Intraoperative management of the no-reflow phenomenon during microvascular fibula free flap reconstruction using alteplase: a case report

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ABSTRACT

This case report describes the successful intraoperative management of a fibula free flap, which demonstrated the no-reflow phenomenon, using locally administered alteplase in an otherwise well 17-year-old male patient with a right mandibular odontogenic myxoma.

Microvascular free flap reconstruction is considered the gold standard for the management of many head and neck surgical defects. The vitality of the flap is reliant on the perfusion of the reconstructed tissue with vascular anastomoses to the recipient site. Alteplase is a fibrinolytic drug normally indicated for use in thrombotic events.

There are very few case reports in the literature to support the use of fibrinolytic agents in microvascular flap surgery, and alteplase may provide an option for intraoperative flap salvage when all other avenues have been exhausted.

Microvascular free flap reconstruction is considered the gold standard for the management of head and neck surgical defects.[1] The success of such flaps relies on the perfusion through local anastomoses and, indirectly, systemic factors. The overall head and neck free flap failure rate is less than 5%, according to a large multicentre prospective study.[2] Khouri and colleagues[2] also observed that identification of intraoperative thrombosis allowed for successful revision of anastomoses at the time, with only 4.1% of these flaps failing. A process known as the "no-reflow phenomenon" describes poor reperfusion of tissue despite the lack of evidence of mechanical vessel obstruction, and may occur during microvascular free flap reconstruction. No-reflow is described across several specialties, such as interventional cardiology, when reperfusion of cardiac tissue fails despite lack of angiographic evidence of thrombosis.[3]

Alteplase is a fibrinolytic drug. Specifically, it is a recombinant human tissue-type plasminogen activator. The usual indication for its use is in thrombotic events such as acute myocardial infarction, massive pulmonary embolism, and acute ischaemic stroke. Alteplase activates plasminogen to form plasmin, which degrades the fibrin clot. Currently, the use of alteplase in free flap surgery is considered "off-label".[4]

There are many publications describing the use of thrombolytics in free flap reconstruction, including streptokinase, urokinase, aspirin, dextran and heparin.[5,6] Alteplase has been described in intraoperative salvage during radial forearm flap reconstruction of the palate and a deep inferior epigastric perforator flap (DIEP) in reconstructive breast surgery.[7,8] However, no literature could be found supporting the use of alteplase to manage a no-reflow situation during a fibula free flap reconstruction in head and neck surgery.

Case description

A 17-year-old male patient was referred to the Oral and Maxillofacial Surgery department at Waikato Hospital (Hamilton, New Zealand) when his dentist found an incidental multilocular lesion on the posterior right mandible during routine imaging (***Figure 1***). A magnetic resonance imaging scan showed intramedullary extension of the lesion towards the angle and symphysis of the mandible. Clinically, a right sided facial deformity could be seen, but the patient was otherwise asymptomatic (***Figure 2***). Incisional biopsy confirmed the lesion as an odontogenic myxoma. The patient was otherwise well, took no regular medications, and did not smoke or drink alcohol.

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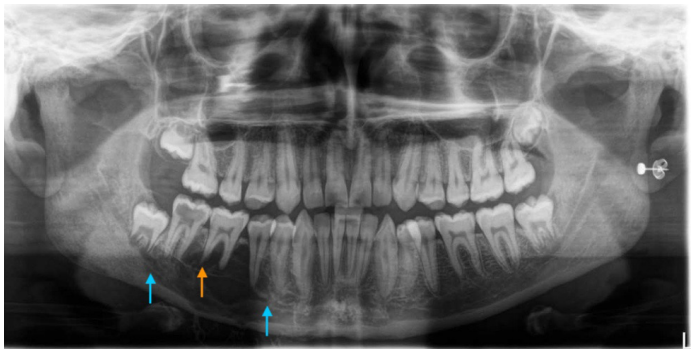


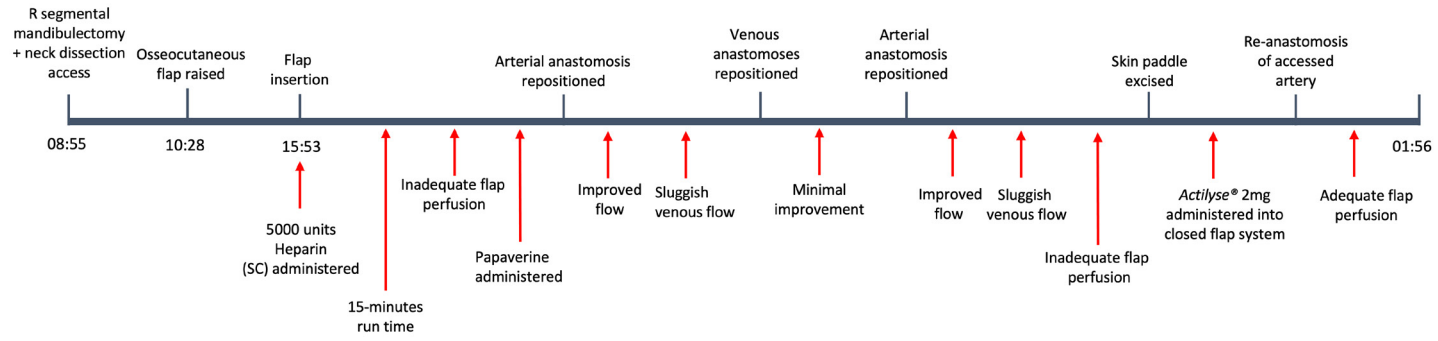
Figure 1. Preoperative mandible orthopantomogram: a multiloculated radiolucency is seen in the right mandibular body associated with teeth 44–47 (blue arrows). Evidence of root resorption of 46 is seen (orange arrow). Expansion of the lesion into the soft tissue seen by the calcified margins of the lesion inferior to the mandibular border

Figure 2. Preoperative photograph demonstrating deformity at the right mandibular body extending towards the mandibular midline

Various treatment options were discussed, and the patient underwent virtual surgical planning to plan his resection and design a fibula free flap to reconstruct the mandible. The fibula bone can be shaped into a structure similar to the native mandible and is therefore commonly used in head and neck reconstructive surgery.[9] He underwent a right segmental mandibulectomy and reconstruction with a left fibula free flap in late 2022. As a young and physically well patient, no preoperative deep vein thrombosis prophylaxis was deemed necessary.

Following tumour resection, a composite osseocutaneous fibula flap was raised without complication. Heparin (5000 units) was administered subcutaneously, as per the department protocol, prior to disconnecting the flap from the donor site. The peroneal artery and two veins were prepared for anastomosis to the facial artery, common facial vein and external jugular vein, respectively. The flap was flushed with heparinised saline (10 000 IU heparin/50 mL saline) solution prior to anastomosis. A total ischaemic time of 42 minutes was recorded between flap disconnection from the donor site to initial anastomosis in the neck. After initial anastomosis, there was adequate flap perfusion, and the flap was left to run for 15 minutes before finalising the inset and closure. However, on assessment of the flap, it was noted that the skin paddle and muscle had lost perfusion. Inconsistent and intermittent blood flow was detected through the veins and artery after clinical assessment and with both implantable and external doppler probes. Application of papaverine, which is an anti-vasospasmodic agent, did not improve the situation. The arterial anastomosis was repositioned to a more proximal location on the facial artery, resulting in improved arterial flow. On inspection of the previous anastomosis, there was no thrombus nor any technical microsurgical error. However, the venous flow continued to be sluggish. After more time to review flow, the distal aspect of the muscle and skin paddle still lacked circulation. The venous anastomoses were also revised, but again no technical microsurgical error or thrombus was noted at either site. The arterial anastomosis was once again revised, with the peroneal artery anastomosed to the external carotid artery. Initially good perfusion was noted, prior to again reduced venous outflow, then poor skin and muscle perfusion.

The decision was made to excise the skin paddle due to future risk of congestion and flap failure and the muscle was debrided to proximal bleeding regions, although this was limited. As an attempt to improve vascularity, the peroneal artery was partially accessed by incision through the vessel wall (arteriotomy) with a small cannula, and alteplase 2 mg (Actilyse 2 mg; Boehringer Ingelheim, New Zealand) was injected into the arterial pedicle over the course of ten minutes with the anatomosed veins clamped closely beyond the anastomosis site (ie, a closed system). The solution was prepared in a 1 mg/1 mL concentration by mixing the 10 mg Actilyse powder with 10 mL sterile water. A 3 cc syringe was used to administer the 2 mL solution through the cannula at 0.2 mL per minute intervals. The flap was allowed to rest and flushed with copious heparinised saline to clear the remaining alteplase prior to clamp removal. A revised arterial anastomosis was performed, yielding positive perfusion results throughout the flap upon clamp release (***Figure 3***).



Actilyse (Boehringer Ingelheim, New Zealand).

Figure 3. Timeline of surgical procedure demonstrating findings and subsequent interventions

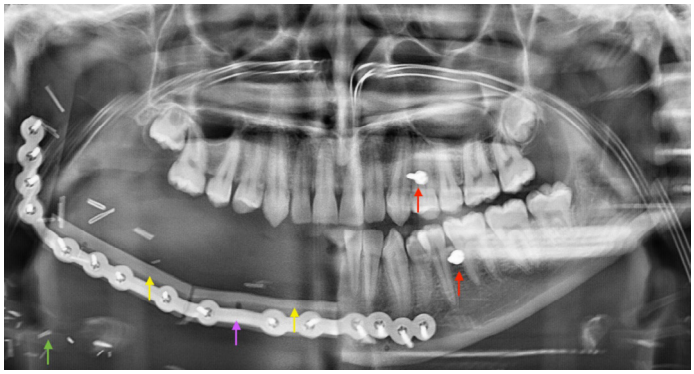


Figure 4. Postoperative orthopantomogram showing fibula flap (yellow arrows) with associated metal ware (purple arrow) and soft tissue vessel clips (green arrow). Left maxillary and mandibular intermaxillary fixation screws (red arrows) in situ for dental approximation. There are plans for dental implant placement and prosthetic rehabilitation in the near future

At the conclusion of the anastomosis, a further 2500 IU heparin was administered subcutaneously, and flap inset was completed with no obvious cause for the previously poor perfusion identified. The patient was haemodynamically stable with blood pressure sufficient for flap perfusion in the postoperative period. A heparin infusion was commenced, and a thrombotic screen and haematology consultation did not reveal any predisposing factors. The patient was discharged on day 13 postoperatively with no signs of flap failure (***Figure 4***).

The patient was reviewed regularly by the oral and maxillofacial surgery team and demonstrated an excellent and uneventful recovery. At the 12-month postoperative review, the flap appeared to have fully integrated and there were no signs of infection, flap failure or odontogenic myxoma recurrence on cone beam computer tomography imaging. He continued with his schooling and has maintained his nutritional intake with a normal diet.

Discussion

Microvascular flap surgery provides patients with head and neck surgical defects an option for reconstruction and rehabilitation. The use of alteplase, a fibrinolytic agent, has only been reported in a small number of case studies for use in microvascular flap surgery. To our knowledge, its use has not previously been reported in a fibula free flap reconstruction. This case demonstrates the successful intraoperative use of alteplase in an otherwise systemically well 17-year-old patient for the salvage of his fibula free flap, which repeatedly lost vascular perfusion, as an example of the no-reflow phenomenon. While the underlying cause was not determined, the administration of intravascular alteplase has proven to be successful, with evidence of complete flap integration 12-months postoperatively.

The failure of a vascularised flap reconstruction is devastating for the patient and surgical team. Therefore, options for flap salvage should be exhausted intraoperatively when there is evidence of flap compromised. This is supported by Khouri and colleagues,[2] who report a lower rate of flap failure when flap thrombosis is identified and managed intraoperatively. The initial procedure provides the best visualisation of the surgical field and is the easiest time to identify anatomical structures before postoperative oedema sets in. In instances where efforts such as re-anastomosis and systemic heparin have been unsuccessful, the off-label use of locally applied alteplase can be considered for flap salvage.

Author contributions

Petterson C: Conceptualisation (present during the surgical procedure and scrubbed during the administration of alteplase, initial discussions with Mr Singh regarding writing the case presentation, gained consent from the patient); data curation (requested clinical records from the Medical Records Department); writing original draft (primary author for the original draft including searching and adding the reference articles); editing; reviewing (provided the initial responses to the review points from the review panel); patient management (gained original consent for the article, managed the patient postoperatively as the on-call staff member).
Singh T: Conceptualisation (primary operator for the surgical procedure, provided expert knowledge on head and neck cancer surgery, and offered to supervise the writing of the article); data curation; writing original draft; editing (primary editor after the original draft was created, provided any additional information about the case and expert knowledge on the topic); reviewing (all responses to review points were checked and contributed to as the supervisor); patient management (provides ongoing review of the patient's progress postoperatively with planned follow-up appointments).
Ananth K: Conceptualisation; data curation (provided the necessary radiological images and clinical data from the onsite computers); formal analysis; methodology; writing original draft (drafted the original case details); editing; reviewing; patient management (remains a staff member within the department and assists with reviews and booking investigations as required).

Patient consent

The patient provided written consent for publication.

Conflicts of interest

All authors declare that they have no conflicts of interest.

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