, Detroit Medical Center/Wayne State University, Detroit, MI, USA
[c]Corresponding Author: Eltiab Saad, Department of Internal Medicine, Saint Francis Presence Hospital, Evanston, IL, USA. Email: Eltaib.Saad@amitahealth.org

doi: https://doi.org/10.14740/gr1504

angle. The rest of the systemic examination was not significant.

Laboratory results reflected an active inflammatory process (white cell count of 15,000/mm^3 and C-reactive protein of 122 mg/dL). The urine analysis revealed microscopic hematuria. Following fluid resuscitation, a contrast-enhanced computed tomography (CT) of the abdomen demonstrated active inflammatory changes with mural enhancement at the distal ileum, nearly 20 cm from the ileocecal valve, with a localized perforation and small gas locules and fluid collection (Fig. 1). In addition, a large but non-occlusive thrombus was visualized at the distal descending thoracic aorta (Fig. 2a, b) and a further smaller thrombus was noted at the level of the left renal artery with a wedge-shaped defect in the left kidney consistent with a left renal infarct (Fig. 3a, b). Notably, these aortic thrombi appeared new compared to the most recent imaging. No evidence of atherosclerotic aortic disease was noted. A mesenteric CT angiogram revealed a patent celiac axis and superior mesenteric artery (SMA) in the setting of the perforated ileum, with no evidence of acute or chronic mesenteric ischemia. Bedside vascular examination revealed bilaterally palpable pulsation at the dorsalis pedis (DP), tibialis posterior (TP), popliteal, and femoral arteries with well-perfused warm distal lower extremities. An electrocardiogram showed sinus rhythm with no ischemic changes.

Vascular surgery consultation advised therapeutic anticoagulation with heparin infusion for aortic thrombosis and renal infarction. Gastroenterology consultation recommended an operative intervention, and the patient underwent an emergent exploratory laparotomy. Operative findings included a perforation at the distal ileum with a focal abscess and adhesive friable small bowel loops around the perforation site. A careful examination revealed no evidence of proximal small bowel or colonic pathology considering the extensive aortic thrombosis visualized on the preoperative imaging. A right hemicolectomy with an end ileostomy was performed due to a substantial

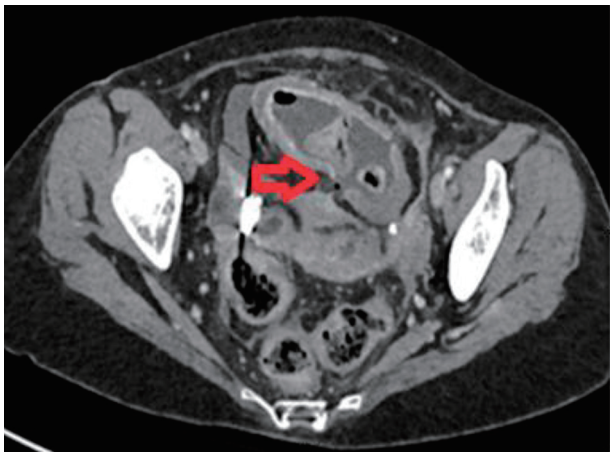

Figure 1. Axial image of contrast-enhanced computed tomography of abdomen with an active flare-up of Crohn's disease showing a localized perforation at the distal ileum (horizontal red arrow).

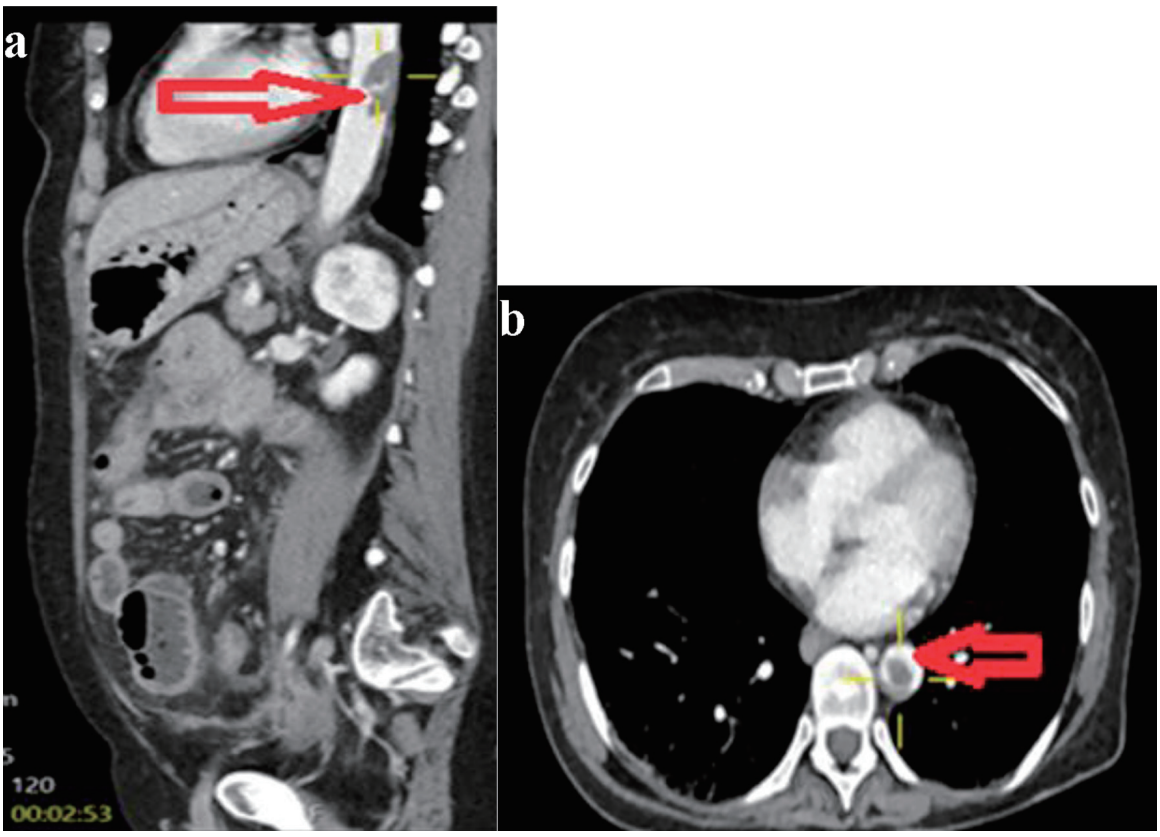

Figure 2. Sagittal (a) and axial (b) image of contrast-enhanced computed tomography of abdomen showing a large thrombus at the distal descending aorta (horizontal arrow).

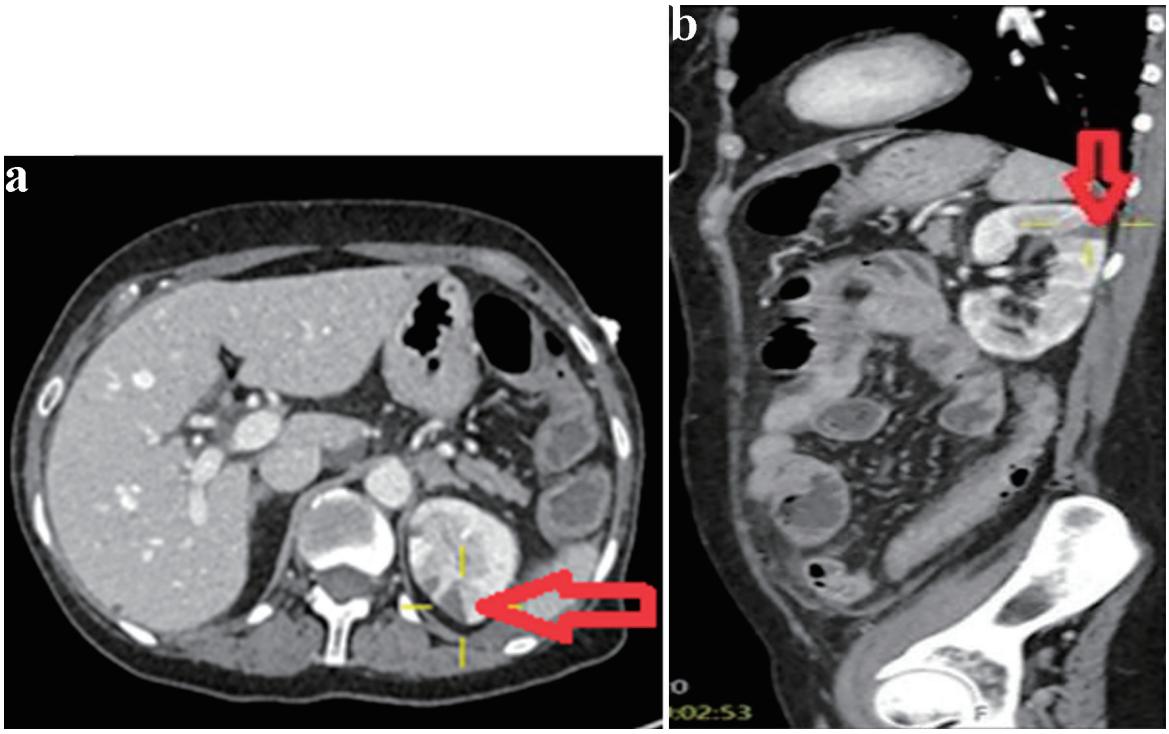

Figure 3. Axial image (a) and sagittal image (b) of contrast-enhanced CT abdomen showing a left renal infarct (arrows).

risk of anastomotic leak. Histopathology of the resected bowel segment confirmed an active CD flare-up.

Hematology services were consulted to evaluate for an underlying etiology of aortic thromboembolism. A detailed vasculitic panel (including p-ANCA, c-ANCA, anti-dsDNA, ANF, and complement levels C3 and C4) was negative. Additionally, a thrombophilia screening was also unrevealing (that included lupus anticoagulant, anti-cardiolipin antibodies, antithrombin III, factor V Leiden, protein C, protein S, and lipoprotein (a)). Transesophageal echocardiography (TEE) with bubble studies showed normal right and left ventricular function with no intracardiac thrombi or masses, and there was no evidence of intracardiac shunts. Continuous cardiac monitoring with an event recorder depicted only very occasional (< 1%) premature atrial contractions (PACs).

The patient was discharged on an oral anticoagulant for 6 months. A repeat CT aortogram 2 months post-operatively revealed an interval decrease of both thrombi sizes with no new lesions.

Discussion

Aortic thrombosis represents an exceedingly rare entity associated with IBD with only a limited number of cases being reported in the reviewed literature [3, 5-19]. This event may be associated with worse outcomes compared to venous thromboembolism (VTE) [1-4]. The management involves a multidisciplinary team of gastroenterologists and IBD specialists, hematologists, and often colorectal and vascular surgeons [3].

Pathophysiology of arterial thromboembolism among patients with IBD remains poorly understood [2-4]. Many theories were postulated, and a multifactorial complex process of interaction between a number of factors was assumed [1, 3, 4]. The chronic inflammatory status and autoimmune activity constitute major triggers of the downstream release of certain procoagulant cytokines (tissue-necrosis factor and interleukin 6 (IL-6)) that trigger endothelial cells injury and initiate thrombotic cascades by enhancing expression of CD40 ligand on platelets surface [1-7]. This hypercoagulable state is further augmented by a range of prothrombotic conditions that encompass disease-associated complications (such as dehydration, reactive thrombocytosis, and vitamins deficiencies that result in elevated homocysteine levels), treatment-related sequelae (such as steroid use, recurrent surgeries with post-operative states, and prolonged immobilization), and exposure to environmental risks (like active smoking and combined oral contraceptive (COCP) use) [1-4].

The review of the medical literature identified a total of 21 cases of IBD-associated aortic mural thrombosis [3, 5-19]. Table 1 briefly summarizes the patient demographics, clinical presentation, thrombosis site, management, and outcome.

The majority of cases were associated with an active IBD status [5, 7-10], in accordance with the literature that reported a markedly reduced level of natural anticoagulants and an upregulated expression of various procoagulants cytokines during disease activity [1, 3]. Furthermore, complicated Crohn's disease (with abscess perforation or enteric fistulae) was strongly associated with systemic endotoxemia that further activates coagulation cascades [20]. Nevertheless, there was only one case that was described with quiescent disease [14].

Most aortic thrombi related to IBD involved infrarenal aorta [7, 8, 10-12, 14, 17], followed by the aortoiliac segment

Table 1. Summary of Cases of IBD-Associated Aortic Mural Thrombosis

Authors/publication year	Patient's age (years)/gender	IBD/activity status	Aortic thrombosis site/embolus site/clinical consequences	Management	Outcome
Novacek et al, 2004 [3]	36/female	UC/active	Distal abdominal aorta with occlusion of the origin of IMA with distal colonic spare due to SMA collaterals	Medical management of UC. Heparin anticoagulation followed by a direct oral anticoagulant	Good outcome with thrombus resolution
Novacek et al, 2004 [3]	41/female	CD/active	Distal abdominal aorta with left iliac embolization and acute left lower extremity ischemia	Thrombectomy with heparin anticoagulation followed by a coumarin derivative	Left leg amputation. Thrombus resolution
Khan et al, 2009 [5]	41/male	CD/active (post-operative)	Extensive proximal abdominal aorta occluding the ostia of celiac, SMA, and left renal artery with left renal infarction and diffuse small bowel and colonic ischemia. Aortic arch thrombus	Heparin anticoagulation with failed IR attempts to cannulate blocked visceral and mesenteric vessels	Death from visceral ischemia and sepsis
Kok et al, 2012 [6]	48/female	UC/active	Large proximal abdominal aorta thrombus with splenic artery embolization and splenic infarction	Heparin anticoagulation followed by warfarin	Good outcome
Talbot et al,1986 [7]	47/male	CD/active	Infra-renal abdominal aorta with colonic ischemia	Unspecified	Death due to colonic ischemia
Perler et al, 1991 [8]	34/female	CD/unspecified	Infra-renal abdominal aorta with distal embolization	Thrombo-embolectomy with heparin anticoagulation	Good outcome
Novotny et al, 1992 [9]	35/female	UC/unspecified	Aorto-iliac thrombosis	Unspecified	Leg amputation
Novotny et al, 1992 [9]	22/female	UC/unspecified	Aorto-bifemoral thrombosis	Unspecified	Unspecified
Novotny et al, 1992 [9]	34/female	UC/unspecified	Aorto-iliac thrombosis	Thrombectomy with heparin anticoagulation	Good outcome
Hahn et al, 1999 [10]	34/male	CD/active (post-operative)	Infra-renal abdominal aorta with distal embolization resulting in blue toe syndrome	Lower extremity embolectomy with heparin anticoagulation followed by warfarin	Good outcome with thrombus resolution
Hahn et al, 1999 [10]	74/male	CD/active (post-operative)	Peripancreatic aorta with severe pancreatitis and distal embolization with blue toe syndrome	Heparin anticoagulation followed by warfarin	Toe amputation. Thrombus resolution
Lehmann et al, 2001 [11]	50/female	CD/active	Infra-renal abdominal aorta with distal embolization to the right popliteal artery resulting in acute lower extremity ischemia	Thrombolysis with urokinase then lower extremity embolectomy with heparin anticoagulation followed by warfarin	Good outcome
Szychta et al, 2001 [12]	42/female	UC/active	Infra-renal abdominal aorta with right renal artery embolization with a right renal infarction	Renal thrombectomy with heparin anticoagulation followed by a coumarin derivative	Good outcome
Grothues et al, 2002 [13]	49/male	UC/active	Aortic arch thrombus in a critically ill UC patient with systemic aspergillosis infection	UC management with antifungal therapy	Death from systemic sepsis
Delay et al, 2014 [14]	33/female	CD/quiescent	Extensive infra-renal abdominal aortic thrombosis extending to both iliac arteries. Extensive workup negative for underlying etiology	The initial IR attempt failed. Aorto-bifemoral bypass with heparin anticoagulation followed by life-long aspirin	Good outcome. Histology showed non-specific occlusive aortitis.
Singh et al, 2012 [15]	28/female	CD/active	Aortoiliac thrombosis. Saddle aortic thrombus at aortic bifurcation extending to both common iliac	Bilateral aorto-iliofemoral bypass surgery. Heparin anticoagulation followed by warfarin for six months	Good outcome with complete thrombus resolution

Table 1. Summary of Cases of IBD-Associated Aortic Mural Thrombosis - *(continued)*

Authors/publication year	Patient's age (years)/gender	IBD/activity status	Aortic thrombosis site/embolus site/clinical consequences	Management	Outcome
Elder et al, 2010 [16]	40/male	UC/active	Aortic arch thrombus with distal lower extremity embolization resulting in acute ischemia of the left lower extremity	Limb salvage with embolectomy. Anticoagulation with heparin	Good outcome
Leblanc et al, 2011 [17]	25/female	CD/active	Abdominal aorta thrombus with distal embolization to the left popliteal artery and acute ischemia of the left lower extremity	Embolectomy and revascularization surgery with heparin anticoagulation	Good outcome
Leblanc et al, 2011 [17]	24/female	CD/active	Abdominal aorta thrombus extending into IMA with distal colon sparing by multiple SMA collaterals	Heparin anticoagulation	Good outcome with complete thrombus resolution
Sinapi et al, 2010 [18]	47/male	UC/active	Distal descending thoracic aorta thrombus and aortic arch thrombus	Heparin anticoagulation and medical management for UC	Good outcome
Stordiau et al, 2011 [19]	56/male	CD/active	Aortic arch thrombus with distal embolization to the left subclavian and axillary arteries resulting in acute ischemia of the left upper extremity	Embolectomy, followed by a series of revascularization surgeries and eventually upper extremity amputation. Bowel resection for perforated ileal disease	Amputation of left upper extremity

IBD: inflammatory bowel disease; CD: Crohn's disease; IMA: inferior mesenteric artery; SMA: superior mesenteric artery; UC: ulcerative colitis; IR: interventional radiology.

[3, 9, 14, 15]. Interestingly, aortic arch thrombosis was found in four cases, either as a solitary lesion [13, 16] or in association with concurrent aortic thrombi [18, 19].

Aortic mural thrombosis results in a spectrum of devastating sequelae such as small bowel infarction [5], colonic ischemia [7] and splenic infarction [6] due to mesenteric emboli, renal infarction complicating renal arteries emboli [5, 12], and acute ischemia of the upper extremities [19] and lower extremities [10, 11, 16, 17].

Therapeutic anticoagulation was employed in most patients in conjunction with medical treatment of IBD flare-up and surgical or endovascular interventions for complications (such as acute extremity ischemia or bowel infarction) that were tailored to each individualized case [5-19].

The Canadian Association of Gastroenterology guidelines for IBD-related venous thromboembolism recommend therapeutic anticoagulation for at least 3 months post-IBD exacerbation [21], but there is no clear consensus yet on the standard treatment duration for the associated arterial disease including aortic events [1, 3].

The outcome of aortic thrombosis associated with IBD included a complete thrombus resolution [3, 10, 15, 17], extremity amputation [9, 19], and death from multisystemic failure due to bowel ischemia [5, 7].

Conclusion

Aortic mural thrombosis is an exceedingly rare extraintestinal complication associated with the flare-up of CD. This condition deserves careful attention as it may result in devastating consequences such as mesenteric infarction or extremities ischemia. Early recognition and timely management are essential to improving the outcome of aortic thromboembolic events.

Acknowledgments

The authors would like to acknowledge the Department of Radiology at Saint Francis Presence Hospital for providing valuable input to this case presentation.

Financial Disclosure

The authors confirm that there is no funding for this case report.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Informed Consent

Informed written consent was obtained from the patient to

write and publish their case as a case report with all accompanying clinical and radiological images. No ethical clearance is deemed required for case report writing as per our local Research Board.

Authors Contributions

ES and AA contributed to the conceptualizing and writing the first manuscript. MA and AB have performed the critical review and editing of the final draft. All authors were involved in the clinical management of the reported patients. All authors agreed to the final draft submission.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

References

1. Pezold M, Pergamo M, Rockman C, Lugo J. Presentation and management of arterial thromboembolisms during active inflammatory bowel disease: case series and literature review. Ann Vasc Surg. 2020;67:532-541.e3.
2. Miehsler W, Reinisch W, Valic E, Osterode W, Tillinger W, Feichtenschlager T, Grisar J, et al. Is inflammatory bowel disease an independent and disease specific risk factor for thromboembolism? Gut. 2004;53(4):542-548.
3. Novacek G, Haumer M, Schima W, Muller C, Miehsler W, Polterauer P, Vogelsang H. Aortic mural thrombi in patients with inflammatory bowel disease: report of two cases and review of the literature. Inflamm Bowel Dis. 2004;10(4):430-435.
4. Di Fabio F, Obrand D, Satin R, Gordon PH. Intra-abdominal venous and arterial thromboembolism in inflammatory bowel disease. Dis Colon Rectum. 2009;52(2):336-342.
5. Khan AB, Bhat N, Hassan A, Al Saied G. Aortic thrombosis complicating Crohn disease: an unusual complication. Can J Surg. 2009;52(5):E182-184.
6. Kok HK, Maguire S, Corr A, Sadlier M, Patchett S, Harewood G. Intra-aortic mural thrombosis and splenic infarction in association with ulcerative colitis. Ir J Med Sci. 2012;181(3):377-379.
7. Talbot RW, Heppell J, Dozois RR, Beart RW, Jr. Vascular complications of inflammatory bowel disease. Mayo Clin Proc. 1986;61(2):140-145.
8. Perler BA, Kadir S, Williams GM. Aortic mural thrombus in young women: premature arteriosclerosis or separate clinical entity? Surgery. 1991;110(5):912-916.
9. Novotny DA, Rubin RJ, Slezak FA, Porter JA. Arterial thromboembolic complications of inflammatory bowel disease. Report of three cases. Dis Colon Rectum. 1992;35(2):193-196.
10. Hahn TL, Dalsing MC, Sawchuk AP, Cikrit DF, Lalka SG. Primary aortic mural thrombus: presentation and treatment. Ann Vasc Surg. 1999;13(1):52-59.
11. Lehmann JM, Shnaker A, Silverberg D, Dayan K, Witz M. Arterial thromboembolism from a distal aortic thrombus in a patient with Crohn's disease. Isr Med Assoc J. 2001;3(3):226-227.
12. Szychta P, Reix T, Sevestre MA, Brazier F, Pietri J. Aortic thrombosis and ulcerative colitis. Ann Vasc Surg. 2001;15(3):402-404.
13. Grothues F, Welte T, Grote HJ, Roessner A, Klein HU. Floating aortic thrombus in systemic aspergillosis and detection by transesophageal echocardiography. Crit Care Med. 2002;30(10):2355-2358.
14. Delay C, Schwein A, Lejay A, Gaertner S, Aleil B, Thaveau F, Georg Y, et al. Aortitis and aortic occlusion in Crohn disease. Ann Vasc Surg. 2015;29(2):365.e5-9.
15. Singh K, Marco SA, Wang ML, Milone L, Deitch JS. Aortoiliac thrombi in inflammatory bowel disease. Ann Vasc Surg. 2012;26(8):1128.e11-14.
16. Elder K, Hawi R, Al Solaiman F. Inflammatory bowel disease-related thoracic aortic thrombosis. South Med J. 2010;103(2):172-174.
17. Leblanc S, Lloret Linares C, Cacheux W, Mouthon L, Chaussade S. Aortic thrombosis in young women with Crohn's disease receiving adalimumab: report of two cases. Inflamm Bowel Dis. 2011;17(3):862-863.
18. Sinapi I, Hammer F, Hainaut P. Aortic mural thrombi associated with ulcerative colitis. Acta Clin Belg. 2010;65(1):54-55.
19. Stordiau GE, Alecha JS, Goni S, Zozaya JM, Centeno R, Tricas JM. Arterial thromboembolism from aortic floating thrombus in a patient with Crohn's Disease. J Crohns Colitis. 2011;5(2):169-170.
20. Cybulsky MI, Chan MW, Movat HZ. Acute inflammation and microthrombosis induced by endotoxin, interleukin-1, and tumor necrosis factor and their implication in gram-negative infection. Pathology Reviews. 1989;1989:103-116.
21. Nguyen GC, Bernstein CN, Bitton A, Chan AK, Griffiths AM, Leontiadis GI, Geerts W, et al. Consensus statements on the risk, prevention, and treatment of venous thromboembolism in inflammatory bowel disease: Canadian Association of Gastroenterology. Gastroenterology. 2014;146(3):835-848.e6.