J Anesth (2012) 26:766–769
DOI 10.1007/s00540-012-1392-8

CLINICAL REPORT

Life-threatening hemorrhagic shock after laparoscopic surgery: a case of postoperative thrombotic thrombocytopenic purpura

Satoru Asano · Masuzoh Taneda · Keiichi Katoh · Kenshi Suzuki

Received: 21 March 2011 / Accepted: 25 March 2012 / Published online: 24 April 2012
© Japanese Society of Anesthesiologists 2012

Abstract We report the successful management of a female patient who developed postoperative thrombotic thrombocytopenic purpura (TTP) after an uneventful laparoscopic oophorocystectomy. The patient underwent uneventful laparoscopic surgery for ovarian cystoma. One hour after completion of surgery, the patient suddenly went into shock, with her blood pressure dropping to 60/40 mmHg. Hemorrhage into the abdominal cavity with an estimated blood loss of 2,000 ml was confirmed by exploratory laparotomy. Initially, anemia and thrombocytopenia were attributed to blood consumption or disseminated intravascular coagulation (DIC). However, blood tests revealed evidence of hemolytic anemia, with fragmented erythrocytes observed on peripheral blood smear examination. Serum levels of lactate dehydrogenase, blood urea nitrogen, and creatinine were elevated. Based on the findings, postoperative TTP was suspected. High-dose steroids and plasma infusions were administered but proved ineffective. Plasma exchange was performed three times, resulting in resolution of postoperative TTP. TTP is an idiopathic disorder, known to be triggered by surgical trauma. Postoperative TTP is difficult to distinguish clinically from DIC because of its close similarity with the latter and subtle differences from other postoperative hematological complications. It is important to bear in mind the possibility of postoperative TTP in patients with unexplained hemorrhagic shock after uneventful surgery.

Keywords Hemorrhagic shock · Thrombotic thrombocytopenic purpura · Laparoscopic surgery

S. Asano (✉) · M. Taneda
Department of Intensive Care Unit, Japanese Red Cross Medical Center, 4-1-22, Hiroo, Shibuya-ku, Tokyo 1508935, Japan
e-mail: gemini1966_jrcmc@hotmail.co.jp

K. Katoh
Department of Anesthesiology, Japanese Red Cross Medical Center, Tokyo, Japan

K. Suzuki
Department of Hematology, Japanese Red Cross Medical Center, Tokyo, Japan

Introduction

Thrombotic thrombocytopenic purpura (TTP) is one category of thrombotic microangiopathy (TMA), and characterized by thrombocytopenia, microangiopathic hemolytic anemia, renal insufficiency, neurological abnormalities, and fever [1]. Functional disorder of intravascular platelet aggregation is among the most distinctive features of TTP, which can result in persistent hemorrhage with a high mortality rate [2]. TTP is a rare disorder with an estimated annual incidence of 3.7 cases per million population [3]. Although TTP is usually idiopathic, it can sometimes occur as a complication of surgery. The etiology of postoperative TTP remains speculative, although surgical trauma is believed to be closely involved.

Case description

A 36-year-old woman underwent laparoscopic oophorocystectomy for a large ovarian cystoma. She had not been taking any regular medications before surgery. Her past medical history was unremarkable. Neither clinical nor laboratory examinations revealed any abnormalities. No unusual indications of risk of hemorrhage were observed.

General anesthesia was induced with 90 mg propofol and 6 mg vecuronium, and maintained with sevoflurane and fentanyl. The operation was completed as planned. Blood loss was insignificant. After the uneventful 90-min operation, her general condition was stable, with an arterial pressure at the end of surgery of 90/40 mmHg, essentially the same as her preoperative average. However, shortly after the patient was transferred to the postoperative care ward, her arterial pressure dropped suddenly to 60/40 mmHg. No response of the low blood pressure to rapid fluid resuscitation and dopamine infusion at 5 μg/kg/min was observed. The hypotension was suspected to be caused by ongoing hemorrhage into the peritoneal cavity. Emergency laparotomy was carried out to identify the site of hemorrhage, and approximately 2,000 ml of blood was found in the abdominal cavity. Four hours and 20 min elapsed before the hemorrhage could be controlled. Dopamine and dobutamine were administered at 10 μg/kg/min each, with 24 units of packed red cells and 8 units of fresh frozen plasma (FFP). Total blood loss was 6,000 ml. The patient was transferred to the intensive care unit for close observation.

Hematological tests indicated mild anemia, with hemoglobin level at 11.0 g/dl. Her platelet count decreased from 271,000 to 98,000/μl despite minimal hemorrhage after the second operation. The findings associated with massive hemorrhage suggested disseminated intravascular coagulation (DIC) or consumptive thrombocytopenia. Gabexate mesilate was administered at a dose of 1,500 mg. Platelets and packed red cells were transfused again to prevent thrombocytopenia and anemia. A total of 6 units of FFP were transfused to supply coagulant factors. However, hemoglobin and platelet counts had decreased further, to 9.1 g/dl and 83,000/μl, respectively. Laboratory data showed no improvement during the next 6 h. Hemoglobin level reached a nadir of 7.0 g/dl, and platelets, nadir of 61,000/μl.

On postoperative day 1, jaundice and dark brown urine were observed. The patient developed fever (body temperature above 37.0 °C), and purpuric spots were found on the trunk. Blood examinations revealed elevation of serum lactate dehydrogenase (LDH) to 1,542 IU/l, blood urea nitrogen (BUN) to 34 mg/dl, and creatinine to 2.8 mg/dl. Platelet count was less than 10,000/μl. Fragmented red blood cells were observed on peripheral blood smears. Therefore, hepatoglobin at 4,000 units was added to the treatment regimen under the suspicion of microangiopathic hemolytic anemia. Direct and indirect Coombs examinations, irregular antibody tests, and the antiplatelet antibody test were all negative. Coagulation studies showed a prothrombin time (PT) of 14.6 s, activated partial thromboplastin time (APTT) of 36.3 s, serum fibrinogen of 165 mg/dl, and serum fibrinogenifibrin degradation products (FDP) of 40–80 μg/ml. On postoperative day 2, the patient developed a headache, and memory lapses were sporadically observed. Considering laboratory data and clinical symptoms together, TTP related to the operation was suspected to be responsible for the condition. Methylprednisolone was administered at 1,000 mg daily for 3 days, starting on postoperative day 3.

On postoperative day 5, laboratory data were hemoglobin 3.9 g/dl, LDH 9,463 IU/l, platelet count less than 10,000/μl, BUN 101 mg/dl, and creatinine 5.1 mg/dl. The serum levels of LDH, BUN and creatinine then rose to 9,718 IU/l, 105 g/dl, and 5.6 mg/dl, respectively. Plasma exchange was performed on postoperative days 6 and 7 with 40 units FFP. Laboratory data showed improvement after two plasma exchanges, with platelet count rising to 129,000/μl, hemoglobin to 7.1 g/dl, and LDH to 1,936 IU/l (Fig. 1). Therefore, the plasma exchanges were suspended because of the improvements in the laboratory data.

On postoperative day 11, however, relapse of the TTP appeared to be imminent, with elevation of serum LDH to 3,169 IU/l and decrease of platelet count to 70,000/μl, suggesting impending TTP. A third plasma exchange was immediately performed.

On postoperative day 13, improvement of the laboratory data was noted: LDH 1,286 IU/l and platelet count 190,000/μl (Fig. 1). Complete remission was considered to have been achieved. The patient was discharged from the hospital on postoperative day 33. She has remained well since, with no signs or symptoms of TTP recurrence.

Discussion

TMA is a pathological condition characterized by platelet thrombi, thrombocytopenia, and hemolytic anemia [1, 3]. Two typical phenotypes of TMAs are TTP and hemolytic-uremic syndrome (HUS) [1, 3, 4]. However, the differential diagnosis between TTP and HUS is clinically difficult. Nowadays, TMA is commonly used instead of TTP/HUS [1].

Life-threatening TTP may be precipitated by surgery, often resulting in misdiagnosis of DIC or consumptive thrombocytopenia as a consequence of the lack of specific clinical symptoms and biological criteria. The survival rate was as low as 10 % as a result of cerebral infarction and renal failure [5] but has been increasing after the recommended application of plasmapheresis and plasma replacement with FFP [3, 5]. At present, the estimated survival rates approach 90 % [2, 3].

Recent reports have shown the close association of von Willebrand cleaving protease (ADAMTS13) with the development of TTP [6, 7]. In the presence of a deficiency of ADAMTS13, unusually large von Willebrand factor

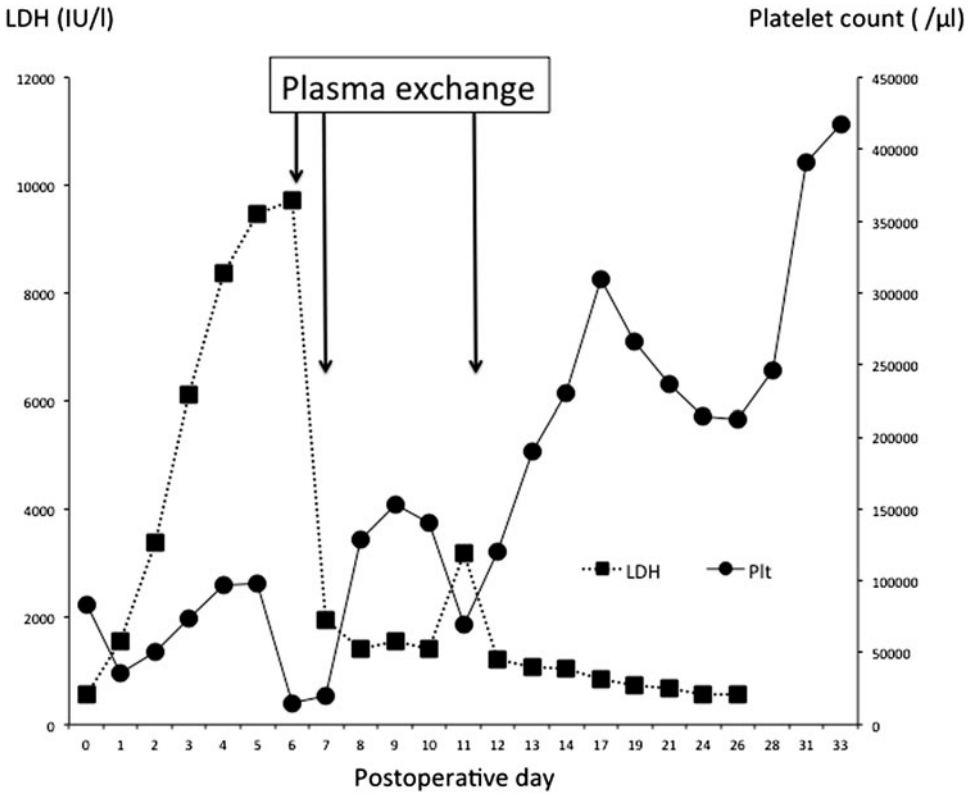

Fig. 1 The serum level of lactate dehydrogenase (*LDH*) decreased and the platelet count increased after plasma exchanges on postoperative days 6 and 7. On postoperative day 11, the serum level of LDH elevated and platelet count decreased. Relapse of thrombotic thrombocytopenic purpura (TTP) was suspected. A third plasma exchange was carried out

(ULvWF) multimers remain in the blood and attach to circulating platelets under high shear stress. As a result, platelet consumption is accelerated and erythrocytes are fragmented by mechanical trauma. Bianchi et al. reported that an ADAMTS13 deficiency (<5 % of the activity in normal human plasma) is a specific finding for a form of TTP [8].

The first effective treatment reported for TTP was plasmapheresis by either plasma exchange or plasma infusion [9]. Thereafter, Rock et al. reported that plasma exchange was more effective than plasma transfusion [5]. Plasma exchange is considered to remove ULvWF multimers and inhibitor antibodies or sufficiently replace vWF cleaving protease. At present, the efficacy of plasma exchange for TTP is widely accepted.

In general, platelet transfusion is contraindicated in patients with TTP, because widespread formation of microvascular thrombi may be accelerated by the platelet transfusion [3, 10]. On the other hand, Coppo et al. [11] reported two patients with TTP who received plasma exchange followed by platelet transfusion preoperatively. The platelet counts increased after the transfusions, with no deterioration of the general condition in either patient. Whether the platelet transfusion is directly responsible for the unfavorable outcomes remains uncertain. Thus, platelet transfusion should probably be employed only if the bleeding is life threatening.

Thrombotic thrombocytopenic purpura is usually idiopathic. However, there have been reports of cases of postoperative TTP, including after vascular surgery, orthopedic surgery, and abdominal surgery, and postgestational TTP [12–20]. It has been hypothesized that capillary endothelial damage results in the release of large amounts of ULvWF, which can overwhelm the existing pool of cleaving enzymes [21, 22]. Certain abdominal surgical procedures may damage the capillary endothelial surface, considering that some abdominal organs and tumors have a rich blood supply [21, 22].

It is said that the complete pentad of TTP is rarely observed. Naqvi et al. [22] noted that the presence of thrombocytopenia and microangiopathic hemolysis is sufficient to carry out plasma exchanges, even if the other three features of TTP have not yet manifested.

The ovarian cystoma of our patient was pathologically confirmed to be a mucinous cyst adenoma and endometrial cyst. Therefore, no chemotherapy was initiated after the surgery. The cause of occurrence of TTP, however, remains to be considered. According to previous reports, we can reasonably speculate that the level of ADAMTS13 was marginally below average, and that even minor endothelial damage could have triggered TTP, otherwise a very rare occurrence. If the cystoma had been highly vascular, the TTP would have already developed, at least by the end of the initial operation. On the other hand, in this

patient, the TTP relapsed on postoperative day 11 after two plasma exchanges. It is considered that the initial discontinuation of plasma exchange may have been premature as the British guidelines have recommended that plasma exchange be continued for a minimum of 2 days after the platelet count returns to normal (>150,000/μl) [23]. We should have continued the plasma exchange until postoperative day 9, even in the face of apparently complete remission.

In conclusion, postoperative TTP can be easily misdiagnosed as DIC because the clinical symptoms and laboratory findings of the two disorders are similar. Neither specific clinical symptoms nor biological criteria are diagnostically useful. Postoperative TTP is, however, not uncommon. We should bear in mind the possibility of TTP in patients with acute postoperative thrombocytopenia and hemolytic anemia. Plasma exchange thereby should not be delayed, as it can be lifesaving.

References

1. Polito MG, Kirstajn GM. Thrombotic microangiopathies: thrombotic thrombocytopenic purpura/hemolytic uremic syndrome. J Bras Nefrol. 2010;32(3):298–308.
2. Bell WR, Braine HG, Ness PM. Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome. Clinical experience in 108 patients. N Engl J Med. 1991;325:398–403.
3. Ruggenenti P, Remuzzi G. Pathophysiology and management of thrombotic microangiopathies. J Nephrol. 1998;11:300–10.
4. Besbas N, Karpman D, Landau D, Loirat C, Proesmans W, Remuzzi G, Rizzoni G, Taylor CM, Van de Kar N, European Paediatric Research Group For HUS. A classification of hemolytic uremic syndrome and thrombotic thrombocytopenic purpura and related disorder. Kidney Int. 2006;70:423–31.
5. Rock GA, Shumak KH, Buskard NA. Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. N Engl J Med. 1991;325:393–7.
6. Furlan M, Robles R, Solenthaler M. Acquired deficiency of von Willebrand factor-cleaving protease in a patient with thrombotic thrombocytopenic purpura. Blood. 1998;91:2839–46.
7. Tsai HM, Lian EC. Antibodies to von Willebrand factor-cleaving protease in acute thrombotic thrombocytopenic purpura. N Engl J Med. 1998;339:1585–94.
8. Bianchi V, Robles R, Alberio L, Furlan M, Lammle B. Von Willebrand factor-cleaving protease (ADAMTS13) in thrombocytopenic disorder: a severe deficient activity is specific for thrombotic thrombocytopenic purpura. Blood. 2002;100:710–3.
9. Bukowski RM, Hewlett JS. Exchange transfusion in the treatment of thrombotic thrombocytopenic purpura. Semin Hematol. 1976;13:219–32.
10. Harkness DR, Byrnes JJ, Lian EC. Hazard of platelet transfusion in thrombotic thrombocytopenic purpura. JAMA. 1981;246:1931–3.
11. Coppo P, Lassoued K, Mariette X. Effectiveness of platelet transfusion after plasma exchange in adult thrombotic thrombocytopenic purpura: a report of two cases. Am J Hematol. 2001; 68:198–201.
12. Pavlovsky M, Weinstein R. Thrombotic thrombocytopenic purpura following coronary artery bypass graft surgery: prospective observations of an emergency syndrome. J Clin Apher. 1997; 12:159–64.
13. Iosifidis MI, Ntavlis M, Giannoulis I, Malioufas L, Ioannou A, Giantsis G. Acute thrombotic thrombocytopenic purpura following orthopedic surgery: a case report. Arch Orthop Trauma Surg. 2006;126:335–8.
14. Kathula SK, Kamana M, Naqvi T, Gupta S, Chang JC. Acute thrombotic thrombocytopenic purpura following orthopedic surgery. J Clin Apher. 2002;17:133–4.
15. Robertson MD, Zumberg M. Post-appendectomy thrombotic thrombocytopenic purpura: a case report and review of the literature. Am J Hematol. 2007;82:224–8.
16. Chang JC, El-Tarabily M, Sharda Gupta. Acute thrombotic thrombocytopenic purpura following abdominal surgeries: a report of three cases. J Clin Apher. 2000;15:176–9.
17. Kathula SK, Kaduri J, Mall S, Chang JC. A case report of total abdominal hysterectomy resulting in acute thrombotic thrombocytopenic purpura with pancreatitis and hepatitis: complete resolution with plasma exchange therapy. Ther Apher Dial. 2003; 7(3):372–4.
18. Hamilton CA, Kao JM, Coutre SE, Teng NNH. Acute postoperative thrombotic thrombocytopenic purpura following hysterectomy and lymphadenectomy for endometrial cancer. Gynecol Oncol. 2007;106:423–6.
19. Ezra Y, Rose M, Eldor A. Therapy and prevention of thrombotic thrombocytopenic purpura during pregnancy: a clinical study of 16 pregnancies. Am J Hematol. 1996;51:1–6.
20. Obeidat B, MacDougall J, Harding K. Plasma exchange in a woman with thrombotic thrombocytopenic purpura or severe pre-eclampsia. Int J Obstet Gynaecol. 2002;109:961–2.
21. Chang JC. Review: postoperative thrombocytopenia: with etiologic, diagnostic, and therapeutic consideration. Am J Med Sci. 1996;311(2):96–105.
22. Naqvi TA, Baumann JC, Chang JC. Post-operative thrombotic thrombocytopenic purpura: a review. Int J Clin Pract. 2004; 58:169–72.
23. Allford SL, Hunt BJ, Rose P, Machin SJ, Haemostasis and Thrombosis Task Force, British Committee for Standards in Haematology. Guidelines on the diagnosis and management of the thrombotic microangiopathic haemolytic anaemias. Br J Haematol. 2003;120(4):556–73.