



Heparin-induced thrombocytopenia causing graft thrombosis and bowel ischemia postendovascular aneurysm repair

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Heparin-induced thrombocytopenia (HIT) is an immune-mediated thrombocytopenia resulting from prior heparin exposure. It can be associated with limb- or life-threatening thrombotic events. Patients undergoing any vascular procedures including endovascular procedures that require heparin administration are at risk. There is very little reported in the literature with regards to thrombosis associated with HIT after endovascular aortic aneurysm repair. All reported cases of HIT thrombosis presented as acute arterial lower limb ischemia or deep vein thrombosis. In this report, we present a case of HIT complicated by stent graft thrombosis and bowel ischemia. (*J Vasc Surg* 2015;61:234-6.)

Heparin is commonly used as an anticoagulant in the prevention and treatment of thromboembolism during cardiac and vascular surgery procedures. Despite the clinical advantage of heparin, some adverse effects with bleeding and thrombosis may occur. Heparin-induced thrombocytopenia (HIT) is a known complication of heparin therapy. It is defined as a sudden fall in the platelet count and usually appears a few days after the start of heparin.¹ It may manifest itself as only a slight decrease in platelet count (HIT-I), or it may be complicated by thrombotic events (HIT-II). For patients undergoing vascular procedures, in particular endovascular interventions, the body of literature for HIT is scarce. Only a few case reports²⁻⁴ have been published, and the presentation and incidence are still unknown. Consent was obtained from the patient to publish these images and clinical history.

CASE REPORT

A 70-year-old man with a medical history of hypertension, hyperlipidemia, coronary artery disease, and prostate carcinoma treated with radio and hormonal therapy underwent elective endovascular repair of an infrarenal abdominal aortic aneurysm. He was treated with an Endurant, (Medtronic, Santa Rosa, Calif) aorto-uni-iliac graft, amplatzer occluder of the left common iliac artery, and a right-to-left femoral-femoral bypass with Dacron graft. The decision to occlude the left common iliac artery and use an aorto-uni-iliac configuration was made intraoperatively due to the high

degree of tortuosity of the left iliac artery. At the time of the procedure, 5000 IU of unfractionated heparin (UFH) was given intravenously. He was discharged on postoperative day 1 after an uneventful postoperative course on aspirin 80 mg daily. Twelve days later, the patient presented to the emergency department with a 1-day history of bloody diarrhea and general malaise. He had no abdominal pain or other symptoms. His abdominal exam was unremarkable; the pulse in the femoral-femoral bypass graft was faint, and distal pedal pulses were not palpable. Platelet count was only 18,000. Noninvasive vascular studies were performed upon readmission. Duplex ultrasound revealed a patent right-to-left femoral-femoral bypass with thrombus visualized throughout the graft. Ankle-brachial indexes were measured and were 0.48 and 0.45 for the right and left side, respectively. Computerized tomography (CT) angiogram of the abdomen and pelvis revealed nonocclusive thrombosis of the aortic graft, the superior mesenteric artery (SMA), as well as the femoral-femoral graft (Fig). There was no technical abnormality such as graft kinking or stenosis demonstrated on the scan. There was no endoleak, the inferior mesenteric artery was thrombosed, and the internal iliac arteries were patent. The CT scan also showed some edema and thickening of the large bowel wall but no evidence of transmural bowel ischemia. Based on the patient's clinical presentation, CT findings, and drop in platelet count, the diagnosis was subclinical bowel ischemia secondary to HIT thrombosis of the aortic stent graft and the SMA. The patient was treated nonoperatively with intravenous anticoagulation using argatroban. Intravenous antibiotics (metronidazole and tazocin) were started at presentation and administered for 24 hours. The patient was examined daily and platelet count followed. The count increased gradually over time (50,000 at 5 days and 80,000 at 10 days after presentation). The diagnosis was confirmed by HIT immunoassay (heparin platelet factor 4), and the bloody diarrhea subsided 10 days after presentation. Two weeks after initiating anticoagulation therapy with the use of argatroban, warfarin was started when the patient's platelet count reached 100,000. Argatroban was stopped after 3 days of combined anticoagulation therapy; the patient was discharged without any symptoms and normal bowel movements. Three months later, the patient remained asymptomatic and

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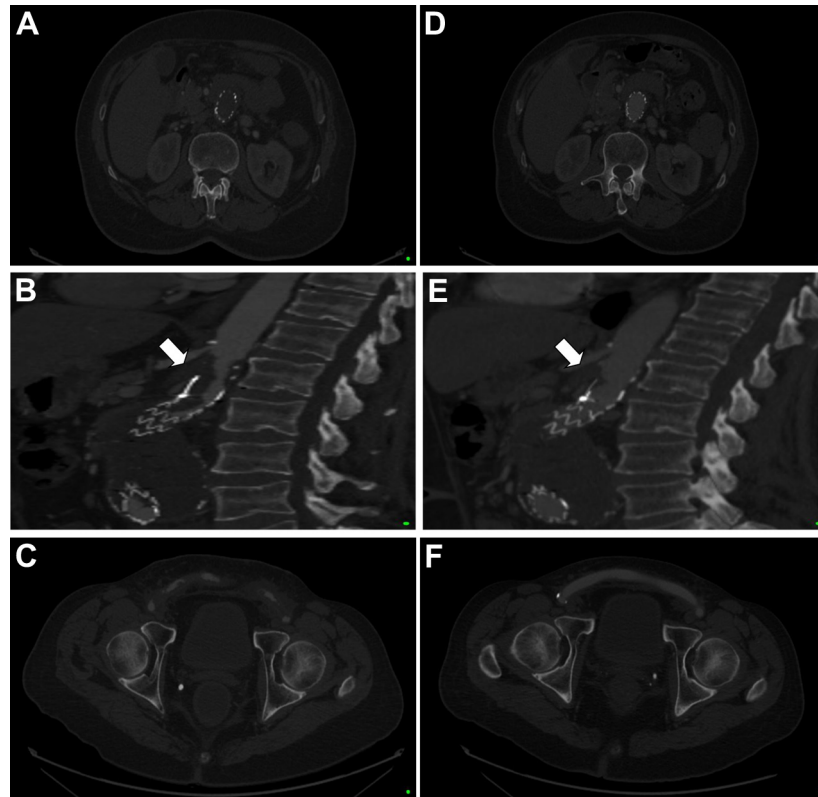


Fig. Representative computed tomography (CT) angiogram images at presentation (A-C) and at 3-month follow-up (D-F) demonstrating significant recanalization of the endograft (A vs D) and the right-to-left femoral-femoral graft (C vs F). Note residual thrombus in the superior mesenteric artery (SMA; arrow) in the follow-up despite significant recanalization of the endograft (B vs E).

follow-up CT angiogram showed near complete recanalization of the endograft and femoral-femoral graft and residual thrombus in the SMA origin (Fig).

DISCUSSION

HIT is a known complication of heparin therapy usually occurring within the first 10 days after heparin treatment has started.¹ Type one (HIT-I), the most common variant, is typically characterized by a fall in platelet count within the first 2 days after initiation of heparin therapy. This will usually correct itself with the discontinuation of heparin therapy.⁵ Thrombocytopenia in this subtype is due to a nonimmune mechanism secondary to a direct effect of heparin on platelet activation.⁵ Type two (HIT-II) is less common and more aggressive than type one and is also known as heparin-associated thrombocytopenia and thrombosis. It is an immune-mediated disorder associated with the formation of antibodies against the heparin-platelet factor 4 complex.

The overall incidence of HIT-II is 2.6%.⁶ The incidence is related to the duration of heparin exposure: 0.2% to 5.0% in patients exposed to heparin for more than 4 days^{6,7}; and 0.2% for those treated with UFH for less than 4 days.⁸ HIT-II has a mortality rate of approximately 20% to 30% and is complicated by limb amputation

in 10% to 20% of unrecognized and untreated patients.⁹ The use of UFH rather than low-molecular-weight heparin, surgical patients, and female gender are all additional but less important risk factors for HIT.^{7,10}

HIT is not uncommon with vascular surgery, although the exact incidence is not clear. An obvious variation is seen in the literature in the incidence of HIT as confirmed by HIT assay. It has been shown to be as low as 1.9% in some reports and as high as 21% in others.^{11,12} Diagnosing HIT based on decreased platelet count is difficult in patients postinsertion of a vascular graft, especially postaneurysm repair, as the postoperative thrombocytopenia could be due to platelet adherence to the graft material.³ To date, HIT secondary to endovascular aneurysm repair is uncommon with unknown incidence.

Five cases of thrombosis-associated HIT-II have been reported in three case reports.²⁻⁴ All of these HIT-II cases presented with either acute lower limb ischemia or lower limb deep vein thrombosis; endograft thrombosis and mesenteric arterial thrombosis with ischemia have not been previously reported in the literature.

The primary finding for diagnosis of HIT is a fall in the platelet count of more than 50% that occurs within 2 weeks after using or starting heparin therapy. Different laboratory

tests, such as enzyme-linked immunosorbent assay,¹³ platelet ¹⁴C serotonin release assay,¹⁴ and heparin-induced platelet aggregation,¹⁵ can all be used for confirmation of the diagnosis. Clinical features of HIT can be either venous thrombosis and/or embolism, including deep venous thrombosis and pulmonary embolism, or arterial thrombosis involving aorta and major limb arteries, resulting in limb ischemia.¹⁶ Unusual thromboembolic events and lack of response to heparin with a history of heparin exposure should raise suspicion of HIT; repeat platelet counts should be done along with other serologic tests. After endovascular procedures, HIT may also rarely manifest as thrombotic complication at the site of intervention.^{16,17}

In this case, we treated the patient primarily with anticoagulation because there was no immediate limb threat and bowel ischemia was incomplete. We did not consider more aggressive intervention such as surgical or endovascular revision or thrombectomy since both would have carried the potential of graft dislodgment and distal embolization. Intra-arterial thrombolysis was contraindicated due to profound thrombocytopenia. Treatment of a patient with HIT starts with immediate cessation of any sources of heparin and replacement with an anticoagulant therapy that does not cross-react with HIT antibodies.^{18,19} Alternative anticoagulants include danaparoid, lepirudin, fondaparinux, and argatroban.^{18,19} Warfarin should not be started for HIT patients until the thrombocytopenia resolves and patients have been stably anticoagulated with one of the above anticoagulants. Low-molecular-weight heparin should not be substituted for UFH after HIT develops because of frequent cross-reactivity with HIT antibodies.

CONCLUSIONS

HIT is a rare but potentially limb- and life-threatening adverse reaction seen in patients exposed to heparin. Patients undergoing vascular and endovascular procedures in which large doses of heparin are used are at risk. A high index of suspicion is required in order to diagnose it and initiate proper therapy to prevent serious thrombotic complications.

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