Free flap failure associated with heparin-induced thrombocytopenia: Is it preventable?

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Heparin-induced thrombocytopenia (HIT) is a serious adverse effect of unfractionated heparin, particularly in the setting of microsurgery, with a reported salvage rate of <25% of free flaps. HIT presenting as venous thromboembolisms (VTEs) can be a more challenging problem to the reconstructive surgeon. The hematology literature reports a prevalence of HIT as high as 12% among patients presenting with VTEs. Complications associated with HIT are preventable if a high index of suspicion is maintained and proper treatment is implemented. A 68-year-old man with VTEs who failed a parascapular fasciocutaneous flap to the forearm secondary to undiagnosed HIT is reported. The authors propose an algorithm to approach such a dilemma and implement adequate treatment measures before commencing any microsurgical procedures in patients to minimize any untoward consequences.

Key Words: Flap failure; Heparin-induced thrombocytopenia; Microsurgery; Pulmonary embolism; Venous thromboembolism

Heparin is commonly used as a method of anticoagulation in surgical patients due to its shorter half-life and the ease of reversal. Patients exposed to heparin can develop heparin-induced thrombocytopenia (HIT). HIT type II (immune-mediated) is a serious hematological sequela, occurring in 0.5% to 5% of patients treated with heparin (1). A devastating complication of HIT in microsurgery is flap failure. HIT-related flap failures have recently been reported in the microsurgical literature, with a salvage rate <25% (2).

We report a patient with venous thromboembolisms (VTEs) whose free flap reconstruction failed due to an undiagnosed HIT. A review of the relationship between VTEs and HIT in the hematology literature is summarized. An algorithm to manage patients with VTEs who are considered for microsurgery is proposed.

CASE PRESENTATION

A 68-year-old man with a history of alcoholism presented to the emergency department following a 7% total body surface area circumferential flame burn of his left forearm and hand. He was admitted for escharotomy, fasciectomy, burn wound care and medical optimization before definitive surgical debridement. Surgery was delayed six days to allow for treatment of newly diagnosed upper gastrointestinal bleeding, acute renal failure and congestive heart failure. Following debridement of the burn, a free tissue transfer was needed to cover exposed tendons, median nerve and radial artery. This urgent procedure was delayed three days due to respiratory failure secondary to bilateral segmental pulmonary embolisms (PEs) and bilateral above-knee deep venous thromboses (DVTs). A multidisciplinary team comprising personnel from hematology, internal medicine and anesthesia assessed and treated these complications. Of note, the patient was kept on prophylactic heparin from admission up until the diagnosis of PEs/DVTs, except for few days when he experienced an episode of upper gastrointestinal bleed. The patient was given therapeutic heparin after diagnosis of PEs/DVTs. Heparin was held the night before surgery.

To cover the upper extremity defect, a fasciocutaneous flap was harvested. Therapeutic intraintravenous heparin was resumed intraoperatively as soon as the donor site was closed. The parascapular fasciocutaneous flap was used to cover the exposed flexor tendons and median nerve as well as hooked to the proximal radial artery outside the zone of injury. Approximately 12 h postoperatively, the distal two-thirds of the flap (the area where the flap was most needed to cover exposed vital structures) was mottled despite good capillary refill proximally and a triphasic Doppler signal. Postoperative laboratory results showed normal blood counts including platelets and coagulation profile. Re-exploration was performed immediately, revealing patent arterial and venous anastomoses. The flap was flushed with heparinized saline and tissue plasminogen activator. Resistance and suboptimal venous outflow were then noted. The pedicle was believed to be at risk for kinking and was, therefore, shortened. After this revision, clinical improvement of the flap was noted. However, over the next few days, a complete flap loss had ensued. Hematological workup confirmed HIT with positive heparin antibodies. HIT type II was, therefore, the most likely cause of flap loss as well as of PEs. The patient’s heparin was discontinued and anagrotaban was started. The patient refused any further reconstructive attempts and later required a below-elbow amputation.

DISCUSSION

HIT is an adverse effect of both prophylactic and therapeutic heparin use (1). HIT type II has an incidence of 0.5% to 5% and is associated with significant arterial and venous thromboses; it usually occurs five to 14 days after the exposure to heparin or earlier in a patient with previous exposure to heparin (1). Risk factors include unfractionated heparin, surgical patients, severe trauma and female sex (3).

The diagnosis of HIT is based on the clinical picture: thrombocytopenia or evidence of thrombosis in a patient treated with heparin for at ≥5 days (1). Thrombocytopenia is considered to be the main diagnostic criterion for HIT, occurring in 85% to 90% of patients (4). HIT should be suspected following a decrease of ≥50% in the peak platelet count in the 14 days following the use of heparin, or in patients without thrombocytopenia who present with thrombosis while on heparin. HIT can also be investigated with laboratory testing such as the serotonin-release assay or the heparin-PF4 antibody testing (1). Susppected patients should undergo serological testing with HIT antibodies (1).

In recent years, studies have shown that patients with normal or even high platelet counts may also develop HIT (1,5). Among patients with flap failure secondary to HIT, thrombocytopenia was the presenting feature of HIT in ~50% (Table 1) (2,6-8). This raises a significant concern regarding the applicability of the 4T scoring system (a pretest probability assessment of HIT) in our patient population, because three of four criteria are related to thrombocytopenia. Patients who manifest their HIT with thrombosis would only be labelled as low probability for HIT according to the 4T score.

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Several reports of failed flap reconstruction attributed to HIT exist in the literature (Table 1) (2,6-8). In cases reported by Schleich et al (7) and Tremblay et al (6), the venous thrombotic events occurred intraoperatively and postoperatively. Our patient, however, had a different presentation, with VTEs as the only manifestation occurring before reconstructive surgery (no thrombocytopenia). It is likely that HIT was present before the microsurgical intervention and was probably the cause of VTEs and flap failure. The flap could likely have been salvaged with treatment of HIT before surgery, as suggested in a case report by Schleich et al (7).

Another possible cause of our patient’s flap failure is the presence of an acute burn injury. Flap failure rates are reported to be as high as 11% to 15% in burn patients (9). However, this patient neither manifested an arterial or venous thrombosis of the flap nor was his burn sufficiently large to stimulate a systemic response. Therefore, in the present case, HIT was most likely the cause of the PEs and flap failure.

The literature reports a 75% incidence of VTEs in patients diagnosed with HIT (10). The prevalence of HIT among patients with VTEs (DVT, PE) is reported to be as high as 12.5% (10). Such an overlooked prevalence of HIT among documented VTEs calls for a prudent approach when planning a microsurgical intervention in patients with documented VTEs, particularly those with strong risk factors (trauma, previous surgery, female sex). We propose an algorithm (Figure 1) outlining the approach for the management of VTEs in patients being considered for microsurgical reconstruction.

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**TABLE 1**

**Summary of studies reporting flap failure caused by heparin-induced thrombocytopenia (HIT)**

| Author (ref) | n | Flap used            | Flap outcome | Type of flap compromise                   | Precipitating factors                        | Initial manifestation of HIT                     |
|-------------|---|----------------------|--------------|------------------------------------------|----------------------------------------------|--------------------------------------------------|
| Busch et al (12), 2009 | 1 | Free ALT             | Failed       | Arterial insufficiency                   | Cancer                                       | Flap compromise                                  |
|             | 1 | Free LD × 2          | Failed × 2   | Arterial insufficiency                   | Trauma, previous heparin exposure            | Flap compromise                                  |
| Schleich et al (7), 2008 | 1 | Free LD              | Salvaged     | Arterial and venous insufficiency        | Cancer; intraoperative heparinization         | Flap compromise; thrombocytopenia                 |
| Tremblay et al (6), 2008 | 1 | Pedicled TRAM        | Failed       | Venous insufficiency distal portion (TRAM zone II) | Cancer; postoperative prophylactic heparin | Flap compromise (delayed-onset thrombocytopenia and DVTs postoperative day 12) |
|             | 1 | RFFF                 | Partial flap loss | Venous insufficiency | Cancer; postoperative prophylactic heparin | Flap compromise (delayed-onset thrombocytopenia and DVTs postoperative day 11) |
| McCleave (14), 2010 | 1 | Free rectus          | Failed       | Arterial and venous insufficiency        | Trauma; prophylactic LMWH                    | Flap compromise; thrombocytopenia                 |
| Medina et al (13), 2010 | 1 | Pedicled soleus      | Failed       | Venous insufficiency                    | Trauma; prophylactic LMWH                    | Flap compromise                                  |
|             | 1 | Free gracilis        | Failed       | Venous insufficiency                    | Trauma; previous prophylactic LMWH, intra- and postoperative full heparinization (UFH) | Flap compromise (delayed-onset thrombocytopenia and DVTs postoperative day 7) |
| Cross-leg   |   |                      | Successful   | None                                     | Diagnosed and treated HIT proper to third flap | None                                             |
| Tessler et al (11), 2014 | 1 | Free ALT             | Failed       | Arterial and venous insufficiency        | Trauma                                       | Flap compromise                                  |
|             | 1 | RFFF                 | Failed       | Arterial and venous insufficiency        | Trauma, previous heparin exposure            | Flap compromise                                  |
| Total       | 6 | 12 flaps             | 9 total loss; 1 partial loss; 2 salvaged | Arterial 7 of 12 (58%); Venous 8 of 12 (67%) | Thrombocytopenia 2 of 12 (17%); late-onset thrombocytopenia 3 of 12 (25%) | Flap compromise                                  |
|             | (8 patients) | (3 pedicles; 9 free) |                                          |                                           |                                                 |

ALT Anterolateral thigh; DVT Deep vein thrombosis; LD Latissimus dorsi; LMWH Low molecular weight heparin; RFFF Radial forearm free-flap; ref Reference; TRAM Transverse rectus abdominis myocutaneous; UFH Unfractionated heparin

**Figure 1** Algorithm for management of venous thromboembolisms in patients undergoing free tissue transfer. HIT Heparin-induced thrombocytopenia
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