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CASE REPORT
Reconstructive

Multiple Thrombi during Microvascular Anastomosis Caused by Decreased Antithrombin Activity: A Case Report

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Summary: With recent advances in microsurgical instruments and technique, microvascular anastomosis has become a universal surgical technique; however, thrombosis still presents in a number of cases. Tension, twisting, and compression to the anastomotic site are the main causes of thrombus; however, disorder of the coagulation–fibrinolysis system also need to be considered. To date, only few reports exist regarding thrombosis caused by disorder of coagulant system in microvascular anastomosis. Here we report our 3 cases in which multiple thrombus formation occurred intraoperatively caused by decrease of antithrombin (AT) activity. AT activity was measured twice a day after vascular anastomosis: after surgery and up to 3 days after surgery. Thrombosis was not observed in any of the 3 patients intraoperatively after the transfusion, or thrombosis was not observed in any of 3 patients intraoperatively after the transfusion or postoperatively, and no other complications were observed. In these 3 cases, the thrombus was not caused by technical error or other previously described factors. The observed intraoperative decrease in AT activity was thought to be caused by thrombus formation. It is important that microsurgeons are reminded that disorders of the coagulation–fibrinolysis system could cause thrombosis. *(Plast Reconstr Surg Glob Open 2020;8:e2872; doi: 10.1097/GOX.0000000000002872; Published online 15 June 2020.)*

With the development of microsurgical technique and instruments, the success rate of microvascular anastomosis now exceeds 95%.[1] In recent years, this surgical technique has been adapted in organ transplantation and composite tissue allografting.[2,3] With expanded application, avoiding thrombosis is increasingly significant for microsurgeons. Technical errors such as tension, twisting, and compression of vascular anastomoses are the major causes of thrombus formation. Other factors frequently mentioned in the literature include arteriosclerotic vessels and inappropriate perioperative management of the patient. However, there are few reports on the relationship between thrombosis and disorders of the coagulation–fibrinolysis system.[4] This study reports 3 cases of intraoperative multiple thrombus formation due to decreased antithrombin (AT) activity. AT is synthesized in the liver, which inhibits thrombus formation and strongly influences the balance of the coagulation–fibrinolytic factors.[5]

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Received for publication November 30, 2019; accepted April 8, 2020.

DOI: 10.1097/GOX.0000000000002872

CASE REPORTS

Case 1

A 70-year-old man presenting with an esophageal and intestinal fistula following gastric tube cancer diagnosis underwent total thoracic esophagectomy and was subjected to jejunal pull-up through the anti-thoracic route. Vascular anastomoses of the jejunal artery and vein to the internal thoracic artery and vein were performed to augment blood flow to the distal part. During the procedure, we observed multiple thromboses in the anastomosed vessels, with 1 arterial and 4 venous thromboses. Intraoperative examination showed AT activity deficiency (50%), and AT transfusion was performed. Then, we performed a second arterial anastomosis and a fifth venous anastomosis.

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

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Subsequently, neither arterial nor venous thrombosis was observed, and the operation was completed. The intraoperative bleeding volume was 1100 mL, and the operation time taken was 12 hours 20 minutes (Fig. 1) (**see figure, Supplemental Digital Content 1**, which displays the perioperative AT activity in 3 cases, **http://links.lww.com/PRSGO/B394**).

Case 2

A 77-year-old man with hilar cholangiocarcinoma presented with a right hepatic artery injury during hepatectomy. The injured artery was resected, and vascular anastomosis was performed. However, thrombosis was observed 3 times. The middle colon artery was harvested as a graft to interpose the vessels. At this time, intraoperative blood tests showed marked depletion of AT activity (25%), and AT transfusion was performed. A fourth arterial anastomosis was done after AT transfusion. Subsequently, no further thrombosis was observed, and the operation was completed. The postoperative course was uneventful thereafter. The intraoperative bleeding volume was 403 mL, and the operation time taken was 13 hours 23 minutes (Fig. 2) (**see figure, Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/B394**). In this case, a slight decrease in AT was observed before the operation (62%), and the AT activity was reduced to 60% at postoperative measurement, but it did not decrease further, and so no AT perfusion was added.

Case 3

A 78-year-old man with extensive left maxillary sinus carcinoma underwent left total maxillectomy, anterior and middle skull base resection, and subsequent free rectus abdominis myocutaneous flap reconstruction. During the operation, arterial thrombosis was observed 5 times in the microvascular anastomotic site. After 4 thromboses were found, the recipient artery was changed to the superior thyroid artery. At this time, intraoperative examination showed AT activity depletion (37%), and AT transfusion was done. A sixth arterial anastomosis was performed after AT transfusion. When no further thrombosis was observed, the operation was terminated. The postoperative course was uneventful. The intraoperative bleeding volume was 1480 mL, and the operation time taken was 18 hours 20 minutes (Fig. 3) (**see figure, Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/B394**).

DISCUSSION

AT inhibits fibrin formation, which is the final form of coagulant factor.[6] AT activity is measured with plasma containing sodium citrate. Since the blood level of AT depends on the balance between productivity and consumption, the significance of the coagulation system in vivo, production status, and the etiology of thrombosis can be known. AT activity is considered to be normal between 70% and 130%.

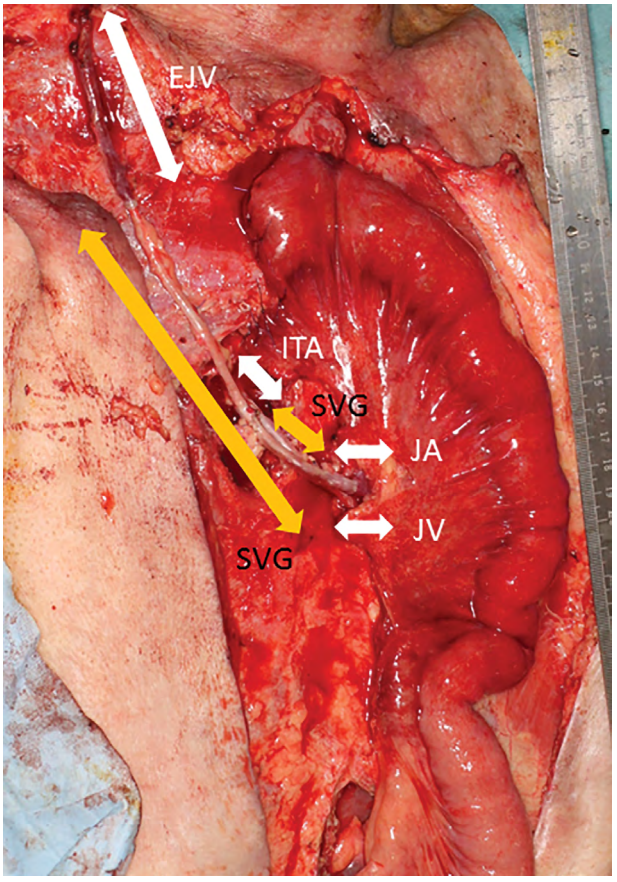

Fig. 1. Case 1: After microvascular anastomosis. After 1 arterial and 2 venous thromboses were confirmed, a left saphenous vein graft was used. After AT transfusion, we performed a fifth venous anastomosis. AT indicates antithrombin; EJV, external jugular vein; ITA, internal thoracic artery; JA, jejunal artery; JV, jejunal vein; SVG, saphenous vein graft.

The causes of AT deficiency are categorized as congenital or acquired. Congenital AT deficiency is an autosomal dominant inherited coagulation disorder reported by Warren[7] in 1935, which is diagnosed by low antigen levels and low AT activity in patients and their families. Although it is estimated that 0.18% of the Japanese population are heterozygous carriers, it is difficult to determine the precise prevalence because it is diagnosed once symptoms appear. The causes of acquired AT deficiency include nephrotic syndrome, consumption in surgery or trauma, hepatic disorders, disseminated intravascular coagulation, and an increased fibrillary state.

The incidence of intraoperative thrombosis due to AT deficiency is rarely reported in the reconstructive surgery field.[8] However, such a condition is seen in the cardiovascular field. In 2013, Ranucci et al[9] reported that preoperative AT supplementation not only avoids excessive postoperative decrease in AT activity but also prevents heparin resistance. In 2018, Nishimura and Takagi[10] described that in AT-deficient patients who undergo cardiac surgery, it is important to perform AT replacement treatment to achieve preoperative AT activity ≥120% and postoperative AT activity ≥80%, while the activated clotting time

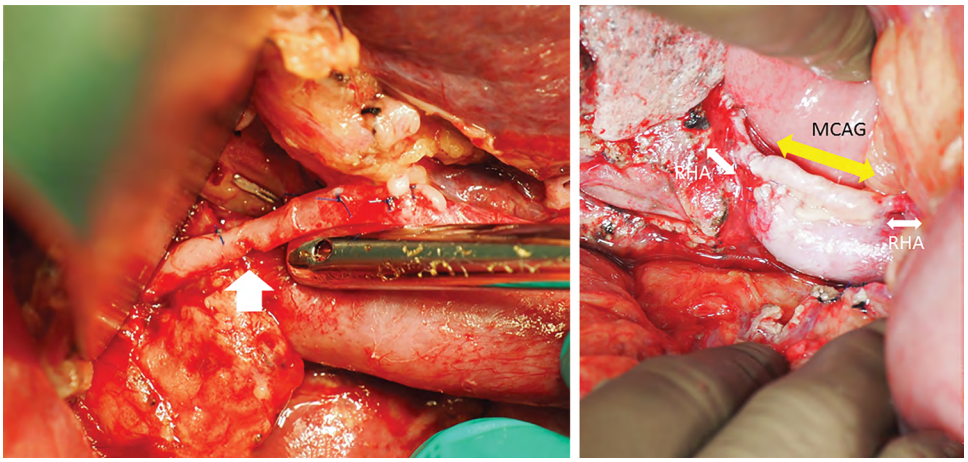

Fig. 2. Case 2. A, Right hepatic artery was injured by electric scalper. The white arrow indicates an injured point. B, After microvascular anastomosis. After 2 thromboses were confirmed, the middle colon artery graft was used. However, thrombus formation was noted in the anastomotic region to the side of the graft and liver. A fourth arterial anastomosis was performed after AT transfusion. The yellow arrow indicates the graft length. AT indicates antithrombin; MCAG, middle colon artery graft; RHA, right hepatic artery.

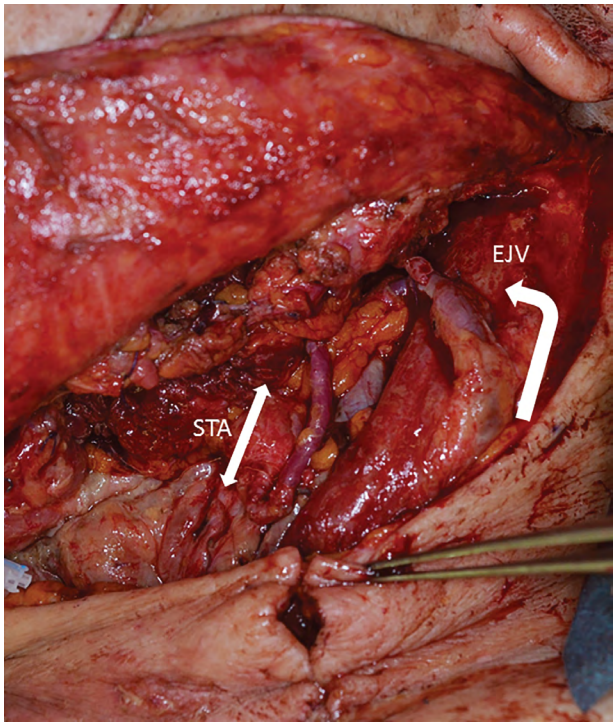

Fig. 3. Case 3: After the final microvascular anastomosis. After 4 thromboses were confirmed, the recipient artery was changed to the superior thyroid artery. A fourth arterial anastomosis was performed after AT transfusion. AT indicates antithrombin; EJV, external jugular vein; FA, facial artery; STA, superior thyroid artery.

is maintained at >400 seconds during cardiopulmonary bypass. In 1 patient (case 2) in our case series, the AT activity value was found to be low before the operation. This patient suffered from impaired liver function due to hilar cholangiocarcinoma, which may be the cause of low AT activity. In this situation, it cannot be determined whether the patient had congenital or acquired AT deficiency. In the other 2 cases, we assumed that intraoperative mass bleeding or extended operation time caused AT exhaustion because both cases exceeded 12 hours and the intraoperative bleeding volume was 1000 mL.

AT transfusion of 1500 U was performed in these 3 cases. As a treatment for AT activity reduction (AT activity <70%) due to disseminated intravascular coagulation etc, 30 U/kg or 1500 U AT preparation was administered intravenously at our hospital, and there was no particular problem. In this case, all patients weighed >50 kg, and AT activity was well below 70%. In consultation with the anesthesiologist, the dose was fixed at 1500 U. The accumulation of future cases will allow us to determine the appropriate AT dose.

SUMMARY

This study reports 3 cases of intraoperative multiple thrombus formation caused by decreased AT activity. Because disorders of the coagulation–fibrinolysis system can cause thrombi in free flap transfer of microvascular anastomosis, surgeons must take care when thrombosis is observed repeatedly.

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