The use of an anti-fibrinolytic agent to reduce endoleak following endovascular repair of multiple aortic aneurysms

Takeshi Uzuka*, Masanori Nakamura, Yohsuke Kuroda and Noriyasu Watanabe

Cardiovascular Surgery, Sapporo City General Hospital, Sapporo, Hokkaido, Japan

* Corresponding author. Cardiovascular Surgery, Sapporo City General Hospital, North 11 West 13 Chuo-ku, Sapporo, Hokkaido 060-8604, Japan.
Tel: +81-11-7262211; fax: +81-11-7267912; e-mail: uzuka@aol.com (T. Uzuka).

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Abstract

This paper reports on the therapeutic use of tranexamic acid in an elderly patient with severe comorbidities that precluded even endovascular reintervention. Orally administered tranexamic acid mitigated and partially reversed two and a half years of progressive aneurysmal expansion and closed a persistent endoleak after thoracic endovascular aneurysm repair and endovascular aneurysm repair for coexisting lesions. Reappearance of the endoleak when tranexamic acid was accidentally stopped and its re-closure after the resumption of tranexamic acid treatment confirmed causality. This singular experience extends prior published observations that administration of prophylactic tranexamic acid before thoracic endovascular aneurysm repair and endovascular aneurysm repair resulted in significantly greater shrinkage, particularly if an endoleak or coagulopathy was present.

Keywords: Tranexamic acid • Endoleak • Endovascular aneurysm repair • Thoracic endovascular aneurysm repair

INTRODUCTION

Tranexamic acid (TXA) is a well-known antifibrinolytic agent that inhibits plasminogen activation and reduces bleeding by stabilizing clots. It has been reported that prophylactic treatment with TXA is associated with Type 2 endoleak reduction and aneurysm shrinkage in endovascular aneurysm repair (EVAR) patients [1, 2]. However, the effects of postoperative administration on enlarged aneurysms and existing endoleak have not been reported.

CASE REPORT

A 70-year old male patient presented with a pulsatile abdominal aortic aneurysm (AAA). He was in a wheelchair due to Parkinson’s disease and had left-side hemiplegia as a result of a past cerebrovascular event. His lung function was also restricted as a result of previous lung tuberculosis. Computed tomographic (CT) angiography (Aquilion ONE; Toshiba Medical Systems, Tokyo, Japan) revealed a 52-mm thoracic aortic aneurysm (TAA) and a 63-mm infrarenal AAA.

Endovascular repair for both aneurysms was offered in accordance with the patient’s preference and his multiple comorbidities. Thoracic endovascular aneurysm repair (TEVAR) using Talent (Medtronic Vascular, Santa Rosa, CA, USA) with coverage of the left subclavian artery (LSCA) and axillary artery crossover bypass was performed without intraoperative endoleak. A month later, the patient underwent EVAR (Zenith Flex, Cook, Inc., Bloomington, IN, USA). Although no endoleak was observed on postoperative CT angiography, follow-up CT a month after EVAR showed a major TAA endoleak without migration of both stent grafts. Further invasive investigation was discussed but not conducted because the size of the TAA did not change.

The endoleak persisted for 2 years in the TAA, which reached 57 mm in diameter. The AAA also enlarged to 76 mm in diameter, but CT showed no endoleak (Fig. 1). Further investigation and possible surgical options were again discussed, but none was undertaken due to the high risk involved. The coagulation profile showed reduced fibrinogen and elevated fibrinogen degradation products (FDP) and D-dimer, and the International Society on Thrombosis and Haemostasis disseminated intravascular coagulation (DIC) score was 5. To treat these enlarging aneurysms and coagulopathy, 750 mg of TXA was administered. Four months later, the previously reduced level of fibrinogen had recovered to a normal level and other coagulation profile variables had also improved (Table 1). Follow-up CT angiography showed no obvious endoleak in the TAA, and revealed that the TAA and AAA had shrunk to 55 and 70 mm, respectively (Fig. 1).

However, re-emergence of the TAA endoleak was observed on the penultimate follow-up CT. The AAA had also enlarged again without endoleak. It later transpired that the patient had not been taking the TXA due to an error at the nursing home where he was resident. After he restarted the TXA treatment, no TAA endoleak was seen on the final CT.

DISCUSSION

Endoleak is a new and unique problem associated with TEVAR and EVAR. In particular, Type 1 and Type 3 endoleaks are reported to
be associated with postoperative rupture, and further intervention is required [3]. The standard approach for preventing endoleak involves securing an adequate landing-zone length, respecting anatomy and avoiding trade-offs. In the case reported here, the LSCA was not embolized after TEVAR because no endoleak was observed on the intraoperative aortogram. However, as a major endoleak emerged on the follow-up CT, it would have been beneficial to block the proximal LSCA to exclude a Type 2 endoleak and diagnose the type of endoleak in the TAA.

The diameter of the AAA increased from 63 to 76 mm in 2.5 years. Although a surgical option was considered, it was not offered due to the high risk involved. We believe that the risk of TXA administration is acceptable compared with the risks inherent in additional surgery. However, most patients with aortic aneurysms have atherosclerotic lesions in other parts such as the brain or heart. Although no major side effects have been reported in TXA administration for EVAR patients [1, 2], TXA administration was started in the case reported here because preoperative screening had already ruled out the presence of any major occlusive disease in the head, neck and coronary artery. However, the long-term effects of postoperative TXA therapy remain unknown, and dosage should be controlled based on coagulation monitoring.

In patients with large aortic aneurysms or persistent endoleak following endovascular repair, consumption of coagulation factors and fibrinolytic activation are observed [1, 2, 4, 5]. In the case reported here, although data on fibrinolysis considerations such as plasminogen activators and the plasmin inhibitor complex are lacking, the coagulation profile indicated that the patient was in a DIC state before TXA therapy. We believe that the reversal of this coagulopathy by TXA triggered mitigation of the major endoleak in the TAA. Depressurization and thrombosis led to the shrinkage of both aneurysmal sacs. This remarkable response to TXA was observed again when TXA was accidentally stopped and later restarted. TXA therapy is therefore considered to be practical for the treatment of existing DIC-related endoleak and to contribute to aneurysm shrinkage.

**CONCLUSION**

TXA therapy was initiated after 2.5 years for a patient with persistent endoleak in a TAA and an enlarged AAA following endovascular repair. After treatment, the major endoleak in the TAA was no longer visible and both aneurysms had shrunk. Accordingly, TXA...
therapy is considered applicable to the treatment of enlarged aneurysms and associated DIC-related persistent endoleaks in patients at high surgical risk.

**Conflict of interest:** none declared.

**REFERENCES**


eComment: Treating endoleak type 2 and disseminated intravascular coagulopathy after EVAR with tranexamic acid: the efficacy of killing two birds with one stone

**Author:** Demetrios Moris

Division of Vascular Surgery, "Laikon" General Hospital, Medical School, Athens, Greece.

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We read with great interest the article of Uzuka *et al.* [1] adding valuable information about the role of tranexamic acid (TXA) in the sac shrinkage in type 2 endoleak after aortic endovascular repair (EVAR).

This article has several interesting findings. First of all, it validates an establishing new knowledge that anti-fibrinolytic agents may be helpful in type 2 endoleak re- guise or stabilization after EVAR [2]. This is of great importance since treatment for type 2 endoleak with sac expansion is still a matter of controversy. It has been reported that a certain type 2 endoleak causes sac expansion and late aneurysm rupture which was often treated with solid agents as coils and vascular plugs or with liquid agents as different glues and thrombin [3].

The role of perisac embolization is another novel technique focusing on all patent arterial branches either from the translumbar or transarterial and transcaval approach [3]. The question raised from TXA administration is the justification of the dose. It is not clear why authors chose the dose of 750 mg. Additionally, the frequency of administration as well as the criteria of this decision are not fully explained. The dose is determined by the progression of the endoleak, the diameter of the sac or other parameters? Moreover, no data are offered about the risk of thrombo-embolic events in that dose that prove effective in that case.

Another interesting finding is that the patient has a disseminated intravascular coagulopathy (DIC), attributed at first to EVAR and its endoleak. This is a point of consideration and discussion. It is well known that DIC is a status of widespread and persistent activation of coagulation in the presence of underlying disease that causes diffuse microthrombi in small blood vessels. In addition to coagulation activation, fibrinolytic activation occurs, but the degree of fibrinolysis varies considerably depending on the underlying disease. With DIC progression, haemostatic factors such as platelets and clotting factors are depleted, thus leading to consumption coagulopathy. So the application of anti-fibrinolytic factors may influence beneficially the fibrinolytic activity in DIC, but at the same time can enhance the thrombotic state of the patient which can have devastating consequences. The authors presented that DIC was improved after TXA administration, result concluded by the differences of the coagulation profile. This should be attributed to the fact that aortic aneurysm, especially abdominal aortic aneurysm, is a rare but important cause of enhanced-fibrinolytic-type DIC in which DIC is associated with marked fibrinolysis activation corresponding to coagulation activation [4]. Fibrinolysis is strongly activated; hemostatic plugs (thrombi due to haemostasis) are more easily dissolved; and bleeding symptoms tend to be severe. Laboratory findings usually show a marked elevation in both FDPs and D-dimers [4]. Because fibrinogen degeneration progresses, the FDP/D-dimer ratio tends to increase (decrease when expressed as the D-dimer/FDP ratio) [4]. At this point, the authors did not clarify if the DIC was a result of endoleak or if there was a pre-existing DIC attributed to original aneurysm and worsen due to failure of EVAR (preoperative D-dimers and fibrinogen values are missing). So, it is not clear if the DIC improvement was directly attributed to the effect of TXA on the coagulation cascade and pathophysiology or it was due to sac shrinkage.

All in all, it seems that TXA therapy is considered applicable to the treatment of enlarged aneurysms and associated DIC-related persistent endoleaks with more well designed studies on investigating this consideration being mandatory.

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**References**


