Management of massive soft tissue defects: The use of INTEGRA® artificial skin after necrotizing soft tissue infection of the chest

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ABSTRACT Necrotizing soft tissue infection, such as necrotizing fasciitis, is a group of highly lethal infections especially when the chest is involved due to increased risk of pulmonary complications. Because aggressive radical debridement of all poorly perfused tissue is required, patients frequently suffer from massive skin defects, which often requires autograft skin grafting or myocutaneous flaps. However, options are limited in patients with limited autograft donor availability, or questionable underlying wound bed viability, such as in scleroderma. Here, we report the case of a 49 year old female with scleroderma who suffered from a necrotizing soft tissue infection of the chest extending to her right upper arm, underwent multiple radical debridements, and reconstruction of the consequent massive chest wall defect with INTEGRA® bilaminar dermal regeneration template. This approach required a thinner skin graft without flaps, allowed for the inherently diseased donor site to heal adequately, and avoided major infections and wound complications. This report highlights an important management option for this challenging disease.

KEY WORDS Chest necrotizing fasciitis; Integra

J Thorac Dis 2012;4(3):331-335. DOI: 10.3978/j.issn.2072-1439.2012.05.12

Introduction

Necrotizing soft tissue infection (NSTI), such as necrotizing faciitis, is a rapidly progressive and potentially fatal soft tissue infection that requires prompt, radical, and often multiple surgical debridements of all necrotic and poorly perfused tissue (1,2). The mortality rate is high especially when the chest is involved because such patients are at even greater risk for pulmonary complications (2-4). Progressive skin necrosis may occur from polymicrobial symbiosis and synergy, infectious spread or hypotension, which require the patient to undergo further debridements as often as necessary, which often result in massive soft tissue defects (2-4).

Traditionally, reconstruction has been performed with skin grafts and flaps, as in burn reconstruction (2). For large defects of the chest, because chest wall muscles are often sacrificed during debridement with difficult wounds to cover, well vascularized tissue flaps have been traditionally advocated (5,6). In cases of massive soft tissue defects, autograft reconstruction may be limited by donor-site availability or questionable underlying wound bed viability, and may require artificial alternatives such as INTEGRA® or Alloderm® (2,7,8). INTEGRA® Dermal Regeneration Template artificial skin is a bilayered membrane consisting of an inner dermal substitute and an outer silicone epidermal layer (7). This product allows for immediate tissue coverage to reduce fluid, protein, and electrolyte loss, protection from microbial invasion, less painful wound care, and an ultrathin autograft harvest with decreased donor-site healing times and decreased hypertrophic scarring (7). Here, we report a case of a patient with a large chest soft tissue defect after multiple debridements for NSTI with reconstruction options limited by a history of scleroderma, who underwent successful reconstruction with INTEGRA®.

Case report

A 49-year-old female with a history of scleroderma and hypertension presented to an outside institution with one week history of worsening swelling, tenderness, and induration of her right anterior chest, extending to her right upper arm. The patient had noticed two "small bumps" one week earlier which she thought was attributable to insect bites. She denied any recent

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Submitted Apr 28, 2012. Accepted for publication May 19, 2012.
Available at www.jthoracdis.com

ISSN: 2072-1439

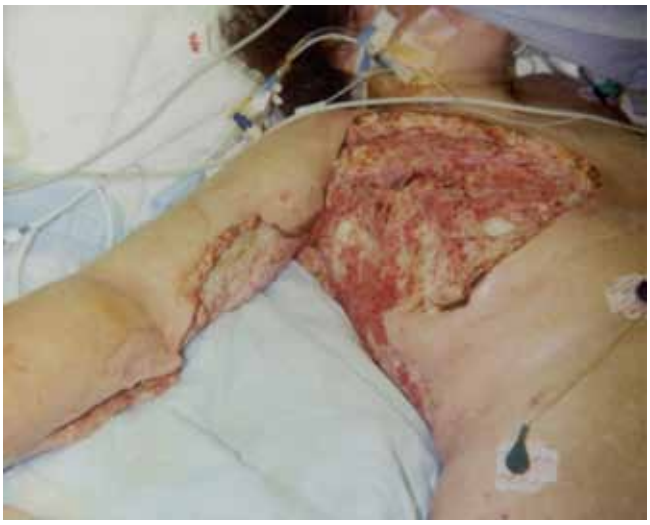

Figure 1. A large skin and soft tissue defect involving her right axilla, anterior and lateral chest was noted after aggressive debridements for necrotizing soft tissue infection.

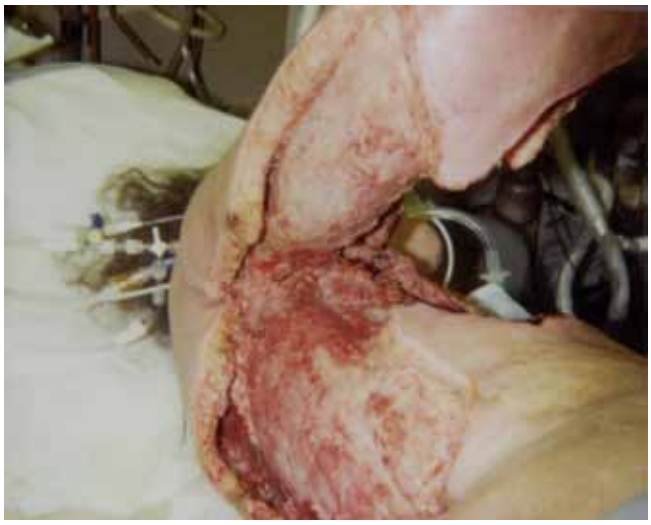

Figure 2. The skin and soft tissue defect after debridements extended to posterior of the chest as well.

trauma, fever or chills. On presentation at the outside institution, she was afebrile and subsequently developed hypotension. Physical examination was consistent with cellulitis of the right anterior chest inferior to the breast. Laboratory findings were significant for leukocytosis of 60,700 with 93 segments, an elevated CPK of 416 and creatinine of 3.5. The patient was admitted to ICU, but her cellulitis progressively worsened despite aggressive antimicrobial treatment with Penicillin, Oxycillin, and Gentamycin. Therefore, extensive debridement was performed on the following day. Operative findings were consistent with necrotizing soft tissue infection (NSTI). Cultures from her blood and wound demonstrated Methicillin Sensitive Staphylococcus Aureus (MSSA). No anaerobes or other organisms were present. Antimicrobial coverage was deescalated to Cefazolin on day 4, and the patient was then transferred to University of California San Diego Medical Center for further wound management.

On admission, the patient was intubated for pneumonia, but afebrile with a leukocytosis of 15,300 with 76 segments, no bands. A large skin and soft tissue defect around her right axilla extending both to anterior of the chest including right medial upper arm (Figure 1), and to posterior of the chest (Figure 2) were noted. The underlying muscle and remaining chest wall were clean with granulation tissue. Initially she was treated with Penicillin G and Clindamycin (9), but then transitioned to Cefazolin due to leukocytosis increased to 37,600 with 64 segments and 22 bands on day 7 from her presentation.

She underwent multiple extensive debridements of the infected tissue of the chest, torso, and right upper arm under general anesthesia on days 7, 13, and 18, eventually losing 15% of her total body surface area, approximately 1,800 cm^2 of her skin. Allograft was applied to the debrided areas and Sulfamylon solution was applied topically. She was successfully extubated on day 15, pseudomonas bacteremia and candida urinary tract infections resolved, and her WBC returned to 10,100. Therefore, the care was transferred to UCSD Regional Burn Center for reconstruction of the skin defect. Due to the massive skin defect extending to her back (Figure 2), myocutaenous flaps using latissimus dorsi muscle were deemed impossible to cover all the defects. Furthermore, given her scleroderma, the donor skin needed to be as thin as possible to secure adequate donor site healing. Therefore, the decision was made to utilize INTEGRA® Dermal Regeneration Template to cover the exposed tissue to reduce fluid, protein, and electrolyte loss, minimize microbial invasion, and allow ultrathin autograft harvest by generation of a neodermis prior to skin graft.

The patient was taken to the operating room for debridement and placement of INTEGRA® on day 25 (Figure 3). INTEGRA® was meshed 1:1 prior to placement, and the wound was dressed with half-strength Sulfamylon solution applied dressing, which remained intact without purulent drainage for a 10-day period. On day 38, a small amount of exudate was removed from the right axilla, which was positive for MSSA. Bactrim was initiated and small pieces of INTEGRA® were removed. The remaining INTEGRA® in the right upper arm, torso, and chest remained intact with good wound bed formation. The outer layer of INTEGRA® was removed on day 46 when good neodermis formation was confirmed (Figure 4). Split-thickness skin graft, meshed at 1:1.5, was performed by harvesting several pieces of autograft set at 0.009 inches with the Zimmer dermatome from her bilateral anterior thighs, with Betaglucan dressing applied to the donor site (Figure 5). Her postoperative course was free from any complication at both her donor and grafted sites, and she was discharged on day

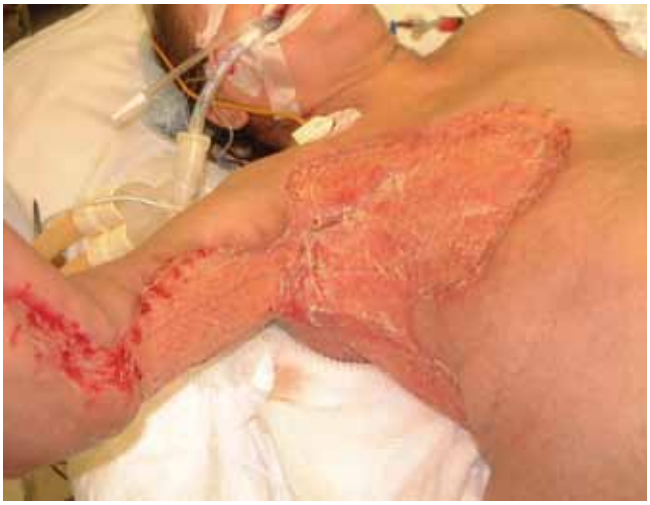

Figure 3. INTEGRA® was placed on Day 25 after meshed 1:1. The wound was dressed with half-strength Sulfamylon solution applied dressing.

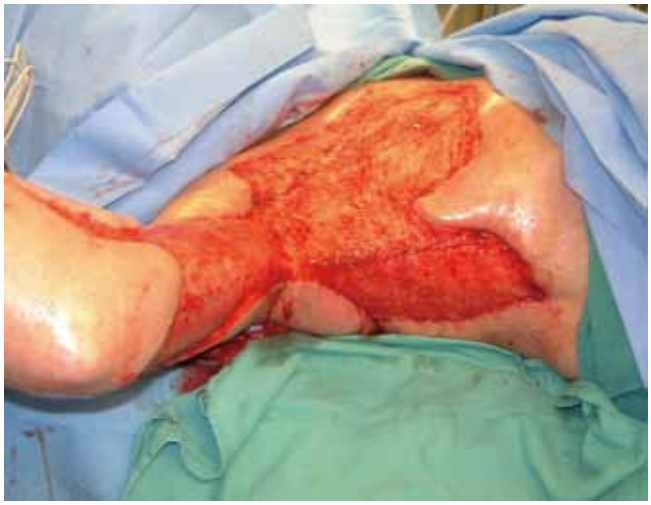

Figure 4. Good "neodermis" formation was confirmed on Day 46 when the outer layer of INTEGRA® was removed.

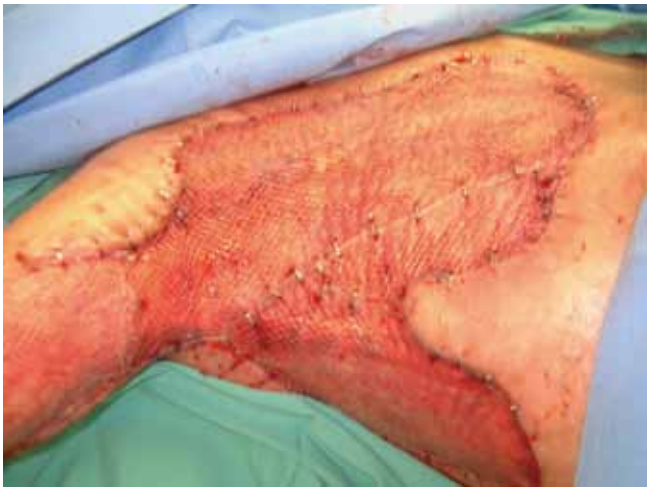

Figure 5. Split-thickness skin graft, set at 0.009 inches and meshed at 1:1.5, was performed.

56. Both the grafts and the bilateral anterior thigh donor sites healed very well, requiring only moisturizer on discharge.

Discussion

Necrotizing soft tissue infection (NSTI) is a critically serious infection of the subcutaneous tissue and fascia which requires timely diagnosis and aggressive, wide, radical debridements of all necrotic and poorly perfused tissue to optimize outcomes (2,10-12). The mortality approaches 70% in reported series, and management is especially challenging when the chest is involved, where mortality is often greater than 89% (2-4,13,14). Hemodynamic instability usually persists postoperatively, and progressive skin necrosis may occur from infectious spread, hypotension, and massive fluid and protein losses. Affected patients must return for further debridements as often as necessary, further exacerbating tissue loss often with wound complications, prolonged sepsis, and poor nutrition (1,2,11-15). There is evidence that aggressive, early surgical debridement in combination with appropriate antimicrobial therapy, resuscitation, nutritional support, and improved critical and wound care limit the extent of soft tissue loss (2,16,17). However, even in such optimal circumstances, soft tissue defects are often massive and pose a challenge to clinicians (2). Once all diseased tissue has been debrided and the patient has been stabilized, soft tissue reconstruction can be considered. Traditionally, reconstruction has been performed with skin grafts and myocutaneous flaps when primary closure is not possible, as in burn reconstruction. In cases with excessively large amounts of soft tissue involvement (>25% Body Surface Area), autograft reconstruction may be restricted by limited donor-site availability or questionable underlying wound bed viability, such as a history of scleroderma in our patient (2).

Scleroderma is a connective tissue disease whose principal features include extensive fibrosis, vascular alterations, and autoantibodies against self-antigens which affect wound healing (18). The progression of the disease is from early microvascular damage, mononuclear-cell infiltrates, and slowly developing fibrosis to densely packed collagen in the dermis, cell loss and atrophy (18). Despite the progressive loss of blood vessels and high serum levels of vascular endothelial growth factor and other angiogenic factors, there is a defect in vasculogenesis (18-21). There is a gradual replacement of the blood vessels and normal architecture with fibrosis and a mixture of collagens, proteoglycans and elastic fibers (18). In addition, fibroblasts which coordinate collagen and extracellular matrix component production, deposition,

and remodeling overexpress cytokines and reactive oxygen species which further the progression of fibrosis and alteration of normal wound healing (18). The process of fibrosis and impaired vasculogenesis are further promoted by autoantibodies which inhibit factors that would otherwise promote normal wound healing and angiogenesis, such as PDGF (18). Because of these features of scleroderma, the challenge of skin defect reconstruction in our patient was that the donor sites of any autograft thick enough to fill the defect, as well as the recipient site itself, would be at high risk of wound complications. To utilize thinner pieces of autograft, a means to develop dermal regeneration was required. Since the skin defect was massive and the wound was not actively infected, we chose to apply INTEGRA® to fill the defect for the following reasons.

INTEGRA® is a bilayered membrane system, consisting of an inner dermal substitute layer and a temporary outer epidermal substance layer. The inner layer is composed of a 3-demensional matrix of cross-linked bovine tendon collagen plus a glycosaminoglycan, and an outer layer is composed of silicone. After application of INTEGRA® the patient's native fibroblasts, macrophages, and lymphocytes infiltrate, and new capillary growth occur into the matrix of the inner layer. The inner layer becomes degraded, and an endogenous collagen matrix is deposited by the patient's own fibroblasts, forming a "neodermis". This process can take place without creating any new wounds in the patient because no donor sites are created. Once engraftment is complete, which usually occurs approximately 2 weeks after application, the outer silicone layer needs to be removed, and an epidermal autograft must placed over the "neodermis".

The advantages of this product are the following: (I) immediate tissue coverage to reduce fluid, protein, and electrolyte loss from the grafted surfaces; (II) protection of the wound from microorganism invasion; (III) less painful wound care after grafting; (IV) thinner autografts with decreased donor-site healing time; and (V) less hypertrophic scarring (22). With these advantages, it was initially developed for treating large burn wounds (22). A contraindication to the use of INTEGRA® is that if there is an active secondary wound infection, "neodermis" will not form. In such circumstances allografts are desirable (23), which would have been the case for our patient if her wound had not stabilized. Because infection was a concern prior to applying INTEGRA® and to avoid infection of the INTEGRA®, we meshed it 1:1 prior to placement. In our anecdotal experience, infection decreased from 55% to 15% with mesh. We have also tried "Pie-crusting" the INTEGRA®, which did not decrease the infection rate. The result was that our patient successfully underwent neodermis formation requiring a thin skin graft just for epidermal coverage without any donor wound site complications.

In summary, NSTI of the chest wall poses a formidable challenge to clinicians, not only in the appropriate early diagnosis and aggressive management of the disease, but also reconstruction of the soft tissue defect after appropriate management of the initial insult. INTEGRA® artificial skin offered the advantages of neodermis formation without the risks of thick autograft harvesting in a patient with a massive defect without major complications, despite a patient history of scleroderma. Therefore, our case highlights an important clinical option to consider for patients with massive chest wall soft tissue defects in whom full thickness skin grafts and myocutaenous flaps would be high risk.

Acknowledgements

Kazuaki Takabe is supported by United States National Institute of Health (R01CA160688, K12HD055881, R01CA154314, and R01DK057543) and Susan G. Komen for the Cure (Investigator Initiated Research Grant (222224) and Career Catalyst Research Grant KG090510). Masayuki Nagahashi is a Japan Society for the Promotion of Science (JSPS) Postdoctoral Fellow for Research Abroad.

Disclosure: The authors declare no conflict of interest.

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Cite this article as: Rashid OM, Nagahashi M, Takabe K. Management of massive soft tissue defects: The use of INTEGRA® artificial skin after necrotizing soft tissue infection of the chest. J Thorac Dis 2012;4(3):331-335. DOI: 10.3978/j.issn.2072-1439.2012.05.12