Successful salvage of thrombosed arterio-venous fistula with thrombolytic therapy using tissue plasminogen activator

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ABSTRACT

A functioning vascular access is crucial to the wellbeing of patients on hemodialysis. Thrombosis is the most common complication of arteriovenous fistula (AVF) resulting in late fistula failure; Its treatment is difficult, and results are often suboptimal. Interventional treatment of AVF thrombosis may not be available all the time, and timely application of an available noninterventional treatment may salvage the fistula. We report the successful treatment of AVF thrombosis using local thrombolytic therapy using tissue plasminogen activator in a patient, for the first time in India.

Key words: Arteriovenous fistula, thrombolysis text, thrombosis, tissue plasminogen activator

Introduction

A functioning vascular access is essential for effective delivery of hemodialysis and, understandably, lack of vascular access or complications developing in an existing vascular access are associated with significant patient morbidity. Thrombosis is one of the most common complications associated with autologous arteriovenous fistula (AVF) for hemodialysis and often results in failure of AVF. Here we report, to our knowledge for the first time in India, salvage of a thrombosed AVF using early thrombolytic therapy (TT) alone, when interventional treatment option was not available.

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Case Report

A 48-year-old man with end stage renal disease (ESRD), on regular thrice-a-week hemodialysis for 4 years, noticed that his AVF for dialysis vascular access had stopped working and reported to the hospital.

He was on regular treatment for hypertension for 17 years before he was detected as having deranged renal function and shrunken kidneys in 2009. The etiology of his kidney disease was unknown, he was not a diabetic. He reached ESRD in May 2010 and was initiated on hemodialysis. He had no history of coronary artery disease, cerebrovascular accidents, peripheral vascular disease, or any other thrombotic events. He did not smoke. The side to side radio-cephalic AVF on the right side was created in 2010, following primary failure of left radio-cephalic AVF. He received hemodialysis thrice a week for 4 h each; the AVF was cannulated by the step ladder technique with the proximal needle being placed more than 5 cm from the AVF anastomosis site. The AVF supported a blood flow of 300-350 ml/min consistently over the past 3 years. He was taking clopidogrel 75 mg/day for the past 3 years.

One year back, on a day when he was due for hemodialysis, he noticed the absence of thrill over the AVF and he reported to the surgeon who created the AVF, in another city. The AVF apparently started working without any

specific intervention at that point of time. No further evaluation was undertaken to assess the AVF.

He had undergone hemodialysis uneventfully, the day before he presented to us. The dialysis session got over by 10:00 PM and the fistula bands were removed by 1:00 AM. He did not notice any abnormality with the AVF the next day morning, when he woke up from sleep. At about 4:00 PM in the evening, he noticed that the AVF appeared "collapsed" and on palpation found the thrill to be absent. He reported to our hospital at 6:30 PM. He denied any history of trauma or prolonged pressure over the AVF, he had mild pain, and noticed a small swelling over the AVF anastomosis site. On examination, there was no bruit over the AVF. Ultrasonography Doppler revealed a thrombus at the anastomotic site with no blood flow. The rest of the AVF was free of thrombus.

After discussing the available and feasible treatment options with the patient, thrombolysis of the blocked AVF was attempted. Written informed consent was taken after explaining the procedure and the possible benefits and risks involved.

An 18G intravenous cannula was placed in the AVF, with the tip of the cannula reaching the thrombus at the anastomotic site [Figure 1]. Flushing was done with 20 ml sterile normal saline to ensure that there was no counter-puncture and resultant extravasation of the thrombolytic agent. Tissue plasminogen activator (tPA - Injection Actilyse, Boehringer Ingelheim India) was reconstituted to a concentration of 0.5 mg/ml. A tourniquet was placed proximal to the IV cannula to prevent the injected tPA from reaching the systemic circulation. A volume of 4 ml (2 mg) of the reconstituted tPA was injected through the IV cannula into the AVF segment, close to the thrombus. Manual manipulation of the anastomotic site where the thrombus was lodged was carried out, during and following injection of tPA, to soften the thrombus. Vascular thrill appeared at the anastomotic site within a couple of minutes. Since the thrill remained feeble, another injection of 4 ml (2 mg) tPA was administered, along with manual manipulation, 5 min after the first injection. A prominent thrill reappeared promptly, and the AVF venous segment demonstrated evidence of good blood flow. The tourniquet was removed after 30 min. The patient was advised limb exercise with a soft ball, and he was started on infusion of unfractionated heparin and tablet aspirin.

An angiogram of the right upper limb (radial artery and the AVF) was performed the next day morning by the cardiologist and showed excellent flow across the AVF anastomotic site with no evidence of stenosis at the anastomotic site or in the venous system, with small thrombus at AVF [Figure 2]. He underwent hemodialysis the same day afternoon, with the AVF supporting blood flow >300 ml/min. He was treated with anticoagulation with heparin for 5 days and discharged with advice to continue aspirin and clopidogrel.

Discussion

Vascular access is the "Achilles heel" of hemodialysis and absence or loss of vascular access is often associated with

Test	Result	Reference value
Hb	10.5 g/dl	13-16.5 g/dl
Platelet count	2.49 lacs/ml	1.5-4.5 lacs/ml
INR	1.04	1.00-1.40
HBsAg	Negative	
Anti-HCV	Negative	
HIV	Negative	

HBsAg: Hepatitis B virus surface antigen, INR: International Normalized Ratio, HCV: Hepatitis C Virus, HIV: Human immunodeficiency virus

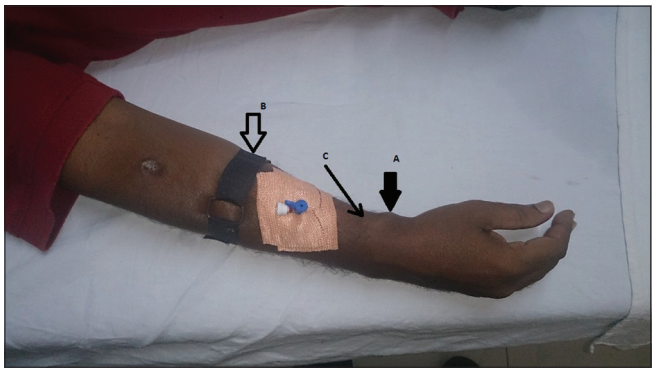

Figure 1: Right forearm of the patient having the arteriovenous fistula (AVF) with the thrombus (solid arrow labeled "A"), 18G IV Cannnula placed in the AVF with its tip close to the thrombus (oblique arrow labeled "C") and a tourniquet applied proximally using a fistula band (transparent arrow labeled "B")

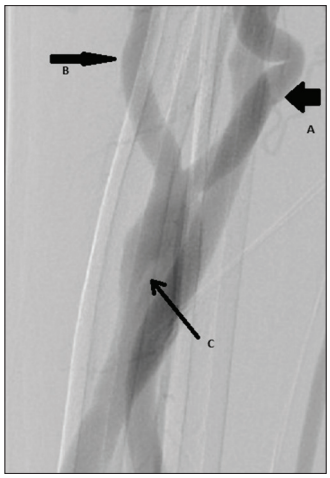

Figure 2: Fistulogram after thrombolytic therapy with tissue plasminogen activator showing the radial artery (thick arrow labeled "A", the arterialized cephalic vein (arrow labeled "B") and a small mobile thrombus near the anastomotic site of the arteriovenous fistula (oblique arrow labeled "C")

significant morbidity and mortality.[1] Even though the thrombosis rate of autologous AVF is one-sixth that of AV graft, thrombosis is still the most common cause for late failure of AVF.[1] Thrombosis is usually the consequence of some sort of anatomic abnormality, like stenosis, in the proximal venous segment; problems with the arterial segment account for only about 17% of AVF thrombosis,[1] but systemic abnormalities in hemostasis like protein C and S deficiency, factor V Leiden, antiphospholipid antibodies, etc., may also contribute. The results of treatment of thrombosed AVF have significantly improved in recent times, with long-term patency reports at 63-89% at 3 months, 52-74% at 6 months, and 27-47% at 1 year.[2-4] For best results, treatment of thrombosis should start as early as possible.[1] Delay in instituting treatment may result in extension of the thrombus, making subsequent intervention or surgical procedures more difficult and less successful. Delay in treating the thrombus also allows a longer period of contact between the thrombus and the vessel wall, making subsequent extraction of thrombus more traumatic to the vessel wall, which in turn could predispose to thrombotic events in the future. Most importantly, early resolution of the thrombosis may allow uninterrupted use of the same AVF for dialysis, avoiding intercurrent use of a venous catheter and attendant morbidity, like in our case. Treatment options available for thrombosed AVF are: (1) percutaneous intervention with thrombectomy and angioplasty of any stenosis detected; (2) surgical thrombectomy; (3) declotting by mechanical techniques (dilatation and aspiration); (4) TT; and (5) combined mechanical declotting and TT. In the absence of robust comparative trials, clinical practice is usually dictated by local expertise and available facilities.[1] Percutaneous intervention is the most preferred option and is usually performed by an interventional radiologist or an interventional nephrologist. Percutaneous interventions as well as surgical thrombectomy were not immediately possible in our patient due to logistic issues. We referred the patient to an intervention center in another city, but the patient refused. Hence it was decided to try TT in his case, in a desperate attempt to salvage the access. Urokinase was not available with us. Published literature on TT with streptokinase as well as tPA are very limited. Only tPA is FDA approved for treatment of thrombosis in hemodialysis catheters (not AVF) in the US and almost all recent reports of TT in clotted AVF also employed tPA. We could not find reports of thrombolysis of AVF using SK after 1995 and the immediate patency rate reported in previous studies was about 50%. The available literature on the use of tPA reported a short-term patency of 90% or even more.[2,4-7] Based on this, we felt that tPA probably offered better chances of success and decided to employ it in our case. We used the protocol described by Tseke *et al*.[7]

It may be prudent to point out that the success in our case may not be generalizable to all cases of clotted AVF. Our patient promptly recognized the absent thrill and reported to hospital within a couple of hours, he had an isolated thrombus at the anastomotic site with the rest of the AVF bearing no thrombi, and we could institute TT within about 4 h of detection of catheter malfunction - all of which likely contributed significantly to the success of the treatment.

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