Esophagectomy for Esophageal Cancer in a Patient with Protein C Deficiency: A Case Report

Naoto Ujiie, MD, PhD, Yusuke Taniyama, MD, PhD, Hiroshi Okamoto, MD, PhD, Chiaki Sato, MD, PhD, Kai Takaya, MD, PhD, Toshiaki Fukutomi, MD, PhD, and Takashi Kamei, MD, PhD

Introduction

Protein C deficiency is a rare genetic disease that predisposes individuals to thrombotic disease. In 1981, Griffin et al.\(^1\) published the first study reporting that low levels of plasma protein C were associated with venous thrombosis. Since then, the incidence of protein C deficiency with clinical symptoms has been estimated at 1 in 20000.\(^2\) Only a few cases of surgery for gastrointestinal cancer with protein C deficiency have been reported, but no reports have considered the perioperative management of these patients in detail. We report a case of esophagectomy for esophageal cancer in a patient with protein C deficiency who experienced complications. We present our case to highlight the necessity of devising perioperative management for patients presenting with protein C deficiency because necrosis of the reconstructed organ is likely.

Case Report

A 63-year-old man with protein C deficiency underwent thoracoscopic esophagectomy and digestive reconstruction using a gastric tube for thoracic esophageal cancer. On postoperative day 3, the gastric tube was removed because of anastomotic leakage and gastric tube necrosis. Digestive reconstruction using a free jejunal graft was attempted 140 days after the first surgery. However, thrombus formation in the artery and vein of the jejunal graft resulted in a failed reconstruction. Ten days after this surgery, digestive reconstruction using the colon was performed with intraoperative heparin administered for anticoagulation control. The surgery was successful, with no thrombus formation afterward. When performing digestive reconstruction in patients with conditions predisposing to thrombus formation, perioperative management should be completed with careful attention toward preventing thrombus formation. In particular, appropriate anticoagulation control, such as the administration of intraoperative heparin, is recommended in patients with protein C deficiency because necrosis of the reconstructed organ is likely.

Keywords: esophagectomy, protein C deficiency, perioperative management, thrombus formation
endoscopy revealed a type 0–IIa tumor, and an esophagogagram showed an irregular-shaped tumor with a 2-cm longitudinal diameter in the middle thoracic esophagus. An endoscopic biopsy indicated squamous cell carcinoma of the esophagus. Computed tomography (CT) revealed no obvious lesion of the esophagus and no enlargement of any lymph nodes suspected of metastasis. The patient was clinically diagnosed with T1bN0M0, stage I squamous cell carcinoma of the esophagus, according to the TNM Classification of Malignant Tumours, 8th edition. The patient opted for surgical treatment for this lesion after proper informed consent. He had no symptoms derived from protein C deficiency preoperatively, and ultrasonography did not reveal the presence of fresh deep vein thrombosis.

He underwent thoracoscopic esophagectomy and digestive reconstruction using a gastric tube via the posterior mediastinal route without anticoagulation management during the surgery. The reconstructed gastric tube seemed to have good blood flow at the time of operation. The operative time was 598 min, the estimated blood loss was 39 ml, and infusion volume was 3234 ml without blood transfusion. Dyspnea and tachycardia were observed on postoperative day 3. Upper gastrointestinal endoscopy showed anastomotic leakage and gastric tube necrosis, whose range was approximately 3 cm (Fig. 1), and CT revealed a right pleural abscess. The gastric tube was removed, and cervical esophagostomy with intrathoracic drainage was performed. CT-guided drainage was performed 1 week after surgery because a residual right pleural abscess was detected.

The patient’s general condition was improved by these treatments, and digestive reconstruction using a free jejunal graft was attempted 140 days after the first surgery. The jejunum was resected, and revascularization of the jejunal artery and vein of the graft was performed using the transverse cervical artery and the internal jugular vein. However, thrombi formed in both the jejunal artery and the vein of the graft, and intestinal blood flow of the jejunal graft was not recovered (Fig. 2). Up to this point, the operation time was 408 min, the time of interruption of blood flow to free jejunal graft was 120 min, and the estimated blood loss was 286 ml. Another jejunum was newly resected after the administration of heparin for the purpose of preventing thrombus formation. However, thrombi formed in the jejunal artery and vein of the graft again, and the plan to use the free jejunum for digestive reconstruction was abandoned.

Ten days after this surgery, digestive reconstruction using the pediculate colon was performed with anticoagulation control based on the activated coagulation time.
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The ACT was adjusted to be more than 200 seconds by administering intraoperative heparin. In addition, vascular anastomosis, such as arterial supercharge and venous superdrainage, was not added. As a result, digestive reconstruction was successful, with no thrombosis (Fig. 3). The operative time was 428 minutes, the estimated blood loss was 371 ml, and the infusion volume was 3063 ml without blood transfusion. Despite maintaining cautious control of anticoagulation by administering an appropriate amount of heparin and monitoring the ACT during surgery, the ACT was prolonged significantly after the surgery. Surgical hemostasis was required as a result of anastomotic bleeding 2 hours after this operation. Thereafter, stricter management concerning anticoagulation was implemented, established to maintain the ACT in the range of 120–150 seconds. Although slight anastomotic leakage was detected, this was improved by conservative treatment. A diet was started 200 days after the first surgery, and the patient was discharged 14 days later. The patient was alive, with no signs of recurrence 1 year later. A histological examination revealed squamous cell carcinoma of the esophagus, and the definitive diagnosis was pT1N0M0, pStage I (TNM Classification, 8th edition).

Discussion and Conclusion

Protein C deficiency is characterized by a tendency to form thrombi and causes deep venous thrombosis and acute pulmonary embolism. The incidence of this disease with clinical symptoms is rare, and no detailed reports have been published regarding the perioperative management of patients with protein C deficiency. We report on the perioperative management of a patient with protein C deficiency, especially in terms of preventing thrombus formation.

No particular perioperative management was taken concerning the prevention of thrombus formation in our patient’s first operation. In addition, when digestive reconstruction using a free jejunal graft was performed, specific perioperative management was not established for his condition. Thrombus formation around the anastomosis site allows the possibility of anastomotic leakage in gastrointestinal reconstruction as a result of the interruption of blood flow to the anastomosis site. In our patient’s first operation, anastomotic leakage and gastric tube necrosis within the early postoperative period may have been caused by thrombus formation in the microvessels around the anastomosis site. Because intraoperative factors such as operation time, estimated blood loss, and infusion volume did not differ significantly compared to usual esophagectomy at the first surgery, there seems to have less association between postoperative thrombosis and intraoperative factors. Moreover, the occurrence of thrombosis during the second surgery, digestive reconstruction using a free jejunal graft, confirmed the importance of careful perioperative management to prevent thrombus formation in patients with conditions predisposing to thrombosis, such as protein C deficiency.

To prevent thrombus formation, perioperative management with anticoagulation control based on the ACT by intraoperative heparin administration was performed eventually. The ACT, which is used widely to monitor the intraoperative anticoagulant effect of heparin, measures the time until clot formation. For our patient, the ACT was set to more than 200 seconds with reference to the value used in the intraoperative management of cardiac and vascular surgery. Digestive reconstruction using the pediculate colon without revascularization was then started. As a result of the intraoperative administration of heparin, the reconstruction was a success, without thrombosis. However, it was considered that the ACT should be set at a lower value because it was prolonged significantly after the operation and surgical hemostasis was required.
because of anastomotic hemorrhage. Although further studies are needed to clarify the appropriate range of ACT, controlling the ACT in-between 120–150 seconds seems to be suitable from our experience.

The administration of an activated protein C concentrate has also been considered as a method of preventing thrombosis caused by protein C deficiency. Activated protein C concentrate has anticoagulant properties, inhibits platelet aggregation, and has a hyperfibrinolysis effect. This formulation would help prevent deep venous thrombosis and acute pulmonary embolism caused by protein C deficiency. However, there are no reports demonstrating that activated protein C concentrate is useful in preventing perioperative thrombus formation. Additionally, the pharmaceutical cost of activated protein C concentrate is so expensive that perioperative management using this formulation is not realistic. Alternatively, perfusion preservation for the jejunal graft might be effective in cases in which digestive reconstruction using a free jejunal graft is selected. Perfusion preservation is used widely for the purpose of preserving the function of the graft during liver and renal transplantation. By applying this method and performing perfusion preservation to the free jejunal graft, it might be possible to prevent thrombus formation of the free jejunal graft.

The issue of choice as to whether treatment should be surgery or conservative treatment for this patient remains as difficult. As a result of esophagectomy with reconstruction, this patient suffered from severe morbidity for a long time. Even though this patient opted for surgery, definitive chemoradiotherapy might have been recommended for patients in such troublesome condition.

Consequently, when performing surgical treatment, perioperative management should be conducted with careful attention toward preventing thrombus formation during digestive reconstruction in patients with conditions predisposing to thrombus formation, such as protein C deficiency. Appropriate anticoagulation control, such as the administration of intraoperative heparin, is recommended in these patients who are likely to develop necrosis of the reconstructed organ as a result of thrombus formation. However, strict management is needed.

Informed Consent

Written informed consent was obtained from the patient for the publication of this report and any accompanying images.

Disclosure Statement

The authors have no conflicts of interest to declare.

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