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Brief Report

Acute Thrombotic Thrombocytopenic Purpura Following Abdominal Surgeries: A Report of Three Cases

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Acute thrombotic thrombocytopenic purpura (TTP) occurred in three patients following abdominal surgeries. One patient underwent extensive lysis for intestinal adhesions with bowel resection, another cholecystectomy for acute cholecystitis, and the third right colectomy and partial intestinal resection for colon cancer. The diagnosis of acute TTP was established on the basis of absent hematologic features of TTP prior to surgery and development of microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and unexplained mental changes after surgery. Hematologic evidence of TTP developed 3 to 9 days after surgery. Other clinical features were acute respiratory distress syndrome (ARDS) in two patients and peripheral digit ischemic syndrome (PDIS) also in two patients. In all three patients, establishing the diagnosis of TTP was delayed. Exchange plasmapheresis in one patient was ineffective due to associated ARDS and two others died soon after the diagnosis was established. In view of our experience, postoperative TTP should be considered in the differential diagnosis of the patient who develops unexplained anemia and thrombocytopenia following an abdominal surgery. Presence of hemolytic anemia, schistocytosis, and unexplained thrombocytopenia should alert the possibility of TTP. J. Clin. Apheresis, 15:176–179, 2000.

Key words: thrombotic thrombocytopenic purpura; microangiopathic hemolytic anemia; adult respiratory distress syndrome; peripheral digit ischemic syndrome

INTRODUCTION

The de novo thrombotic thrombocytopenic purpura (TTP) is thought to be an uncommon clinical syndrome typically characterized by microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and neurologic manifestation. However, in the past two decades, with an availability of exchange plasmapheresis as effective treatment, more cases of TTP, including atypical and secondary cases, have been recognized and treated with a better outcome in clinical practice [1–5]. Recently, postoperative TTP has been reported following renal and liver transplants [6,7], vascular surgeries [8,9], and coronary artery bypass grafts [9,10]. Yet, in the literature there is no well-recorded case of postoperative TTP after abdominal surgery. In this article, we report three cases of acute TTP that developed following abdominal surgeries. Hematologic and laboratory features are reviewed, and possible pathogenesis is discussed.

MATERIALS AND PATIENTS

All the known cases of TTP at the Good Samaritan Hospital, Dayton, Ohio have been carefully documented and recorded in the computer system since 1981. From January 1981 to July 1999, the diagnosis of TTP was established in a total of 64 patients. Among these patients 21 patients had postoperative TTP. Out of these 21 patients, 3 patients developed TTP following abdominal surgeries. These cases are briefly illustrated and the confirming clinical and hematologic data are presented. In all three patients, the platelet counts were normal and schistocytes not present in the blood slide prior to surgery. Known causes of postoperative thrombocytopenia, including heparin-induced thrombocytopenia, consumption coagulopathy, drug-induced immune thrombocytopenia, alloimmunization, sepsis, and posttransfusion thrombocytopenia, were excluded on the basis of clinical findings and laboratory evaluation, when available, as previously described [11].

CASE REPORTS

Patient 1 (AN)

A 72-year-old woman with recurrent episodes of diverticulitis of the colon and past history of total abdomi-

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nal hysterectomy and bilateral salpingo-oophorectomy was admitted because of left lower quadrant abdominal pain, low grade fever, and rectal bleeding. An exploratory laparotomy showed a distended bowel from the sigmoid colon to the ileocecal valve due to extensive dense adhesions from the previous surgeries and diverticulitis. The patient underwent extensive de-adhesion surgery and segmental large bowel resection. Initial postoperative recovery was slow as anticipated after an extensive surgery. Five days postoperatively, the patient developed dyspnea and fever of 101°F and gradually became confused and disoriented. Evaluation for infection, including pneumonia, urinary tract infection, and other sites, was negative. While on ampicillin/sulbactam sodium postoperatively, multiple blood cultures grew no organisms. The patient progressed to acute respiratory distress syndrome (ARDS). This diagnosis was established on the basis of persistent hypoxia of about 60 mmHg on 60% FiO2 with diffuse pulmonary infiltrates and without evidence of congestive heart failure, pulmonary emboli, pneumonia, pleural effusion, and other lung disease. The patient was intubated and mechanical ventilation started. Although the platelet count was normal before and 2 days after surgery, on the 4th postoperative day the platelet count dropped to 120,000 and the 5th postoperative day to 22,000. The patient was transfused with platelet concentrates. Two days later, her mental status worsened and she became unresponsive. Peripheral digit ischemic syndrome (PDIS) also developed with progressive gangrene of the toes. When seen by a hematologist, the hemoglobin was 8.6 gm% and platelet count was 62,000/μL. The reticulocyte count was 8.6%. Consumption coagulopathy was excluded on the basis of normal prothrombin time, activated partial thromboplastin time, and fibrinogen level. Additionally, there was no evidence of bleeding. The 14-C serotonin release assay for heparin-dependent platelet antibodies was negative. The serum lactic dehydrogenase level was markedly increased to 697 U/L (normal: 91–180). The blood smear showed approximately 5% schistocytes among red blood cells. The diagnosis of TTP was established. A daily 3.5 L exchange plasmapheresis, using fresh frozen plasma replacement, was performed for 7 days. Neither hematologic nor clinical response occurred, but serum lactic dehydrogenase level gradually decreased to 480 U/L after seven exchanges. The patient died on the 15th postoperative day.

Patient 2 (RD)

A 70-year-old man underwent cholecystectomy for acute cholecystitis and cholelithiasis. Preoperative hemogram was normal other than mild anemia. On the 2nd postoperative day, the patient became hypotensive, confused, and developed respiratory arrest. The patient was resuscitated and an intra-aortic balloon pump was placed to support the unstable hemodynamic status. While on mechanical ventilation, no clinical improvement occurred. On the 1st postoperative day the hemoglobin was 10.4 gm% and platelet count 132,000/μL, and on the 3rd day the hemoglobin was 10.5 and platelet count 88,000. In addition, PDIS occurred with progressive gangrene of the fingers and toes. Extensive evaluation for infection was negative. Multiple cultures from the blood, urine and bronchial secretion grew no pathogenic organisms. On the 10th postoperative day, hematology consultation was requested for unexplained thrombocytopenia. At the time hemogram showed the hemoglobin of 9.7 gm%, white blood cell count was 21,400/μL, and platelet count was 35,000/μL. The peripheral blood smear showed 3–5% schistocytes among red blood cells and prominent polychromasia, and the reticulocyte count was 5.0%. Consumption coagulopathy was excluded on the basis of normal prothrombin time and activated partial thromboplastin time and lack of bleeding tendency. Advanced TTP was diagnosed. Shortly after hematology consultation, the patient expired.

Patient 3 (MC)

An 83-year-old woman with advanced diabetes mellitus and coronary artery disease underwent right hemicolectomy and partial small bowel resection for colon cancer in the ascending colon. Preoperative hemogram was normal other than mild anemia. The blood smear was normal. Immediate postoperative recovery was uneventful. On the 9th postoperative day, the patient became anemic with the hemoglobin of 9.9 gm% and the platelet count decreased to 103,000/μL. Retrospective review of the peripheral blood smear showed prominent polychromasia and occasional schistocytes. Next day the patient became confused and disoriented and began to have shortness of breath. On the 14th postoperative day, fever developed to 100.2°F, and she became unresponsive. Hemogram showed gradual changes with the hemoglobin of 7.7 gm% and platelet count 106,000/μL on the 15th postoperative day and 8.7 gm% (after transfusion) and 86,000/μL, respectively, on the 16th day. Severe hypoxia of PO2 of 68 mmHg was noted in spite of a high flow of oxygen. The chest roentgenogram was abnormal with diffuse bilateral pulmonary infiltrates. The diagnosis of ARDS was established. Extensive evaluation for infection, including in surgical sites, urinary tract, and lung, was negative and sepsis was ruled out with multiple negative blood cultures. Supportive care was recommended because of her poor general condition, underlying pathology and old age. On the 20th postoperative day, just before her death, hematology consultation was requested for unexplained thrombocytopenia. Further changes of hemogram noted with the hemoglobin of 6.1 gm%, and platelet count was 44,000/μL. Many schistocytes were present in the peripheral blood smear. Later the haptoglobin was reported to be less than

TABLE I. Patient Hematologic Data*

Patient number	Normal value	Prior to surgery[a] 1	2	3	After surgery 1	2	3
Hemoglobin (gm%)	14–18	11.2	10.8	11.7	8.6	9.7	8.7
Hematocrit (%)	40–50	33.2	34.1	32.2	25.5	30.1	24.6
Platelets (μL)	150,000–450,000	312,000	201,000	249,000	62,000	35,000	86,000
Reticulocyte (%)	1–2	ND	ND	ND	8.6	5.0	6.9
Blood smear (schistocyte)	None	None	None	None	2+	2+	3+
Haptoglobin (mgHb%)	20–200	ND	ND	ND	65	40	<5

*Schistocytes among red blood cells: 1+, 1–2%; 2+, 3–5%; 3+, 5–10%; 4+, more than 10%.
[a]ND, not done.

5 mg% and the reticulocyte count 6.9%. The diagnosis of postoperative TTP was established after death.

HEMATOLOGIC DATA

To confirm the diagnosis of acute TTP following abdominal surgeries, the pertinent hematologic and laboratory parameters were reviewed when available (Table I). Preoperatively, in all three patients, the platelet count was normal, but mild anemia was present. The hemoglobin level gradually decreased further during the post-surgical period. Anemia was partly due to bleeding from surgery in the beginning, but progressive anemia after surgery was mainly due to MAHA. This diagnosis was supported by reticulocytosis, appearance of schistocytes and prominent polychromasia in the peripheral blood smear, and increased lactic dehydrogenase or decrease of haptoglobin level. Postoperative thrombocytopenia was evaluated and other known causes excluded [11]. Two patients had persistent hypoxia due to ARDS, presumably due to microthrombi involving alveolar capillaries.

COMMENTS

In all three patients, the diagnosis of postoperative TTP was established on the basis of triad of TTP: MAHA, thrombocytopenia, and progressive neurological (mental) changes. ARDS and PDIS also support the diagnosis since these syndromes have been documented as a part of TTP, especially after cardiovascular surgeries [3,9,12,13]. However, unfortunately because of low index of suspicion during post-surgical care, the diagnosis was delayed and all three patients died of serious complications without getting the benefit of timely exchange plasmapheresis.

Postoperative TTP has been described as a clinical syndrome characterized by acute onset of TTP occurring after open heart or vascular surgeries, usually 3 to 7 days after the operation [9,10]. The surgical procedures that have been associated with postoperative TTP include coronary artery bypass graft, valvular heart surgery, endothelial and myocardial surgery, femoro-popliteal bypass graft, arteriolar-venous fistula formation, and repair of aortic aneurysm [8–10]. As anticipated, all these surgeries may result in considerable damage to the arteriolar endothelial surface by direct physical injury. The pathogenesis of TTP, in some instances, is thought to be related to the release of unusually large von Willebrand factor (ULvWF) multimers from either diseased or injured endothelial cells. Normally, these ULvWF multimers should be cleaved to intermediate or small molecular weight multimers by a von Willebrand factor (vWF)-cleaving metalloprotease or other enzyme [14–16]. In a situation where there is a deficiency, either hereditary or acquired, of a vWF-cleaving protease, persistent ULvWF multimers may cause platelet activation leading to aggregation of platelets and thus in microcirculation promote attachment of aggregated platelets to shear stress-altered receptors of the endothelial surface [17]. This theory may also explain occurrence of acute postoperative TTP due to formation of extensive microthrombi in the arteriolar capillaries following surgical vascular injuries.

Postoperative TTP has not been reported following abdominal surgeries. Very little injury to the vascular endothelium is presumed to occur during an uncomplicated surgery. However, because abdominal organs are rich in blood vessels, certain surgical procedures that require extensive manipulation of the organs and tissues may damage the arterial endothelial surface and trigger postoperative TTP seen in our patients. TTP itself presented as acute abdomen due to extensive arteriolar microthrombi in the gastrointestinal tract [12,18]. As seen in postoperative TTP following cardiovascular surgeries, our three patients also developed the evidence of TTP, 3–9 days after abdominal surgeries.

In two patients (Patients 1 and 3), ARDS was the main clinical feature, which contributed to their demise. Two patients (Patients 1 and 2) had PDIS. ARDS [3,12,13] and PDIS [9] have been reported with TTP. Both conditions are explained by extensive platelet microthrombi involving the alveolar capillaries and arterioles of the peripheral digits [9,12,13]. Although we have seen several cases of ARDS and PDIS as complications of TTP, no emphasis, in the literature, has been placed on that these clinical syndromes could be a part of TTP. In clinical situation, the diagnosis of TTP might be missed or delayed when ARDS and PDIS are prominent clinical pictures even though thrombocytopenia is present in postoperative patients.

The most important aspect of recognizing postoperative TTP is a high index of suspicion when a postsurgical patient presents with unexplained progressive anemia, thombocytopenia, and progressive neurological or mental changes. However, to give the benefit of exchange plasmapheresis, which is a life-saving treatment for TTP, MAHA and unexplained postoperative thrombocytopenia should be sufficient criteria for presumptive diagnosis of TTP and enough features to initiate the treatment [9]. Once ARDS and mental deterioration occur, the demise of the patient is likely with further progression to multi-organ dysfunction. Early recognition of the disease is of paramount importance for a favorable outcome since timely institution of exchange plasmapheresis is a very effective treatment.

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