

Efficacy of Local Delivery of Recombinant Tissue Plasminogen Activator for Vein Thromboembolic Syndrome

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Abstract: Tissue plasminogen activator (tPA) is a potent thrombolytic agent and as a consequence, bleeding is a major side effect associated with its use. We here describe a 72 year-old woman with a single kidney who was admitted to our hospital because of renal trauma associated with an accident. A large thrombus associated with the central venous line developed close to the wall of the inferior vena cava two weeks after embolization. To manage this complication, we locally delivered 6350 IU/Kg of recombinant tPA (monteplase) through a pulse infusion catheter. This represents only one-half to one-quarter of the usual dose of tPA. One day after this local delivery, the thrombus had disappeared with no bleeding complications despite sub-acute sub-cortical hematoma of the injured kidney. We propose that local delivery of small amounts of recombinant tPA into thrombi may mediate efficient thrombolysis with less bleeding complications as a side effect.

Keywords: Catheter, pulse infusion, thrombus, thrombolysis.

CASE REPORT

A 72 year-old woman was admitted to our hospital because of renal trauma sustained after falling from cliffs 5 metres in height. She had a single kidney because of a congenital anomaly, and suffered from type 3 renal trauma. Coil embolization was required due to sub-cortical bleeding of the single kidney. A central venous line was inserted due to hemorrhagic shock. A dopamine infusion drip was administered at a dose of 7 µg/kg/min through the central venous line. A large thrombus associated with the central venous line developed close to the wall of the inferior vena cava two weeks after embolization (Fig. 1A), although no pulmonary thromboemboli were present. An inferior vena cava (IVC) filter was placed on the IVC close to the hepatic vein, because a large thrombus occupied the body of the inferior vena cava. We delivered 400,000 IU of recombinant tPA (monteplase) locally through a pulse infusion catheter (Fig. 1A, B). One day after local delivery, the thrombus had disappeared with no bleeding complications despite the recent trauma to the kidney (Fig. 2). We were able to replace the original IVC filter with another applied to the usual delivery site, namely the IVC body, since the large thrombus had been minimized.

DISCUSSION

Tissue plasminogen activator (tPA) is a potent thrombolytic agent and as a consequence, bleeding is an important side effect associated with its use. We are therefore confronted by the dilemma of whether to dissolve a thrombus using systemic tPA in an effort to protect against lethal

pulmonary thromboembolism, or to avoid serious bleeding from multiple organs. Because tPA strongly binds to fibrin monomers promptly and irreversibly, we hypothesized whether tPA locally delivered into a large thrombus would retain efficacy, with more minor complications than systemic delivery.

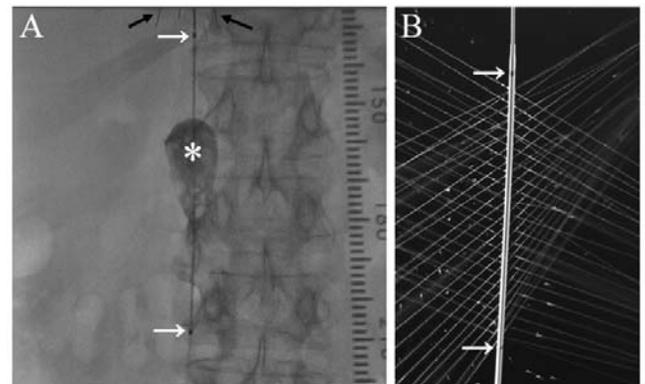


Fig. (1). Local delivery of recombinant tPA with contrast dye. Panel A shows a thrombus developing close to the inferior vena cava. After spraying with tPA + contrast medium into the area of the large thrombus, a large and sluggish thrombus was visible. Black arrows show the feet of the inferior vena cava filter. *: The bulk of the large thrombus. Panel B is a photogram made while infusion materials were being sprayed through the pulse infusion catheter tip. White arrows indicate the radiopaque marker positioned at the infusion points of the catheter tip.

Yamagami *et al.* [1] showed that thrombolysis with monteplase (recombinant tPA) was effective for treatment of deep venous thrombosis. They administered 2,170,000 IU of monteplase, and while deep vein thrombosis (DVT) had been completely resolved in 67% of cases, unfortunately 12.5% of patients had a hemorrhage at the puncture side and

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Fig. (2). Local delivery of alteplase (recombinant tPA) + contrast dye into the thrombus. Upper panel shows a single plane computed tomography image acquired one hour after local delivery of tPA + contrast medium. The black circle shows that the contrast dye, which was delivered intra-thrombus with alteplase, remained in the thrombus close to the inferior vena cava wall. Bottom panel also shows the single plane computed tomography image one day after local delivery. The thrombus has disappeared.

at the gingiva. The efficacy of local delivery of thrombolytic agents through a pulse infusion catheter has been demonstrated [2]. In the present case, alteplase was present for a considerable period after local delivery and successfully achieved complete thrombolysis though delivered at one quarter of the usual dose.

CONCLUSIONS

Local delivery or catheter-directed thrombolysis performed under imaging guidance delivers a thrombolytic agent directly to the thrombus through a catheter inserted in

the vein. Intra-thrombus delivery of a fibrin-specific thrombolytic agent such as alteplase may be an alternative to systemic thrombolysis and may minimize the risk of bleeding complications.

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