

Salvage of venous congested free flaps: It's TBA for subcutaneous tPA



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Objective

Between 5 to 10% of tissue free flap (FF) transplants are complicated by vascular thrombosis, with approximately half the flaps being salvaged through re-exploration.¹ There is limited evidence for salvage therapies when FF have vascular compromise. The objective of this case report is to highlight the use of subcutaneous alteplase (rt-PA) to salvage a FF with vascular compromise, and review the literature for this practice.

Clinical Features

A 61 year old male was admitted for a left mid-foot fusion and FF transplantation, after falling and sustaining a Lisfranc fracture.

The first FF failed 6 days post transplantation after recurrent venous thrombosis and attempted revisions including the use of leeching and intra-arterial alteplase.

Two days later, a second (anterolateral thigh) FF was used to reconstruct the left dorsal foot. Eight hours post-operatively the flap darkened and tissue turgor increased. Re-exploration revealed a venous thrombus crossing the anastomosis.

Interventions and Case Progress

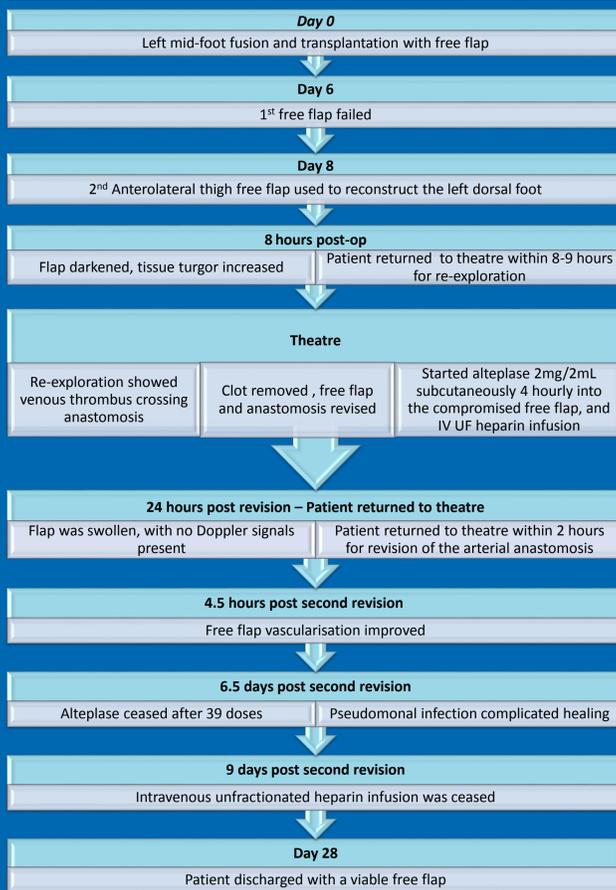
The clot was removed, and the flap and anastomosis were revised within 9 hours of venous congestion identification. At this point the team prescribed 2mg/2mL alteplase administered subcutaneously into the compromised FF 4 hourly.

Two-hourly observations were performed on the flap after the revision. This involved nurses examining the flap, noting colour, temperature, capillary refill time, tissue turgor, and assessing Doppler signal strength.

The patient was concomitantly administered an intravenous unfractionated heparin infusion aiming for an APTT of 60 to 100 seconds. The therapeutic intravenous heparin infusion was initiated around 12 hours prior to the first injection of alteplase and continued for 9 days. It was imperative that heparin and alteplase were administered via different routes as they are physically and chemically incompatible intravenously, resulting in the formation of crystals, reduced alteplase activity and erratic heparin activity. Hence, the unfractionated heparin was administered intravenously and alteplase was administered subcutaneously.

Within 24 hours, the FF became swollen and Doppler signals were unable to be found. The patient returned to theatre 2 hours later for revision of the arterial anastomosis, due-to signs of arterial insufficiency.

Figure 1. Patient Timeline



Outcomes

Within 4.5 hours of the second anastomosis revision, thrombolysis appeared successful. Flap vascularisation improved, and the flap became pink and warm with strong Doppler signals present.

Alteplase was administered for a total of 6.5 days.

The FF eventually succeeded, and the patient was discharged home 28 days following his initial operation, however the midfoot fusion was complicated by a pseudomonas infection. (See Figure 1. Patient Timeline).

Table 1. Microvascular thrombosis prophylaxis/treatment modalities

Medication	Mechanism of Action
Aspirin	Reduce platelet function
Dextran	Decrease blood viscosity
IV Unfractionated Heparin	Inactivate thrombin
IV Papaverine	Vasodilatation
IV Lidocaine	Vasodilatation
Manual Thrombectomy	Surgical removal of thrombus
Intra-arterial thrombolysis	Dissolve blood clot with thrombolytic
Subcutaneous Alteplase	Dissolves blood clots in FF microvasculature

Case Discussion and Literature Review

In the last year, subcutaneous alteplase has been used in at least three cases at our hospital in attempts to salvage FF complicated by vascular thrombosis, with varied success. In this context, the pharmacy team were asked to investigate the evidence to support this practice.

We undertook a literature review to investigate the subcutaneous administration of alteplase to improve vascularisation and salvage venous compromised FF.

The most critical factor for FF salvage appears to be the time to re-exploration, thrombectomy and anastomotic revision. The window for successful intervention that allows FF salvage appears to be the first 24 hours following thrombosis.¹

A literature review identified various prophylactic strategies to prevent microvascular thrombosis. Strategies include the use of aspirin, dextran, intravenous heparin, papaverine or lidocaine, manual thrombectomy, intra-arterial thrombolysis or a combination of these treatment modalities.² (See Table 1). There have also been five reported cases of successful thrombolysis of venous congested FF with 2mg alteplase injected subcutaneously into multiple sites in the FF upon identification of vascular compromise. In these cases, the administration of alteplase was not repeated.^{1,3,4}

Whilst subcutaneous administration of alteplase is not a licensed route of administration, we found evidence to support high alteplase activity following subcutaneous administration of recombinant human tissue-type plasminogen activator (alteplase)⁵.

We also found that response times following subcutaneous injection of alteplase into FF seems to differ greatly and this may be explained by differing flap sizes and varying distribution of alteplase, or by different severity of thrombosis in the flap vasculature.^{3,4}

Conclusion

We report a case of successful thrombolysis following the use of subcutaneous alteplase and concomitant revision of the anastomosis that resulted in salvage of a venous compromised free flap. Whilst more research is required, this adds to the limited evidence from case series to support this practice.

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