

Acute Subdural Hematoma Complicating Heparin-induced Thrombocytopenia: A Case Report

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Abstract

Heparin-induced thrombocytopenia (HIT) is an antibody-mediated drug reaction to heparin use that causes platelet aggregation, followed by thrombocytopenia. Despite the thrombocytopenia, the main complications of HIT are thromboembolic in nature rather than hemorrhagic, and in particular, intracranial hemorrhage is rare. Herein, we describe a case of atraumatic acute subdural hematoma secondary to HIT, which was treated by platelet transfusion and surgery. A 77-year-old woman was admitted to our hospital for the treatment of severe aortic valve stenosis. Unfractionated heparin was administered during the preoperative period and during the aortic valve replacement surgery. Three days after the cardiac surgery, the patient presented with coma consistent with an acute subdural hematoma in the posterior fossa and obstructive hydrocephalus. Laboratory examination revealed a marked decrease of the platelet count to 40000/ μ L, and subsequent serological assay confirmed the diagnosis of HIT. The patient was treated by transfusion of platelets and fresh frozen plasma, and surgical removal of the hematoma. We started the administration of argatroban for substitution of heparin 4 days after the craniotomy. On day 13 after the neurosurgery, the patient developed cerebral infarction due to left middle cerebral artery occlusion and persistent right hemiparesis. We presented a rare case of the patient who developed acute subdural hematoma complicating HIT. Emergency craniotomy was successfully performed after administering platelet transfusions. Our experience with the present case suggests that platelet transfusions may be effective for performing emergency surgery for intracranial hemorrhage, even in patients with HIT.

Keywords: spontaneous acute subdural hematoma, heparin-induced thrombocytopenia

Introduction

Heparin-induced thrombocytopenia (HIT) is an immune-mediated drug reaction to administration of heparin, characterized by thrombocytopenia, as well as a hypercoagulability state associated with thrombosis. The diagnosis is made by demonstrating the presence of platelet-activating immunoglobulin reactive with the platelet factor 4-heparin complex, which promotes aggregation of platelets and stimulation of the vascular endothelial cells.¹⁾

In contrast to other consumptive thrombocytopenic states, HIT mainly manifests as thromboembolic complications, and hemorrhagic complications are

rare.²⁾ There are only a few reported cases of intracranial hemorrhage associated with HIT.^{3–6)} No cases of subdural hematoma complicating HIT have ever been reported before. Because of its rare occurrence, a standard management strategy for intracranial hemorrhage complicating HIT still remains to be established.

Prophylactic platelet transfusions for thrombocytopenia have been thought to be contraindicated in patients with HIT, because they may induce thrombotic events.^{7,8)} The 2012 American College of Chest Physicians (ACCP) clinical practice guidelines recommend avoidance of prophylactic platelet transfusions to correct low platelet counts. The guidelines also recommend limiting platelet transfusions to only those presenting with bleeding or scheduled for some invasive procedure,⁹⁾ although this also remains controversial.

For neurosurgical procedures, the generally accepted threshold for platelet transfusion, to minimize the

Received August 5, 2021; Accepted October 5, 2021

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risk of hemorrhagic complications, is 100000/ μL .^{10,11)} Herein, we describe the case of a patient with HIT complicated by subdural hematoma who underwent platelet transfusions and subsequent surgical treatment.

Case Report

A 77-year-old woman, with a previous history of atrial fibrillation and hypertension, was admitted to our emergency department with a history of recurrent episodes of syncope. Transthoracic echocardiography revealed that episodes of syncope were caused by severe aortic valve stenosis, and aortic valve replacement surgery was planned. She had no history of trauma, including head injury, related to her episodes of syncope. Examination at admission revealed no neurological deficits. On the day after admission, preoperative coronary angiography was performed. During the examination, the patient received intravenous administration of unfractionated heparin. Furthermore, unfractionated heparin was also used to prevent coagulation of the peripheral venous catheter. Five days after admission, mechanical aortic valve replacement was performed, and the patient received continuous administration of unfractionated heparin during and after the surgery. Three days after the aortic valve replacement, the patient showed rapid deterioration of her consciousness level (Glasgow Coma Scale score 6: eye opening 1, verbal response T, motor response 4) from an alert state within an hour. There were no signs of any paralysis. Computed tomography (CT) revealed bilateral acute subdural hematomas in the posterior fossa (Fig. 1).

As compression of the brainstem and obstruction of the fourth ventricle caused obstructive hydrocephalus, emergency surgery was considered as being indicated for removal of the hematoma. Preoperative laboratory investigation revealed that the platelet count had declined to 41000/ μL , from 96000/ μL on the day before. Coagulation studies revealed a prothrombin time-international normalized ratio (PT-INR) of 1.13, activated partial thromboplastin time (APTT) of 58.6 seconds, plasma fibrinogen level of 460 mg/dL, and plasma D-dimer level of 8.7 $\mu\text{g}/\text{dL}$. As no other cause was apparent, we considered HIT as the most probable cause of the acute thrombocytopenia. The 4T's score, which is widely used to diagnose HIT and described later, was 6, indicating a high probability of HIT. Serological testing by enzyme-linked immunosorbent assay showed an antibody titer of 0.7 units/mL for the heparin/PF4-complex, and this value did not meet the criterion for the diagnosis of HIT at that time.

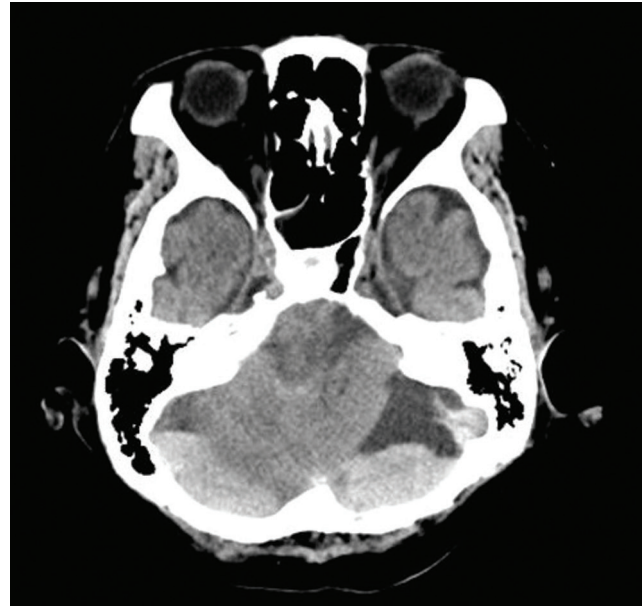


Fig. 1 Preoperative brain CT. Bilateral subdural hematoma compressing the brainstem and fourth ventricle. CT: computed tomography.

For emergency surgery, protamine sulfate was administered to neutralize the effect of the continuous heparin infusion. Then, following transfusions of platelets, fresh frozen plasma and red blood cells, bilateral suboccipital decompressive craniectomy, dural incision, and evacuation of the hematoma were performed. A ventricular catheter was placed. The hematoma was red-to-brown in color, and not capsulated. There was no obvious point of active bleeding.

Postoperative CT showed sufficient decompression of the cerebellum and brainstem (Fig. 2), and we removed the ventricular catheter. The platelet count immediately after the operation was 141000/ μL . However, 4 days later, the platelet count decreased again to 48000/ μL , as shown in Fig. 3. At this time, a serological testing revealed a positive result (higher than 5 units/mL) for antibody to heparin/PF4-complex, which fulfilled the criterion for definitive diagnosis of HIT. To avoid postoperative hemorrhagic complication, we stopped administering any anti-coagulants for first 3 days after the craniotomy. Four days after the craniotomy (day 11 of the admission), we initiated the patient on treatment with argatroban as a substitute for heparin. We administered argatroban from day 11 to day 18 of admission, and switched to warfarin since day 19.

The patient's consciousness gradually improved after the craniotomy and there was no evidence of paralysis. On day 13 after the craniotomy, the patient developed right hemiparesis of sudden onset, and

magnetic resonance imaging (MRI) showed a left cerebral infarction due to left middle cerebral artery occlusion. CT showed no evidence of recurrence of the hematoma. The left hemiparesis was persistent and the patient was transferred to long-stay hospital on day 60 after admission.

Discussion

Clinically, decrease of the platelet count by more than 50% or a thrombotic event occurring within

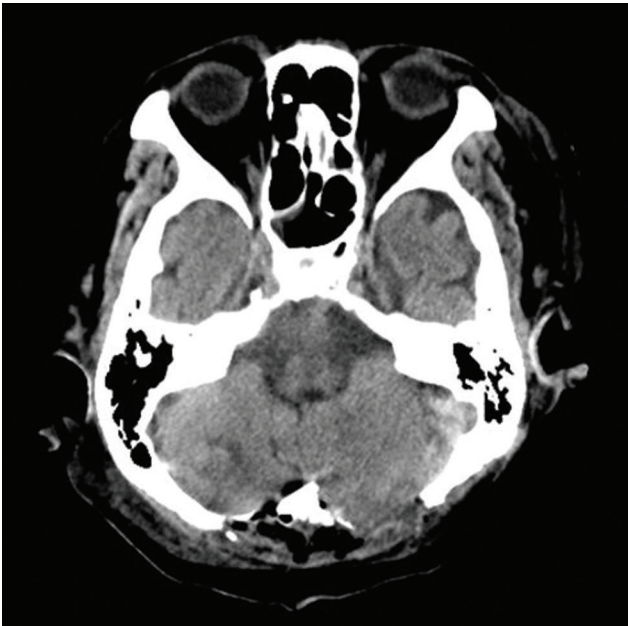


Fig. 2 Postoperative brain CT. The subdural hematoma had been completely evacuated. Sufficient decompression of the cerebellar hemispheres and brainstem was observed. CT: computed tomography.

5–10 days after the start of heparin use, in association with the appearance of the PF4-heparin antibody, lead to the diagnosis of HIT.²⁾ The 4T's score is a widely used scoring system to estimate the probability of HIT,^{12,13)} and is especially helpful for the diagnosis and treatment of HIT before the results of the test for PF4-heparin antibody become available, as in our case. In our patient reported here, the 4T's score was 6 (platelet count decrease by more than 50% and nadir greater than 20000/ μ L, onset from days 5 to 10 of heparin use, no thrombosis, no other cause to explain the thrombocytopenia), which corresponds to a high score. While serological test for the PF4-heparin antibody was negative on the day of the emergency craniotomy, it became positive (above 5 U/L) 4 days after the surgery. This clinical course supports the diagnosis of definitive HIT.

In contrast to other consumptive thrombocytopenic states, HIT is mainly complicated by thromboembolic events, and hemorrhagic complication is rare.²⁾ According to the retrospective study of thrombocytopenic diseases conducted by Goel et al., only 5.7% of cases of HIT develop a bleeding event during the course of their admission, and central nervous system bleeding was reported in 0.9% of cases.¹⁴⁾ Another retrospective study of HIT showed that central nervous system complications occurred in 9.2% of cases; however, there was no case of primary intracerebral hemorrhage.¹⁵⁾ A few case reports have been published of intracranial hemorrhage associated with HIT,^{3–6)} although no case of subdural hematoma complicating HIT has ever been reported. Because of its rarity, the most suitable therapeutic strategy for intracranial hemorrhage complicating to HIT still remains to be established.

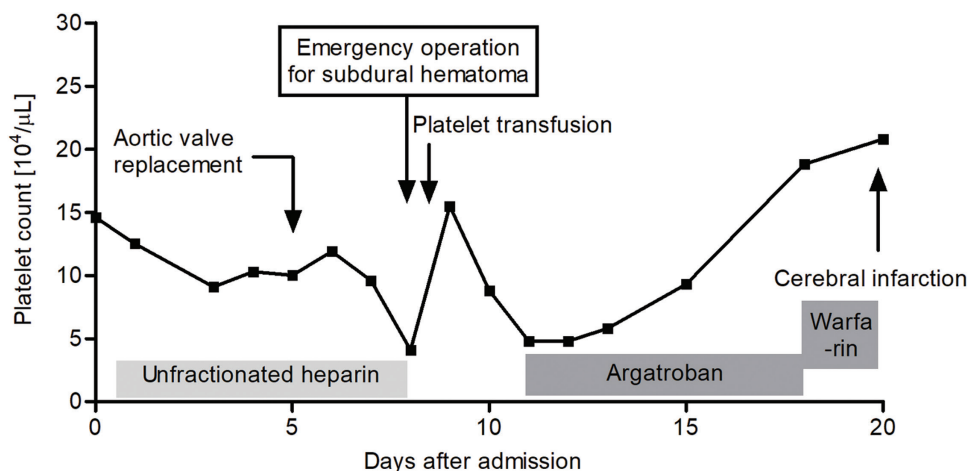


Fig. 3 Platelet counts and clinical course. The platelet counts were restored after platelet transfusion at the time of surgery, but decreased rapidly thereafter. The platelet count began to restore 4 days after the craniotomy.

Various causes of acute subdural hematoma, including thrombocytopenia other than HIT, have been reported previously. A systematic review of published cases of non-traumatic acute subdural hematoma showed that in 8.7% of cases, acute spontaneous subdural hematoma is caused by coagulopathy, including thrombocytopenia.¹⁶⁾ A review of seven patients of immune thrombocytopenic purpura (ITP) with subdural hematoma showed that the platelet count at the onset of subdural hematoma was in the range of 16000/ μ L–30000/ μ L.¹⁷⁾ In the present case, the nadir of the platelet count suggests that HIT led to acute subdural hematoma, although there has never been any previous report of acute subdural hematoma developing secondary to HIT. In our case, we could not obtain any history of head trauma; however, it is not impossible that the patient got subtle head trauma before admission associated with syncopal attacks resulting from the cardiac disease. It is also plausible that minor head trauma had some effect on the development of intracranial bleeding. Furthermore, atraumatic acute subdural hematoma is known to be rare but life-threatening perioperative complication following open-heart cardiovascular surgery, occurring in 0.1%–0.4% of postoperative patients.¹⁸⁾ Some plausible mechanisms of subdural hematoma development after cardiovascular surgery are tearing of the bridging vein resulting from fluid shift to the brain after cardiopulmonary bypass,¹⁹⁾ cerebral dehydration and volume change caused by massive urine excretion,²⁰⁾ and the bleeding tendency induced by heparin use.¹⁹⁾

Prophylactic platelet transfusion for thrombocytopenia has been thought to be contraindicated in the cases of HIT, as it is thought to have the potential to provoke thrombotic events.^{7,8)} To date, four studies on patients with HIT who receive platelet transfusions have been published. Goel et al. analyzed 6332 patients with HIT, 450 of whom received platelet transfusions. Patients receiving platelet transfusions were more likely to develop arterial thromboses than those who did not receive platelet transfusions (odds ratio 3.4, 95% CI: 1.2–9.5).¹⁴⁾ In contrast, a retrospective analysis of 37 patients with HIT who receiving platelet transfusions revealed no case of thrombotic events by day 30 of platelet transfusion, but six patients died of unknown cause.²¹⁾ Hopkins et al. reported that four patients with HIT who received platelet transfusions experienced no thrombotic events.²²⁾ The evidence is insufficient to confirm the safety or prove the adverse effects of platelet transfusion. The 2012 ACCP clinical practice guidelines recommends avoidance of

prophylactic platelet transfusions to correct low platelet counts. The guideline also recommends that platelet transfusion be limited only to those with active bleeding or undergoing invasive procedure,⁹⁾ although this remains controversial.

For neurosurgical procedures, the generally accepted threshold for platelet transfusion minimizing the risk of hemorrhagic complications is 100000/ μ L.^{10,11)} In our case, because nadir platelet count was 41000/ μ L, we administered platelet transfusions when performing the craniotomy.

As shown in Fig. 3, the platelet counts increased after platelet transfusion, but decreased rapidly again on day 10, suggesting that the transfused platelets may have been destroyed or become aggregated through antibody-mediated immune reaction. It also remains controversial whether platelet transfusions should be administered even after the neurosurgical operation, in cases where the thrombocytopenic state persists because of HIT. In our case, the platelet counts gradually began to restore 4 days after the craniotomy, without platelet transfusion.

Finally, we consider the occurrence of a thromboembolic event in our case. On day 13 after the emergency craniotomy, the patient developed right hemiparesis and aphasia caused by left middle cerebral artery thrombosis although we administered anticoagulants. As acute ischemic stroke is common in patient with HIT, especially within 2 weeks after the onset of HIT,²³⁾ it could also have been a manifestation of HIT in our case, besides subdural hematoma. However, a retrospective study by Goel et al. showed that platelet transfusions in a patient with HIT were associated with arterial thromboses, but not stroke (odds ratio, 0.5; 95% CI: 0.06–3.5).¹⁴⁾ Therefore, in our patient, it still remains unclear if the preoperative platelet transfusion could have led to the occlusion of the middle cerebral artery 13 days later.

In conclusion, we have presented the rare case of a patient who developed acute subdural hematoma complicating HIT after undergoing cardiac surgery. Emergency craniotomy and evacuation of the hematoma were successfully performed after administering platelet transfusions, suggesting that platelet transfusions may allow emergency surgery for intracranial hemorrhage to be effectively performed, even in patients with HIT.

Conflict of Interest Disclosure

The authors have no interest in any of the materials and drugs in the article.

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