Preoperative Long-term Therapeutic Subcutaneous Heparin Administration into Abdomen: Possible Cause for Nonobstructive Microvascular Flap Failure

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Summary: The anterioabdominal wall is the most common site for low molecular weight heparin administration for anticoagulation, either for prophylactic or for therapeutic indications. Occasionally, this could be associated with damage of the abdominal pannus microvasculature, which could possibly jeopardize the reliability of free abdominal flaps as deep inferior epigastric perforator and muscle sparing transverse rectus abdominis muscle, especially with therapeutic anticoagulation therapy. These flaps are reliant on a highly intricate complex vascular anatomy and perforasomes for their adequate perfusion and survival. The authors report a case of nonobstructive microvascular failure of a free muscle sparing transverse rectus abdominis muscle utilized for soft tissue coverage following resection of a chest wall breast cancer recurrence on a background of portacath-induced deep venous thrombosis of the axillary and subclavian vein whilst on chemotherapy. History of long-term therapeutic low molecular weight heparin administration in the abdomen resulted in microangiopathic densities evident on computerized tomography scan with subsequent flap failure due to possible jeopardization of the flap microvasculature and perfusion. Following exclusion of common local and systemic factors that can cause vascular compromise, a debridement and salvage re-reconstruction procedure utilizing a contralateral free latissimus dorsi flap was performed. Reconstructive surgeons should be cautious when planning to utilize free abdominal-based flaps on the background of long-term therapeutic low molecular weight heparin administration in the abdomen and may possibly explore other alternative options of using non-abdominal free flaps from the reconstructive armamentarium within this unique context. *(Plast Reconstr Surg Glob Open 2021;9:e3400; doi: 10.1097/GOX.0000000000003400; Published online 17 February 2021.)*

INTRODUCTION

Muscle-sparing transverse rectus abdominis musculocutaneous (MSTRAM) and deep inferior epigastric artery perforator (DIEP) free flaps have become the gold standard for autologous breast reconstruction.[1,2] Given their

well-known superiority, they also have an important role in chest wall reconstructions by virtue of their size, reliability, and anatomy, with the ability to resurface substantial wound defects.[3,4] Notably, vascular anatomy and perforasomes ex vivo and in vivo studies demonstrated a complex spatial model of perforator anatomy that highlighted the highly intricate vasculature that these flaps are reliant on for adequate perfusion and survival.[5–7]

Despite the delicate intra-flap vasculature, these flaps also exhibit a significant degree of resilience to previous trauma, including multiple liposuction procedures[8,9] and long-term abdominal subcutaneous low molecular weight heparin (LMWH) injections.[10,11]

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CASE REPORT

We report a case of a failed MSTRAM flap in a 49-year-old woman, a nonsmoker, who had undergone a chest wall resection and reconstruction after developing a second local recurrence of triple negative breast cancer. Preoperative CT angiography (CTA) demonstrated patent perforators of good caliber, length, and perfusion. Following her first chest wall recurrence, she developed portacath-induced DVT of the axillary and subclavian vein whilst on chemotherapy. This was managed with self-administered subcutaneous injection of 1.5 mg/kg LMWH once daily, in the lower abdomen for 6 months before being replaced with oral anticoagulation. After multidisciplinary team en bloc right chest wall resection, skeletal reconstruction was performed with soft tissue coverage achieved using a fascial-sparing free MSTRAM flap (Fig. 1). Postoperatively, she was commenced on 75 mg daily aspirin and a prophylactic dose of LMWH (40 mg daily). In the immediate postoperative period, the flap demonstrated good vascularity with strong Doppler signals detectable at the sites of the cutaneous perforators, and a good capillary refill, temperature, and color, indicating adequate perfusion, particularly in zones I and II. However, within 72 hours, the flap developed progressive ecchymosis and swelling followed by fixed violaceous staining and epidermolysis (Fig. 2). Despite these changes, the Doppler signals of the cutaneous perforators remained normal. Re-exploration of the flap revealed intact anastomoses confirmed by the Acland test and an intraoperative Doppler, which demonstrated an audible venous hum and a triphasic arterial flow signal. (**See Video [online],** which demonstrates the management of 49-year-old woman who had undergone a left chest wall resection and reconstruction after developing a second local recurrence of triple negative breast cancer. Nonobstructive failure of the free MSTRAM was attributed to the previous history of administration of LMWH in her lower abdomen for management of DVT. Note the intact microvascular anastomoses confirmed by an intraoperative Doppler, which demonstrated an audible venous hum and a triphasic arterial flow signal on re-exploration of the flap.)

Following debridement, re-reconstruction with a contralateral free LD flap and split thickness skin graft was successfully performed using the same ipsilateral recipient internal mammary pedicle for microvascular anastomosis, reaffirming the patency of the recipient vessels (Fig. 3). Respectively, the patient showed an uneventful recovery and healed without complications. As part of the assessment to determine the cause of flap failure, all her previous CT staging scans performed during her previous treatments were reviewed. Surprisingly, they revealed numerous areas of densities in her lower abdomen 3 months after the discontinuation of LMWH therapy, which were believed to be caused by the chronic local inflammation resulting from the LMWH injections, leading to subcutaneous fibrosis and calcification (Fig. 4). Of note, these densities appeared to have resolved by the time she had had her CTA before management of her second recurrence.

Fig. 1. Intraoperative photograph showing the skeletal reconstruction with cement mesh and titanium bar of right chest wall defect post en bloc resection, including partial sternectomy and 4 ribs with the simultaneous harvesting of free MSTRAM based on the left inferior epigastric pedicle before transfer to the chest. Venous anastomosis was performed using a 3-mm coupler, and arterial anastomosis was performed using 9/0 nylon hand-sewing technique. The total ischemia time was 77 minutes, and there was a good intraoperative Doppler signal at the sites of the anastomoses. Note the hyperemic changes in zone 4, but normal skin perfusion in zones 1 and 2.

Fig. 2. Intraoperative photograph of the flap 72 hours post primary surgery, revealing swollen, ecchymotic congested flap with fixed violaceous staining and epidermolysis.

DISCUSSION

In essence, this case report does not demonstrate direct causality between long-term LMWH therapy and free flap failure, although several key findings would support this as a potential hypothesis. Firstly, despite progressive flap failure, both arterial and vascular anastomoses remained demonstrably patent, and the cutaneous perforators showed intact perfusion on Doppler in an otherwise hemodynamically stable patient. There was no evidence of pedicle thrombosis, vasospasm, or external compression. Other systemic potential causes were discounted, including vascular disease, diabetes or coagulopathy, or local causes as in previous abdominal surgical procedures. The recipient vessels were qualitatively good, as confirmed by the successful revisional microvascular reconstruction with free LD

Fig. 3. Postoperative photograph after 1 year showing complete healing of the re-reconstruction with a contralateral free LD flap and split thickness skin graft. The revisional microvascular anastomosis was successfully performed using the same ipsilateral recipient internal mammary pedicle for reaffirming the patency of the recipient vessels. Of note, the ipsilateral LD flap was previously utilized for her right breast reconstruction, which was subsequently resected as part of the en bloc resection when she experienced her first recurrence.

Fig. 4. A CT scan image taken 18 months before the patient's surgery for the second left chest wall recurrence, revealing numerous areas of densities in her lower abdomen 3 months after the discontinuation LMWH therapy, caused by the chronic local inflammation resulting from the LMWH injections, leading to subcutaneous fibrosis and calcification.

flap using these same recipient vessels. This would suggest that the causes of the MSTRAM flap failure were merely intrinsic due to the affection of its microvasculature.

LMWH administration induced abdominal cutaneous and subcutaneous microvasculature damage with scarring; fibrosis and even necrosis (skin and fat) have been previously reported.[10,12] This microangiopathy has been attributed to several pathological mechanisms, including immunological, hemotoxic, and mechanical factors.[10,12–15] On the other hand, successful outcomes have been reported in patients planned for DIEP breast flap and who had abdominal wall LMWH administration up to 24–32 hours preoperatively.[10,11] Duncumb et al reported 3 cases of LMWH-induced subcutaneous densities in the anterior abdominal wall before DIEP flap following management of DVT during chemotherapy. Despite that all their flaps survived, there was no indication on the long-term effects of the quality of breast reconstruction.[10] Interestingly, in our case, these densities were still evident several months after discontinuation of the LMWH therapy on follow-up CT staging, although they have been resolved by 18 months on CTA. These microangiopathic densities can damage the subdermal plexus which the flap would be dependent on, therefore affecting its viability. Potentially, this could reasonably explain the total flap failure in our case, with over 160 injections. Although there are currently no formal guidelines on the administration site for LMWH subcutaneous injections before free flap harvest, the anterior abdominal wall remains the site of choice. Alternatively, other sites considered are the upper thigh and arms, and although at prophylactic doses there is no difference in bruising or Activated Prothrombin Time (APTT) when used in comparison with the lower abdomen, it would be preferably avoided at therapeutic doses due to an increase in incidence of complications and inconvenience.[16–18]

To the best of the authors' knowledge, this case report is the first to demonstrate the fact that therapeutic LMWH-therapy-induced microangiopathy can potentially have an impact on the reliability of flap perfusion. Reconstructive surgeons should be cautious when planning to utilize free abdominal-based flaps on the background of long-term therapeutic LMWH administration in the abdomen. Accordingly, they may possibly explore other alternative options (such as non-abdominal free flaps) to be used from the reconstructive armamentarium, within this unique context.

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