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Case Report

Abdominal Aortic Aneurysm with Essential Thrombocythemia: A Case Report Describing Perioperative Management in Open Surgery

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We report perioperative management and open surgery to treat a case of infrarenal abdominal aortic aneurysm with essential thrombocythemia (ET), a chronic myeloproliferative disorder associated with arterial or venous thrombosis, idiopathic bleeding, and heparin-resistant diathesis. Following careful preoperative management, including assessment of heparin resistance, open surgery was successfully performed to treat the aortic aneurysm of our patient. This report shows that optimal preparation for surgery is important to safely perform abdominal aortic aneurysm repair and prevent perioperative thrombosis and bleeding in patients with abdominal aortic aneurysm with ET.

Keywords: abdominal aortic aneurysm, essential thrombocythemia, heparin resistance

Introduction

Essential thrombocythemia (ET) is a chronic myeloproliferative disorder associated with vascular thrombosis, idiopathic bleeding, and heparin-resistant diathesis.[1–3] Heparin resistance may lead to systemic thrombotic events, particularly during cardiovascular surgery requiring anticoagulation management. However, no clear guidelines exist for the intraoperative and perioperative management of abdominal aortic surgery, including preoperative assessment for heparin resistance, in patients with abdominal aortic aneurysm (AAA) with ET. Here we describe a perioperative management for open surgical intervention to treat an AAA with ET.

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Case Report

A 76-year-old man (body weight, 70.5 kg; height, 164.5 cm) underwent preoperative screening examinations before bladder stone treatment. Computed tomography showed a 56-mm fusiform infrarenal AAA (**Fig. 1A**). The patient was referred to our department for AAA treatment following surgery for a bladder stone. The patient's medical history included hyperlipidemia, diabetes mellitus, glaucoma, lacunar infarction, and ET with *JAK2* V617F mutation. To treat the lacunar infarction and ET of the patient, he was prescribed to take oral aspirin (100 mg/day) 6 years earlier. The patient had no family history of cardiovascular diseases. Preoperative coronary angiography showed noncritical stenosis in the distal left anterior descending artery. Routine laboratory data were within normal limits except for mild renal dysfunction and a high platelet count. A complete blood count showed a significantly elevated platelet count of $639 \times 10^3/\mu L$ (normal range, $158–348 \times 10^3/\mu L$), a mildly elevated white blood cell count of $115 \times 10^2/\mu L$ (normal range, $33–86 \times 10^2/\mu L$), and a hemoglobin level of 13.3 g/dL (normal range, 13.7–16.8×10^2 g/dL).

The patient was referred preoperatively to a hematologist to determine surgical risk. The hematologist authorized invasive treatment for AAA because ET was stabilized with aspirin. The patient's operative tolerance was acceptable; therefore, open surgical intervention was selected for the radical treatment of AAA. The problems associated with open AAA surgery were whether (1) the antiplatelet drug for ET treatment could be discontinued preoperatively and (2) intraoperative heparin resistance would occur. The hematologist determined that perioperative discontinuation of antiplatelet medication was feasible; hence, aspirin was discontinued 10 days preoperatively. To rule out heparin resistance, we decided to administer heparin to our patient on the ward preoperatively to con-

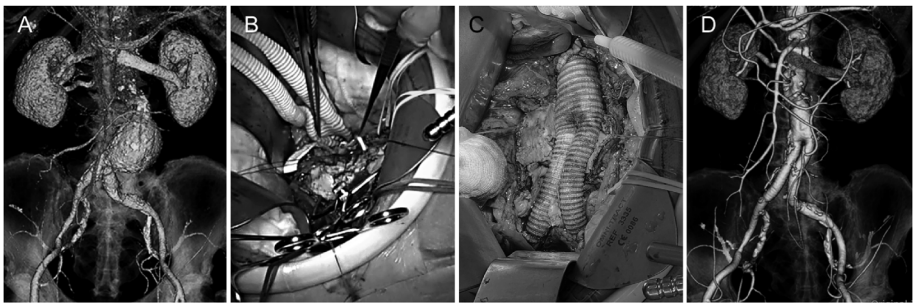

Fig. 1 CT and surgical findings. (**A**) Initial three-dimensional CT image of infrarenal AAA. (**B**) Proximal anastomosis under appropriate anticoagulation management using heparin. (**C**) Surgical field showing a Y-shaped Dacron graft and good hemostasis. (**D**) Postoperative three-dimensional CT image.
AAA: abdominal aortic aneurysm; CT: computed tomography

firm an anticoagulant response. The patient was injected intravenously with a standard starting heparin dose of 5000 units into the forearm, and venous blood was drawn from the opposite forearm 10 min later. This heparin sensitivity test (HST) showed an activated coagulation time (ACT) of 176 s (preadministration value, 109 s) and an activated partial thromboplastin time (APTT) of >150 s (above the upper limit of the measurable value; preadministration value, 30.3 s; normal range, 23.7–34.8 s). HST showed that intraoperative anticoagulation management with heparin was feasible because the ACT value after the standard starting heparin administration was <200 and the APTT value was >1.5 times higher than the preadministration value. Additionally, the preoperative platelet factor-4 (PF-4) value, a possible indicator of heparin resistance, was 13 ng/mL (normal range, ≤20 ng/mL), supporting the likelihood of no heparin resistance. Other preoperative coagulation tests showed a prothrombin time–international normalized ratio of 1.02 (normal range, 0.85–1.15), fibrinogen of 359 mg/dL (normal range, 200–400 mg/dL), and antithrombin-III (AT-III) of 83% (normal range, 79–121%), all within normal limits.

Open surgical repair was performed 4 days after the preoperative HST. During surgery, a median abdominal incision was made and the infrarenal aorta was replaced with a Y-shaped Dacron graft (J graft 20×10 mm, Japan Lifeline Inc., Tokyo, Japan). Intraoperative ACT values were controlled within 195–256 s (pre-heparin administration value, 134 s) using a heparin dose of 10,000 units in total. Because the preoperative HST showed that the standard starting dose of 5000 units did not reach the targeted ACT >200, a modified weight-based heparin dosage was used. Specifically, heparin of 7000, 2000, and 1000 units was administered before aortic and arterial clamping, at 1 h, and at 2 h, respectively. The aortic and arterial clamping time was 1 h and 44 min in total. After graft replacement, the effect of heparin was neutralized with 100 mg protamine sulfate, resulting in an ACT value of 137 s. Hemostasis was achieved without platelets and fresh-frozen plasma, and surgery was successfully performed without any embolic events or critical bleeding (**Figs. 1B** and **1C**). Aspirin was restarted on postoperative day 2. Platelet counts remained at 299–673×10^3/μL during postoperative hospitalization. The patient did not experience complications and was discharged on postoperative day 16. At the 1-month postoperative follow-up, the platelet count and PF-4 value were 505×10^3/μL and 11 ng/mL, respectively, both of which were not higher than the preoperative values. Additionally, no clinical symptoms, such as thrombosis and bleeding diathesis, were observed 6 months after surgery (**Fig. 1D**).

Discussion

ET is a chronic myeloproliferative disorder characterized by marked platelet count increase associated with thrombosis and bleeding.[1,2] Patients with ET may develop heparin resistance,[2,3] which can interfere with the treatment of cardiovascular diseases. AAA accompanied by ET is very rare, and there are no clear guidelines for the perioperative management of these concurrent conditions. In this report, we present a case of a 76-year-old man with an infrarenal AAA accompanied by ET. The patient underwent open surgical intervention for AAA after a preoperative HST. The surgery was completed with intraoperative anticoagulation using heparin administration dosed according to the preoperative HST result.

ET is characterized by conflicting symptoms of thrombosis and bleeding.[2] Thrombosis is more frequently observed in patients with high platelet counts, whereas bleeding is not associated with platelet counts.[4] The conflicting symptoms make it difficult to estimate which pathology is more likely to occur, especially in patients with high platelet counts during perioperative periods. Therefore, it is important to be aware of possible thrombotic and bleeding symptoms regardless of platelet counts

during the perioperative period in patients with AAA accompanied by ET.

In aortic surgery, it is necessary to maintain the patient in an anticoagulated state. However, patients with AAA with ET may develop heparin resistance and therefore may require the use of alternative drugs, rather than heparin, to maintain intraoperative anticoagulation. Many cases of intraoperative decisions to use argatroban hydrate due to failure of anticoagulation after heparin administration have been reported.[5,6] Nevertheless, there are no clear guidelines on whether heparin or alternative drugs should be used during cardiovascular surgery for patients with ET.

Patients with ET exhibit heparin resistance due to the marked increase in PF-4, a platelet-specific protein present in platelet α-granules that is released into the blood when platelets are activated.[2,3] The released PF-4 binds to heparin-like substances such as heparan sulfate on vascular endothelial cells and remains in the vessel wall. When heparin is administered, it acts on platelets and vascular endothelial cells to release PF-4, which binds strongly to heparin, inhibiting the formation of a complex between AT-III and heparin and thus neutralizing the anticoagulant effect of heparin.[2,3] In contrast, argatroban hydrate is a selective antithrombin agent that does not require cofactors such as AT-III and does not increase PF-4. Argatroban hydrate exerts its anticoagulant effect without the neutralizing effect of PF-4, and argatroban-induced anticoagulation can be confirmed by ACT during surgery and cardiovascular management.[5] However, the method of selecting anticoagulants for heparin-resistant patients based on intraoperative judgment may lead to three clinical problems: (1) switching to an alternative drug may increase operative time; (2) an ineffective drug may be administered, leading to adverse events; and (3) heparin may contribute to platelet activation[7] that could be avoided using an alternative drug. In the absence of guidelines for the surgical treatment of AAA in patients with ET, realistic strategies are needed to address these clinical problems.

In this case, heparin sensitivity was examined preoperatively to determine if heparin could be used intraoperatively as anticoagulation therapy. Preoperative heparin administration confirmed anticoagulant activity, and a normal PF-4 value supported the assessment of heparin efficacy. Additionally, in our patient, the standard starting heparin dose of 5000 units[8] did not result in an ACT >200, a useful threshold for intraoperative management of AAA surgery. Therefore, we used weight-based heparin dosing during surgery.[9] This strategy avoided the use of argatroban hydrate, which carries a high risk of bleeding and requires frequent anticoagulation testing using ACT during surgery.[5,6] However, intraoperative heparin administration may cause platelet activation and subsequent heparin resistance. Therefore, PF-4 was measured 1 month after the AAA surgery. The PF-4 value was normal, with no residual effects of intraoperative heparin administration on platelet activation.

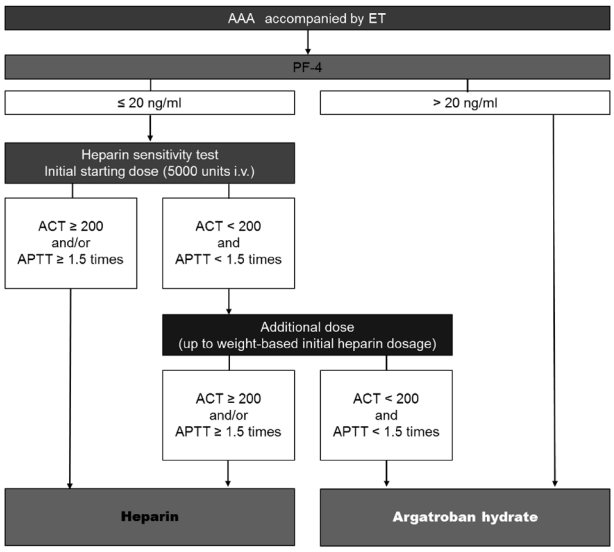

Fig. 2 Our strategy for anticoagulant selection during surgery for AAA accompanied by ET.
AAA: abdominal aortic aneurysm; ACT: activated coagulation time (seconds); APTT: activated partial thromboplastin time (seconds); ET: essential thrombocythemia; i.v.: intravenous; PF-4: platelet factor-4

Another important factor affecting platelet activation is the selection of either open surgery or endovascular aneurysm repair (EVAR) as the therapeutic intervention for AAA. Although EVAR causes less tissue trauma than open surgery, postoperative platelet activation due to catheter manipulation has been reported in previous literatures.[10] Furthermore, endoleaks may remain after EVAR, disrupting the coagulation–fibrinolytic system and causing continued platelet consumption, leading to concerns for bleeding and thrombosis. Therefore, in our patient with AAA with ET, who had an increased risk of bleeding and thrombus formation, open AAA surgery was selected because of the patient's ability to tolerate it.[10] Finally, we show our strategy regarding the selection of intraoperative anticoagulants for patients with AAA accompanied by ET in **Fig. 2**. However, further studies are needed for deeper consideration of intraoperative anticoagulation.

Conclusion

Preoperative HST and PF-4 assessment was useful in safely and effectively performing open AAA surgery in a patient with ET.

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Disclosure Statement

All authors have no conflicts of interest to declare.

Informed Consent

Written informed consent for publication of patient information and images was obtained from the patient.

Author Contributions

Study conception: all authors
Data collection: all authors
Writing: NY
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

Data Availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during this report.

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