Iran J Vasc Surg Endovasc Ther
Volume 1, Number 2, 2021
http://ijvset.gums.ac.ir
eISSN: 2783-1590

Case report

Free floating thrombosis of aorta in three patients with COVID-19 infection

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Abstract

There is evidence that current coronavirus disease (COVID-19) is responsible for thromboembolic events in a number of affected patients. One of this potential thrombotic event is aortic free floating thrombosis (FFT). We report three cases of aortic FFT in COVID-19 patients. All three cases were female. The first case had mesenteric ischemia with descending thoracic aorta (DTA) FFT. The patient underwent resection and anastomosis of small intestine and stent graft placement in DTA. The second patient had right lower extremity ischemia and abdominal aortic FFT. This patient underwent open aortic and right femoral thromboembolectomy. The third patient had mesenteric ischemia and FFT of abdominal aorta. This patient was managed by resection and anastomosis of small intestine, splenectomy and anticoagulation. All three patients were discharged from the hospital in appropriate condition. FFT of aorta is a potential complication of current COVID-19 infection. Precise attention is necessary to diagnose and manage this condition and prevent further complications.

Keywords: Coronavirus, Severe Acute Respiratory Syndrome, Aorta, Thrombosis

Introduction

The current coronavirus disease (COVID-19) pandemic, which causes severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has affected all medical specialties including vascular surgery [1, 2]. One of the devastating complications of COVID-19 infection is thromboembolic events [3, 4]. The thromboembolic complications of COVID-19 include deep venous thrombosis, pulmonary embolism, cerebrovascular events, cerebral vein thrombosis, acute limb ischemia and acute aortic thrombosis [5, 6]. Thromboembolic complications of COVID-19 are associated with high risks of death [7-10]. Herein, we report three cases of free floating thrombosis (FFT) of aorta in COVID-19 patients from Iran.

Case report

We report three consecutive cases of aortic thrombosis in COVID-19 patients. All three cases had severe COVID-19-related hypoxia. During the hospitalization, aortic FFT was found on specific radiological examinations. The diagnosis of COVID-19 was confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) in the patients. All three patients were managed at our vascular surgery center at Shohada-Tajrish Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. The management of coronavirus infection was done by infectious disease attending physicians of our center. The reported patients were checked for thrombophilia factors and these were negative in all three cases. These factors included

factor V Leiden, antithrombin III deficiency, protein C deficiency, protein S deficiency, lupus anticoagulant, cardiolipin antibodies, hyperhomocysteinemia and lipoprotein (a). Furthermore, rheumatoid factor (RF), antinuclear antibody (ANA) and antineutrophil cytoplasmic antibodies (C-ANCA and P-ANCA) were negative in all three cases. Table 1 tabulates clinical and laboratory characteristics of the presented patients.

Case 1

The first patient was a 38-year-oll woman referred to our center with thrombosis of descending aorta with progression to superior mesenteric artery (SMA). The patient had undergone laparotomy for acute abdomen in another hospital. During that laparotomy, 40cm of jejunum was resected due to necrosis. A computed tomography angiography (CTA) was performed after the laparotomy to assess the etiology of mesenteric ischemia and the patient was scheduled for a second look. The CTA revealed non-obstructive descending thoracic aorta (DTA) thrombus and superior mesenteric artery (SMA) thrombosis. The rest of the GI tract was intact at second look. The patient was anticoagulated with heparin for a week.

The patient was referred to our center because of DTA thrombosis. The patient was asymptomatic at our center. We repeated the CTA to assess the burden of thrombus and the effect of anticoagulation on it. The same results were present at the repeat CTA despite full anticoagulation for a week (Figure 1; A to D). We scheduled the patient to stent graft placement in DTA to exclude the thrombus and prevent further embolization to distal arterial territories. A 24mm diameter, 130mm length stent graft was deployed in the DTA (Figure 1; E). The procedure was performed under sedation and local anesthesia through the femoral access. The postoperative course was uneventful. The patient was asymptomatic and thus the thrombosis of SMA was managed by anticoagulation. The patient was discharged and warfarin was administered.

This patient was admitted to the first center with respiratory symptoms and her COVID-19 infection was confirmed there. She had an 0_2 saturation of 80-85% at her admission to our center. She had bilateral pulmonary involvement (40-50%) on chest CT. This patient received oseltamivir, dexamethasone and azithromycin in the first center. The patient received O_2 and dexamethasone at our center and her respiratory status did not have significant impact on the endovascular procedure. The patient was discharged with a good respiratory condition without requiring home oxygen.

The clot in DTA was managed by endovascular stent graft placement in this case. Thus, we do not have pathological assessment of the thrombus. The gross investigation of the resected small intestine revealed a portion of intestine measuring 40cm in length and 6cm in diameter with hemorrhagic and exudative serosal surface. The microscopic investigation revealed foci of transmural necrosis with extension of inflammatory cells into the surrounded fibrofatty tissue.

Case 2

A 67-year-old woman was admitted to our center with COVID-19 infection. She had a vascular surgery consult due to acute right lower extremity ischemia. A CTA was performed and there was FFT of infra-renal aorta and a thromboembolism in common femoral, superficial femoral and deep femoral arteries (Figure 2; A to C). The patient underwent open abdominal aortic thrombectomy and femoral embolectomy. The thromboembolectomy was performed through right femoral incision and mid-line laparotomy. The postoperative course was uneventful. The patient was discharged on fourth postoperative day and warfarin was administered.

This patient was found to have COVID-19 infection during routine investigations. She had mild cough and bilateral pulmonary involvement (20-25%) on chest CT. The patient had respiratory compromise on her eighth day of admission and her O_2 saturation was 82-90%. This patient received favipiravir. The respiratory status of the patient did not have substantial effect on surgical management and the patient was discharged with a good respiratory condition without requiring home oxygen.

Table 1. Demographic, clinical and laboratory findings of the patients

Variable	Patient No. 1	Patient No. 2	Patient No. 3
Age, years	38	67	50
Sex	Female	Female	Female
Clinical characteristics	Mesenteric ischemia	Right lower limb ischemia	Mesenteric ischemia
Cardiovascular risk factors	None	DM, HTN	HTN
Symptoms at disease onset	Acute abdomen	Lower extremity ischemia	Acute abdomen
Localization of emboli	SMA	Right CFA	SMA, Celiac branches
Time from COVID-19 onset to thrombotic event	10 days	8 days	4 days
Manifestation of the embolic event	Necrosis of 40 cm of jejunum	Right lower limb acute ischemia	Ileal necrosis and splenic infarct
RT-PCR of COVID-19	Positive	Positive	Positive
WBC, per mm^3	16000	7300	13500
Total neutrophils, percent	85%	77%	85%
Total lymphocytes, percent	10%	23%	15%
Platelet count, per mm^3	474000	338000	454000
Hemoglobin, gr/dl	9.7	12.9	5.7
PT	13.7	13	13.1
PTT	36	30	30
INR	1.1	1	1
Creatinine, mg/dl	0.62	0.96	0.86

CFA – Common Femoral Artery, *COVID* – Coronavirus Disease, *dl* – deciliter, *DM* – Diabetes Mellitus, *gr* – Gram, *HTN* – Hypertension, *INR* – International Normalized Ratio, *mg* – milligram, *mm* – millimeter, *pg* – pico gram, *PT* – Prothrombin Time, *PTT* – Partial Thromboplastin Time, *RT-PCR* – Reverse-Transcriptase Polymerase Chain Reaction, *SMA* – Superior Mesenteric Artery, *WBC* – While Blood Cell

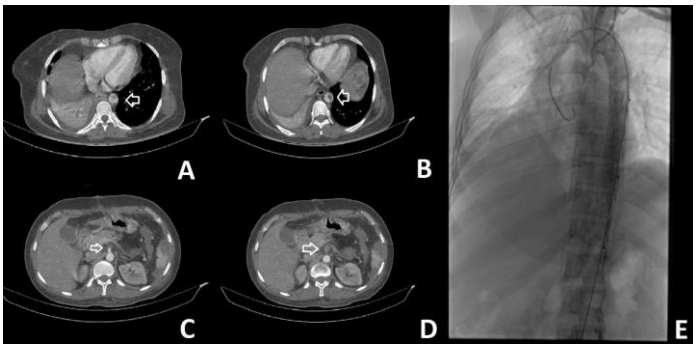

Figure 1. Free floating thrombosis of descending thoracic aorta (A and B, arrows); Thrombosis of superior mesenteric artery (C and D, arrows); Deployment of stent graft in descending thoracic aorta (E)

The retrieved blood clot through femoral and aortic thromboembolectomy was investigated. The femoral specimen was blood clot and contained inflammatory cells and cellular aggregation and congestion. The aortic specimen was partial vessel wall together with blood clot. There were ruptured vascular section with necrotic tissue and inflammatory cells together with cellular aggregation and congestion. Figure 3 illustrates the thromboembolectomy specimen of the abdominal aorta.

Case 3

The third patient was a 50-year-old woman who presented with acute abdomen to the emergency department of our center. The patient was transferred to the operating room because of generalized rebound tenderness and guarding. Following laparotomy, there were segmental gangrene of ileum and splenic infarct. Thus, segmental resection and anastomosis and splenectomy was performed. The patient was scheduled for a second look. After the operation, a CTA was performed. There was a free floating thrombosis at the abdominal aorta (Figure 4: A and B). The patient was anticoagulated since her first operation. The second look was performed and it was uneventful. On fourth postoperative day, the patient had severe dyspnea and she was hypoxic. An RT-PCR confirmed COVID-19 infection. The patient was anticoagulated and due to her poor general condition, vascular procedure was not performed. The patient had respiratory compromise and not suitable to another procedure. However, her abdominal examination was normal after the second look. Thus,

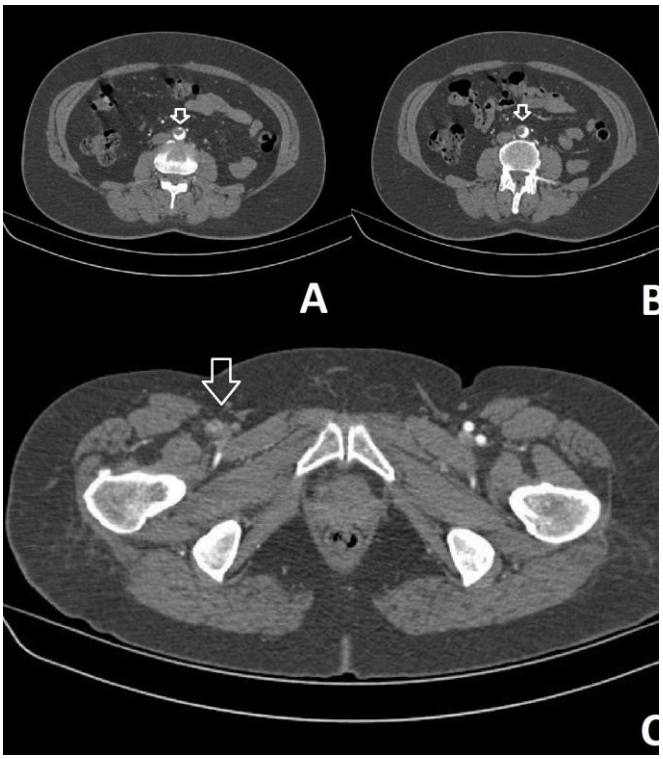

Figure 2. Thrombosis of infra-renal abdominal aorta (A and B, arrows); Thrombosis of common femoral artery (C, arrow)

it was decided to manage the aortic thrombosis conservatively. The repeat CTA of this patient revealed substantial regression of thrombosis.

This patient was found to have COVID-19 infection during work-up of her dyspnea. She had mild to moderate cough and bilateral pulmonary involvement (30-40%) on chest CT. This patient received conservative treatment for coronavirus infection. O_2 saturation of this patient was more than 90% at her admission but it fell to 80-85% on her fourth postoperative day. For this reason, the patient was managed conservatively and she was discharged after full recovery of her respiratory status.

The intestinal specimen of this patient revealed multiple foci of necrosis. The splenectomy specimen reveled multiple infracted areas together with normal splenic tissue. There were also multiple foci of atherosclerosis within the vessel walls of the spleen. Figure 5 illustrates the microscopic pathology of the resected spleen.

Discussion

Aortic mural thrombus of aorta in the non-atherosclerotic and non-aneurysmal segment is a rare

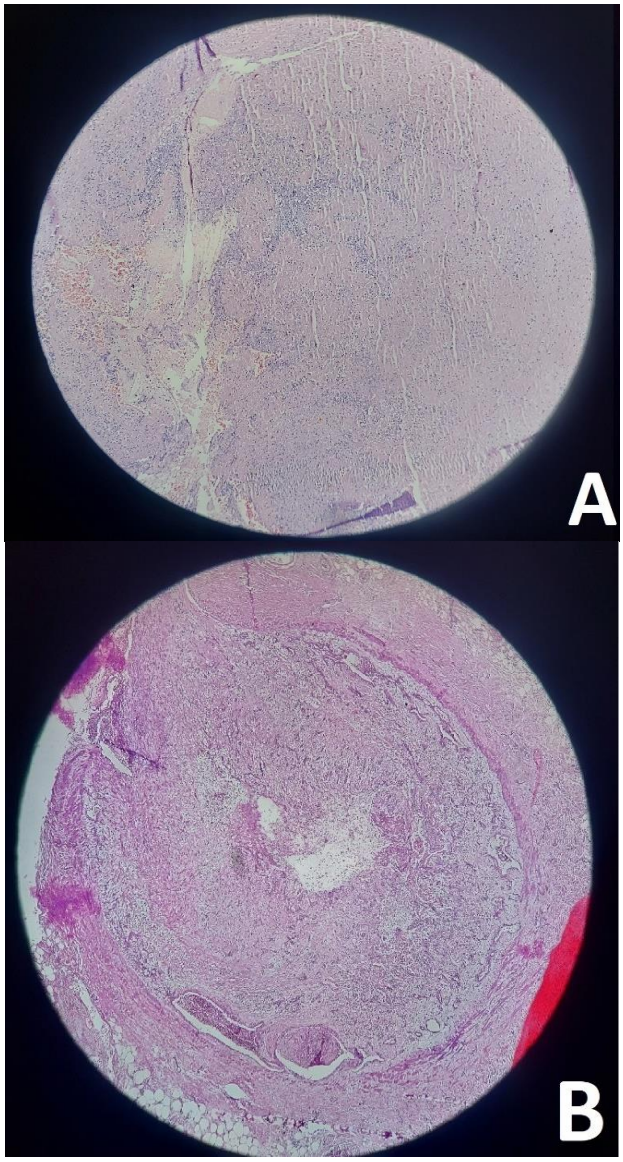

Figure 3. The thromboendarterectomized specimen from the abdominal aorta; 4X (A) and 10X (B)

entity. The known predisposing factors are hypercoagulable states, thrombophilia and malignancy [11]. This sequence is frequently seen in younger patients and these patients should be separated from the typical atherosclerotic process taking place in older patients. In the presence of FFT of aorta, an underlying cause should be suspected [12].

Although the prognosis of patients hospitalized with COVID-19 disease is often determined by the extent of pulmonary lesions, vascular complications can also substantially affect the outcome. Many authors have recently demonstrated the existence of a

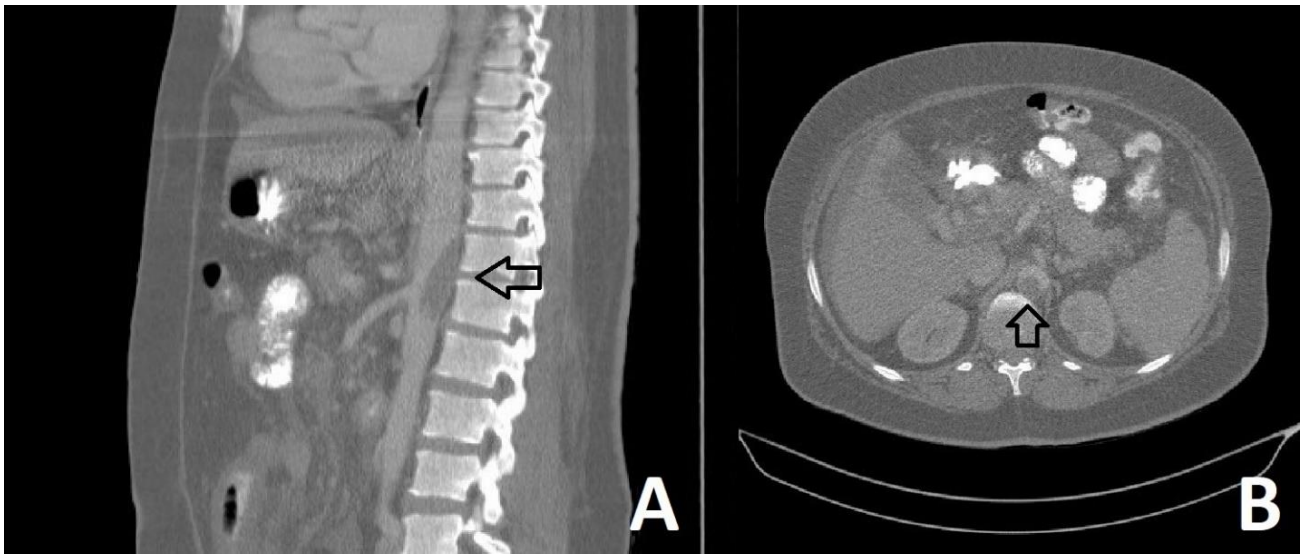

Figure 4: Non-obstructive thrombosis of abdominal aorta (A and B, arrows)

strong link between COVID-19 infection and thromboembolism [5-10]. The physiopathology, however, has not yet been fully elucidated. Dysfunction of platelets and endothelial cells are possible mechanisms that have been proposed by a number of investigators [13, 14]. However, all these proposed mechanisms are based on postulations. For instance, other investigators have proposed that greater fibrinolysis resistance plays a significant role in COVID-19-related thromboembolism and greater platelet aggregation does not have a significant impact in this regard [15]. We ruled out other hypercoagulable states in our patients. Nonetheless, the causality of COVID-19 infection and thromboembolism should be interpreted with caution due to numerous pathologies which can augment thrombosis and coagulation in affected patients.

To our knowledge, there are few reported cases of aortic thrombotic events in COVID-19 patients. Wengerter et al. recently reported four cases of acute aortoiliac and infrainguinal arterial thrombotic events in COVID-19 patients. In their series, two patients had aortic thrombosis. One patient had aortoiliac and femoropopliteal thrombosis and underwent surgical thromboembolectomy. The other patient had partial thrombosis of infra-renal aorta and was managed non-operatively with anticoagulation [8]. We also performed femoral and aortic thromboembolectomy in our second patient. Furthermore, we used non-operative management in our third patient after resection & anastomosis of the small intestine and splenectomy.

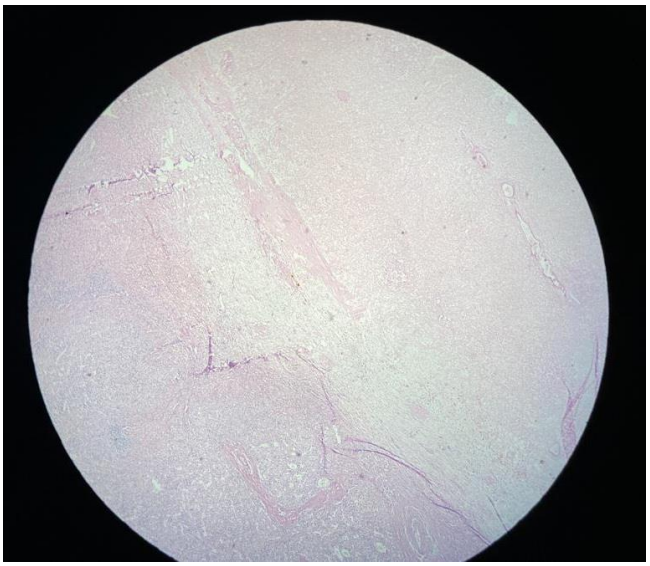

Figure 5. The microscopic pathology of splenectomy specimen (4X)

We also performed femoral and aortic thromboembolectomy in our second patient. Furthermore, we used non-operative management in our third patient after resection & anastomosis of the small intestine and splenectomy [9]. Woehl et al. also reported four COVID-19 patients with acute aortic thrombosis. One patient had non-obstructive thrombosis in DTA. Three patients had infra-renal aortic thrombosis. Axillobifemoral bypass was performed in one of the patients with abdominal aortic thrombosis. Two patients with infra-renal

aortic thrombosis and one patient with DTA thrombosis managed non-operatively with anticoagulation [13]. Recently, Patel et al. reported a case of acute aortoiliac and lower extremity arterial thrombosis who was managed by thrombolysis [16]. Furthermore, splenic infarct has also been reported in association with COVID-19 infection [17, 18]. Our third reported patient had also splenic infract associated with aortic thrombosis.

The management of FFT of aorta is still controversial and there is no consensus regarding the best therapy. Anticoagulation, open surgical thrombectomy, and in certain cases endovascular procedures are possible treatment options [19-22]. Verma et al. suggest that all thoracic and abdominal aortic primary mural thrombi be covered with either stent grafts or closed-cell metal stents or be managed with open thromboembolectomy [23]. In the cases of acute aortic occlusion, open surgical or endovascular management is proposed [24]. However, successful management of the aortic thrombus with anticoagulation has also been reported [23-25]. Dougherty et al. reported two cases of distal lower extremity embolization resulting from primary mural aortic thrombus. They used thrombolysis to treat popliteal emboli. Aortic thrombi were managed by thrombolysis in one case and anticoagulation in the other. The postoperative courses were uneventful in both cases [26]. Thus, anticoagulation alone is considered to be a potential treatment strategy in primary mural aortic thrombosis in selected patients.

The treatment of choice for this condition in COVID-19 patients is more challenging. According to the limited literature review, it seems that surgical thrombectomy, endovascular therapies and non-operative management with anticoagulation alone are possible treatment options. The best management strategy of FFT of aorta in COVID-19 patients should be individualized in each patient according to the general condition and vascular presentation of the thrombosis.

Author contribution

NT, SMH, MZ and SZ managed the patients. HT was involved in anesthetic and intensive care of the patients. SAH did data collection. MA did the pathological analysis. The article was written by NT, SMH and SZ. All authors read and confirmed the final format of the manuscript.

Conflict of Interest

Authors declare no conflicts of interest.

Ethical declaration

Informed consent was obtained from the patients to report these cases.

Funding source

There was no source of funding.

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