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CASE REPORT
Reconstructive

Reducing Wound Hemorrhage: Use of Bilayer Collagen Matrix in Chronic Myelogenous Leukemia

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Summary: Donor site preparation is a critical step before the application of an autologous split-thickness skin graft (STSG). Comorbidities can lead to complications and graft loss, including that due to hematoma. In this case, a bilayer collagen matrix was used as a temporary wound dressing in a 25-year-old woman with active chronic myelogenous leukemia. She presented with a bleeding diathesis and spontaneous intramuscular and intracompartmental hematomas of the right leg. She experienced ongoing high-volume blood loss from her fasciotomy wounds, requiring wound care to be performed in the operating room under general anesthesia, and requiring multiple blood and platelet transfusions. Instead of immediate STSG, a bilayer collagen matrix was placed to reduce the bleeding and further prepare the wound bed over a 9-week period while she underwent medical optimization. Once stabilized from a hematologic standpoint, STSG was performed with total graft take. Both uncontrolled chronic myelogenous leukemia and its therapy, tyrosine kinase inhibitors, have a risk of hemorrhagic and thrombotic complications. Bilayer collagen matrix serves as an adjunct in the limb salvage algorithm that can reduce transfusion needs whereas a temporary bleeding diathesis is medically corrected before the application of an autologous skin graft. *(Plast Reconstr Surg Glob Open 2019;7:e2532; doi: 10.1097/GOX.0000000000002532; Published online 27 November 2019.)*

Autologous split-thickness skin graft (STSG) is a commonly used modality in the reconstructive algorithm. However, concomitant medical conditions can increase the risk of complications and autograft loss, including loss due to hematoma. Chronic myelogenous leukemia (CML) is a rare hematologic malignancy affecting 1 in 100,000 individuals annually. The characteristic transposition between chromosomes 9 and 22 creates the *BCR-ABL* gene, a tyrosine kinase. CML is associated with spontaneous hemorrhage due to platelet dysfunction. During the rapid generation of malignant cells, bone marrow enters blast crisis, with resultant giant platelets, vitamin K deficiency, and thrombocytosis. However, platelets are abnormal in morphology, membrane function, and the metabolism of arachidonic acid. In many cases, CML can be successfully treated with tyrosine kinase inhibitors (TKIs), which can halt blast crisis and reverse the platelet dysfunction. In these cases, temporization of the wound with an artificial skin substitute can improve the ultimate success of skin grafting. Here, we present a case in which a bilayer collagen matrix was used as an intermediate wound dressing in the algorithm of limb salvage.

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CASE

A 25-year-old woman with active CML and no history of trauma presented with spontaneous intramuscular and intracompartmental hematomas of the right leg, causing acute compartment syndrome. Her most recent CML treatment was with imatinib 400 mg twice daily started 2 months before her admission; however, she had been noncompliant with the regimen, taking the medication intermittently. On presentation, her white blood cell (WBC) count was 341,000/mL (normal 3,400–10,800/mL), hemoglobin was 5.8 mg/dL (normal 11.1–15.9 g/dL), and platelet count was 140,000/mL (normal 150,000–379,000/mL). Despite this thrombocytopenia, she had a left popliteal deep vein thrombosis. She was taken urgently to the operating room for evacuation of the hematomas and 4-compartment fasciotomies. Intraoperatively, she experienced significant enough hemorrhage that through-knee amputation was considered; ultimately, the bleeding was controlled to the point where she could be transferred to a tertiary care center.

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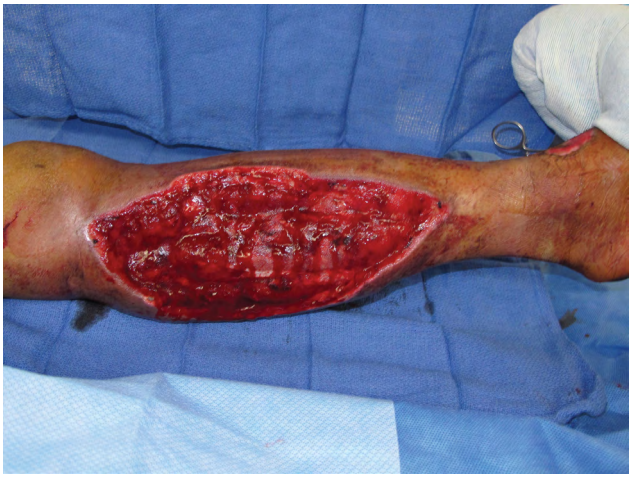

Fig. 1. Before application of bilayer collagen matrix, the fasciotomy wounds experienced frequent and persistent hemorrhage.

Serial wound debridements were performed, then transitioned to wet-to-dry dressing changes on a petroleum gauze base as the fasciotomy wounds stabilized. She experienced persistent high-volume blood loss during each dressing change, which required the care to be performed in the operating room under general anesthesia every other day (Fig. 1). Her limb appeared salvageable.

Once the wound was free of necrotic tissue, autologous skin grafting was planned; however, she was deemed high risk for donor and recipient site bleeding with the resultant potential for graft loss. After considering alternative reconstructive options, Integra bilayer dermal matrix (Integra Lifesciences, Plainsboro, NJ) was placed (Fig. 2). The dermal matrix promoted further wound bed preparation with minimal trauma and bleeding, which allowed wound care to be performed at bedside for an extended time period of hematologic optimization. Over a 9-week period, her bleeding diathesis was corrected by initiating bosutinib and managing her thrombocytopenia with

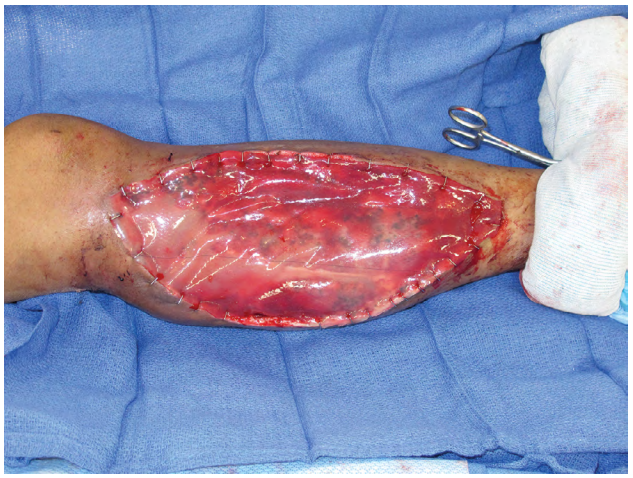

Fig. 2. Bilayer collagen matrix was placed so dressings could safely be changed at bedside while the bleeding diathesis was corrected medically.

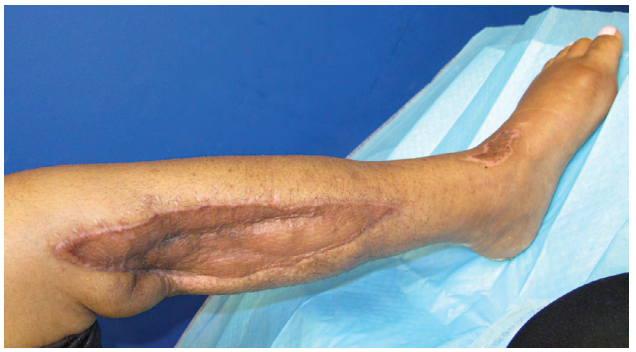

Fig. 3. STSG was completed 2 months after the placement of bilayer collagen matrix.

hydroxyurea. Her nutrition was improved with high-protein supplements, a multivitamin, zinc, and additional vitamins A and C. Once she was cleared from a hematologic standpoint (WBC 6,300/mL, platelets 310,000/mL), STSG was performed with total graft take. Two weeks postoperatively, she was discharged home. At her 3-month follow-up, her wound coverage was stably healed (Figs. 3 and 4) and she was ambulatory with a 4-point cane.

DISCUSSION

Poorly controlled CML is associated with both bleeding and thrombotic complications.[1] Bleeding commonly has cutaneous and mucosal manifestations ranging from petechiae to bruising to hemorrhage.[2] Platelet function and response are abnormal due to altered platelet morphology, membrane abnormalities, and reduced response to epinephrine.[2] After initiation of TKI therapy, thrombohemorrhagic complications are less common and are typically limited to patients in accelerated phase or blast crisis. Moderate chronic CML is associated with a 20% incidence of spontaneous hemorrhage, whereas patients in accelerated phase or blast crisis have nearly triple the risk.[1]

Although disease control lowers the risk of bleeding, TKI therapy itself is associated with the risk of hemorrhage and may increase the risk of arterial and venous thrombotic events. TKI therapy is associated with thrombocytopenia, platelet dysfunction, and platelet membrane defects.[3–5] Coagulopathy can be compounded by nutritional deficiencies. Vitamin K is essential for the carboxylation of coagulation factors, facilitating subsequent activation and clotting functionality. As such, nutritional status should be carefully evaluated in patients with spontaneous hemorrhage. To our knowledge, acute compartment syndrome secondary to spontaneous intra- and intermuscular hematoma has not been described with either CML in blast phase or with TKI therapy.

In general, limb salvage offers better functional outcomes, improved cost-effectiveness, and decreased mortality compared to amputation for traumatic or chronic conditions.[6,7] Limb salvage techniques range from simple to complex. In patients unsuitable for immediate reconstruction due to medical comorbidities, use of a bilayer dermal matrix can bridge wound healing until comorbidities

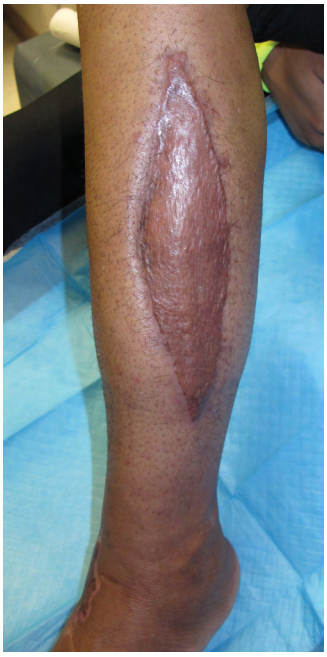

Fig. 4. The wounds demonstrated total graft take, which was stable at the 3-month follow-up.

are better controlled and STSG is appropriate. With cross-linked collagen and glycosaminoglycans, the matrix serves as a scaffold for dermal regeneration. It facilitates recruitment of macrophages, fibroblasts, and lymphocytes that aid in reepithelialization and angiogenesis, with graft evolution often mimicking the natural stages of wound healing.[7,8] The use of bilayer collagen matrix is well accepted in the algorithm of lower extremity reconstruction, notably in cases of exposed bone, nerve, or tendon.[8–10] This is the first report of using a bilayer collagen matrix as a temporary dressing during the correction of bleeding diathesis.

In the current case, a bilayer collagen matrix was used to allow time for improved medical control of CML, with fewer return trips to the operating room, less pain, and higher patient satisfaction as compared to conventional wound dressings. It allowed for vastly reduced blood loss and, therefore, a much lower chance of alloantibody formation from transfusions, which is a constant concern with hematologic oncology patients. The product cost was easily offset by the savings in operating room time, ongoing blood and platelet transfusions, and the lifetime morbidity and psychological cost of an above-knee amputation in a 25-year-old woman.

CONCLUSIONS

Use of a bilayer collagen matrix is well-accepted in cases of bone, tendon, or nerve exposure. Added to these indications should be that of a temporary bleeding diathesis with the potential for medical correction before application of an autologous skin graft.

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This case report represents clinical care provided to an individual patient and conforms to the standards of the Declaration of Helsinki.

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