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APIXABAN FAILURE IN A POST-BARIATRIC SURGERY FEMALE PATIENT WITH THORACIC AORTIC THROMBUS SECONDARY TO COVID-19

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ABSTRACT

A floating thrombus in the thoracic aorta represents a rare vascular condition frequently associated with morbidity and mortality. There is no standardised management approach, but options potentially include anticoagulation therapy, surgical intervention or a combination of these. Clinicians are increasingly selecting direct oral anticoagulants (DOACs) due to predictable pharmacokinetics. Here, we present a 37-year-old female with a history of Roux-en-Y gastric bypass surgery for obesity, who was found to have an incidental floating thrombus in the thoracic aorta during evaluation for generalised weakness and altered mentation following a recent COVID-19 infection. The patient was initially treated with intravenous heparin and subsequently transitioned to apixaban. Despite medication adherence, she presented two weeks later with worsening mental status and bilateral leg swelling. Repeat imaging revealed rupture of the thrombus, leading to right renal and bowel infarctions. The failure of anticoagulation was attributed to malabsorption secondary to her bariatric surgery. Despite aggressive interventions, the patient ultimately developed multisystem organ failure and succumbed to her illness. Literature suggests that DOACs may be less effective in post-bariatric patients due to altered pharmacokinetics. Due to the absence of clinical guidelines for post-bariatric patients, we recommend full-dose anticoagulation with warfarin, a vitamin K antagonist, to enable therapeutic international normalised ratio (INR) monitoring and necessary dose adjustments. DOACs are less effective in this population, particularly in hypercoagulable states, and the lack of monitoring increases the risk of treatment failure and subsequent life-threatening complications. This case report is of apixaban treatment failure in a female patient with a Roux-en-Y gastric bypass.

KEYWORDS

Apixaban failure, aortic thrombus, COVID-19, post-bariatric surgery, direct oral anticoagulants, DOACs

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LEARNING POINTS

- There is no established management of floating aortic mural thrombus detected by computed tomography.
- The efficacy of oral anticoagulants after bariatric surgery is uncertain.

INTRODUCTION

A floating thrombus in the thoracic aorta is a rare vascular condition associated with significant morbidity and mortality due to embolic complications, including stroke, visceral ischaemia and limb ischaemia. Although the aetiology is often unknown, contributing factors include hypercoagulable states, vascular injury, malignancy and atherosclerosis. A viral-induced coagulopathy, such as coronavirus disease-2019 (COVID-19), is frequently overlooked in clinical practice. COVID-19 is hypothesised to cause an exaggerated immune response through systemic activation of inflammatory cytokines, leading to lymphopenia, thrombocytopenia and haemostasis[1]. This prothrombotic state increases the risk of venous thromboembolism (VTE), myocardial infarction and disseminated intravascular coagulation[1]. Venous thrombosis is a common complication in COVID-19 patients, whereas arterial thrombosis is rare and has only been reported a few times[1,2]. Only a small number of COVID-19 patients have been affected by aortic thrombosis, primarily males with comorbidities such as VTE history and coronary artery disease[3,4].

Currently, no standardised management approach exists for aortic thrombi due to their rarity. Potential treatment options include anticoagulation therapy, surgical intervention or a combined approach. Houmsse et al. reported a successful case of treating a de novo ascending aortic mural thrombus with apixaban[5]. Direct oral anticoagulants (DOACs), such as apixaban, a factor Xa inhibitor, are increasingly used for thromboembolic disorders due to their predictable pharmacokinetics and ease of use compared to vitamin K antagonists. However, their efficacy in patients with altered gastrointestinal anatomy, such as those with a history of bariatric surgery, presents challenges. Limited studies have investigated how bariatric surgery affects drug pharmacokinetics. Changes in drug absorption, distribution and metabolism may alter the efficacy of oral medications, including DOACs[5,6]. This case study presents a rare scenario of a female patient with a Roux-en-Y gastric bypass and recent COVID-19 infection, who was incidentally found to have an aortic thrombus with no known thromboembolic risk factors. She was treated with apixaban and despite adherence, the thrombus ruptured, emphasising the complex nature of managing anticoagulation in patients with altered gastrointestinal anatomy.

CASE DESCRIPTION

A 37-year-old female who had Roux-en-Y gastric bypass surgery 17 years previously for obesity with revisions, gastroesophageal reflux disease and chronic lower back pain on opioids, presented with generalised weakness and altered mentation. Three weeks prior, she was diagnosed with COVID-19 but began experiencing difficulty ambulating with increased bilateral leg swelling since that time.

In the emergency department, she was afebrile and haemodynamically stable, but disoriented. Laboratory studies showed elevated blood ammonia (142 mmol/l), WBCs (12.3 $\times 10^3$/µl) and influenza A positivity. Neurological evaluation and brain imaging were unremarkable. A CT angiogram of the chest revealed bilateral upper lung ground glass opacities consistent with multifocal pneumonia and an incidental floating thrombus in the lower thoracic aorta measuring 0.9 × 0.9 × 3.5 cm *(Fig. 1)*. Arterial doppler revealed complete occlusion in the bilateral distal posterior tibial arteries without clinical signs of acute limb ischaemia.

The patient's condition worsened with progressive obtundation secondary to encephalopathy, requiring mechanical ventilation and intensive care unit transfer. She received intravenous (IV) piperacillin-tazobactam, vancomycin for pneumonia, lactulose, rifaximin and IV levocarnitine for hyperammonaemia. After neurological improvement, she was extubated after nine days.

Cardiology and vascular surgery were consulted for the incidental aortic thrombus. Hypercoagulability workup, including thrombophilia screening, was unremarkable. A transoesophageal echocardiogram revealed an echogenic mass in the descending thoracic aorta *(Fig. 2)*, consistent with a thrombus, with no valvular vegetation and preserved ejection fraction (66%). She was started on IV heparin, later transitioned to oral apixaban 5 mg twice daily, clopidogrel 75 mg daily and atorvastatin 40 mg daily. Vascular surgery

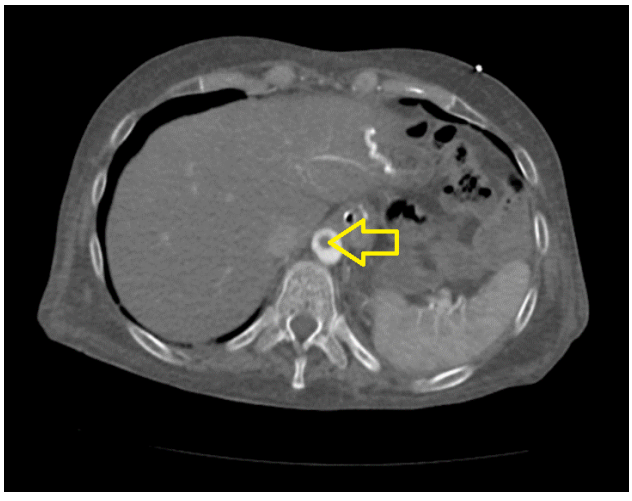


Figure 1. CTA of the chest with and without contrast shows a floating thrombus in the non-aneurysmal lower thoracic aorta, measuring 0.9 × 0.9 × 3.5 cm.

did not recommend surgical intervention due to absent limb ischaemia symptoms. She was discharged with outpatient follow-up.

Two weeks later, she returned with worsening bilateral leg weakness. Despite medication adherence, a repeat CT angiogram showed rupture of the aortic thrombus and worsening bilateral posterior tibial artery occlusions. Subsequently, this progressed to right renal and bowel infarctions. Apixaban failure was suspected as a malabsorptive complication secondary to bariatric surgery, prompting a switch back to IV heparin. Despite aggressive interventions, she developed hypotension, lactic acidosis, cardiomyopathy, disseminated intravascular coagulation and eventually succumbed to multisystem organ failure.

DISCUSSION

COVID-19 induces a proinflammatory response triggering thrombus formation. Venous thrombosis is a common COVID-19 complication, with a prevalence of 60.8 to 85.4% in critically ill patients, compared to 3 to 47.9% in non-COVID-19 patients[2]. In contrast, arterial thromboembolic events are rare, with a 3.9% incidence[1]. Abdominal aortic thrombosis is exceedingly rare. Our case highlights a female patient with COVID-19 and influenza A who developed an aortic thrombus despite no prior thromboembolic risk factors.

A literature review by Giannetta et al. identified six cases of abdominal aortic thrombosis, only two of which were associated with COVID-19[3]. Woehl et al. reported a case series in which all patients were male with significant comorbidities, such as coronary artery disease and prior VTEs[4]. Our patient was female, lacked traditional risk factors and had no history of thromboembolic disorders, making this case particularly rare.

Floating thrombi, also known as pedunculated thrombi, are rare but highly emboligenic, with a 73% risk of embolic complications[7,8]. Most cases remain asymptomatic until presenting as severe events such as stroke, renal infarction, visceral ischaemia or peripheral limb ischaemia[1]. A study of 10,671 autopsies found a 0.45% incidence of aortic thrombus, with 17% showing distal embolisation and 6% identified as cause of death[9,10]. Early detection and intervention are crucial to prevent life-threatening complications.

Due to its rarity, no strict diagnostic criteria exist for aortic thrombus. Management involves radiological confirmation, ruling out atherosclerotic and thrombotic risk factors, and thrombophilia testing[9].

Venous thrombosis is managed conservatively with anticoagulation, whereas arterial thrombosis may require immediate heparinisation to prevent new thrombi formation[11]. Treatment should be tailored based on patient-specific factors. In some cases, surgical intervention is necessary[8]. Woehl et al. reported that half of COVID-19 patients with arterial thrombosis did not survive, emphasising early detection and intervention. In our patient, transoesophageal echocardiogram facilitated early diagnosis, and systemic IV anticoagulation was initiated.

Yang et al. analysed five cases, demonstrating a preference for conservative treatment with anticoagulation, yet some patients experienced disease progression[12]. Our case similarly depicts the unpredictability of anticoagulation efficacy, with thrombus rupture transpiring despite apixaban therapy. Unlike the cases in Yang et al., our patient lacked aortic disease or stent placement but had undergone bariatric surgery, introducing an uncommon risk factor.

Apixaban was chosen for its ease and efficacy in managing thromboembolic events, but our patient's history of Roux-en-Y gastric bypass introduced challenges. This surgery alters gastrointestinal anatomy, potentially compromising oral drug absorption. Bypassing critical absorption sites

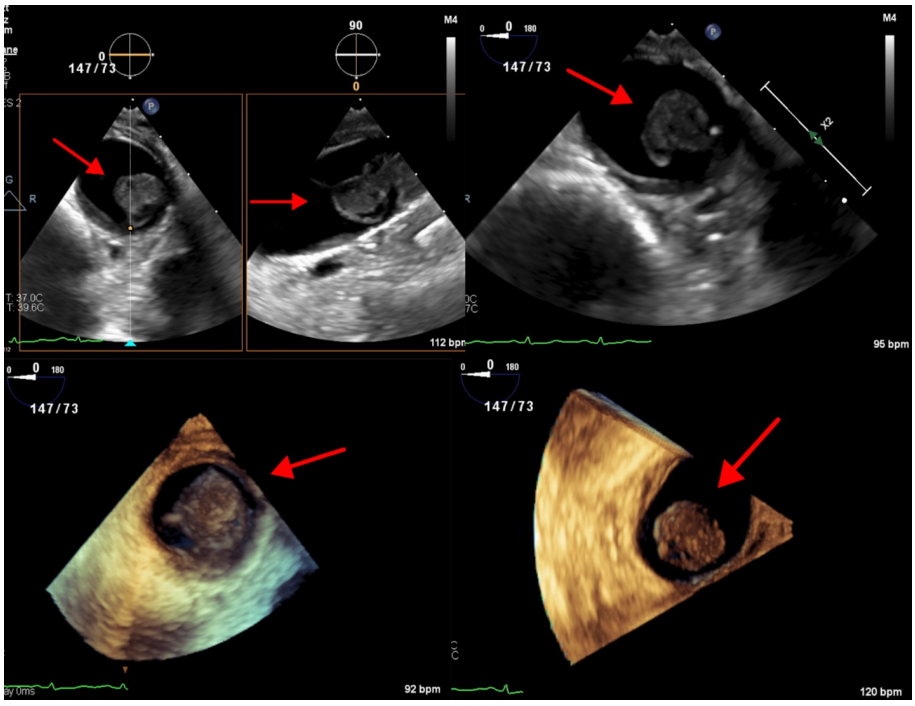


Figure 2. Transoesophageal echocardiogram shows a large non-occlusive pedunculated thrombus in the distal descending thoracic aorta, measuring 1.01 × 0.87 × 2.7 cm in diameter.

in the proximal intestine and altered transit time can result in subtherapeutic drug levels. While routine DOAC concentration monitoring is unnecessary, it may be required in cases like our patient as this likely contributed to thrombus rupture and subsequent complications[11].

The long-term effects of bariatric surgery on medication efficacy are crucial. A study of 28 postoperative gastric bypass patients found significantly lower factor X activity, attributed to surgical effects rather than apixaban pharmacodynamics[13]. Martin et al. reviewed how Roux-en-Y gastric bypass impacts oral anticoagulant pharmacokinetics, reporting reduced absorption of DOACs and recommending warfarin due to its ability to be monitored with INR[14]. This aligns with our case, where apixaban failure led to catastrophic embolic complications. Given the limited data on DOAC use in this population, our case emphasises the importance of careful anticoagulation selection and highlights the need for further pharmacokinetic studies.

CONCLUSION

This case underscores the multifactorial nature of arterial thrombosis in COVID-19 and the impact of bariatric surgery on drug absorption. COVID-19-induced coagulopathy likely contributed to the aortic thrombus. While DOACs such as apixaban are favoured, their efficacy in altered gastrointestinal anatomy remains uncertain. This case is one of apixaban treatment failure in a female patient with a Roux-en-Y gastric bypass. The anticoagulation failure resulted in thrombus rupture. Given the absence of clinical guidelines for post-bariatric patients, we suggest full-dose anticoagulation with warfarin, a vitamin K antagonist, to enable therapeutic INR monitoring and necessary dose adjustments. DOACs may be less effective in such patients, particularly if they have a hypercoaguable state, and the lack of monitoring increases the risk of treatment failure and subsequent life-threatening complications.

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