Necrotizing Soft Tissue Infection or Sweet Syndrome: Surgery Versus No Surgery?: A Case Report

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The authors report a case of necrotizing Sweet syndrome in a 24-year-old transsexual male who presented with recurrent myonecrosis of the neck/upper chest. On index admission, computer tomography revealed gas and fat stranding of the sternocleidomastoid and pectoralis major muscle— ndings suggestive of a necrotizing soft tissue infection. Despite debridement procedures and intravenous antibiotic therapy, myonecrosis of the affected areas persisted. Evaluation of tissue samples by dermatopathology revealed neutrophilic in ltration extending into the dermis and muscle necrosis, ndings consistent with necrotizing Sweet syndrome. The initiation of IV corticosteroids, the gold-standard treatment for necrotizing Sweet syndrome, lead to signi cant clinical improvement. When soft tissue infections do not respond to debridement and broad-spectrum antimicrobial coverage, perioperative care providers should consider necrotizing Sweet syndrome as an underlying cause. By facilitating the early diagnosis and appropriate management of unique conditions such as necrotizing Sweet syndrome, anesthesiologists can not only play a more visible role as leaders in the emerging perioperative surgical home model, but they may also prevent signi cant patient morbidity and reduce unnecessary utilization of health care resources. (A&A Case Reports. 2017;8:182–5.)

Sweet syndrome, also known as acute febrile neutrophilic dermatosis (AFND), is clinically characterized by acute-onset fever with painful, demarcated erythematous nodules, and described on pathology as a dense neutrophilic in ltrate of the dermis. [1,2] Sweet syndrome with necrosis of muscle and/or adipose tissue is rare, but it has been recently reported as a subtype of Sweet syndrome known as necrotizing Sweet syndrome.[1] The standard features of AFND with necrosis of deep soft tissues can effectively mimic a necrotizing soft tissue infection (NSTI). Although surgical debridement is the rst-line treatment in the latter, [3] this therapeutic intervention is essentially contraindicated in the former, because the condition of the patient would worsen rather than improve. [1]

The primary goal of this case report is to raise awareness of necrotizing Sweet syndrome so that perioperative specialists, such as anesthesiologists and intensivists, can lead providers toward the most appropriate therapeutic regimen. The early recognition of necrotizing Sweet syndrome is essential in decreasing morbidity by circumventing unnecessary and potentially harmful surgical interventions, as is early dermatologic consultation.[1] Necrotizing Sweet syndrome should be strongly considered in all patients suspected of NSTI with a recalcitrant course, as well as in those who remain tissue and/or body uid culture negative.

Consent

Written consent was obtained from the patient to publish this report.

CASE PRESENTATION

Our patient was a 24-year-old transsexual, female-to-male, with a medical history of testosterone-induced cystic acne and Hashimoto thyroiditis who initially presented to a community hospital with a 2-day history of increased submental swelling and pain. On admission, broad-spectrum antibiotic therapy was initiated, which consisted of vancomycin, piperacillin/tazobactam, and clindamycin. Given the high suspicion of NSTI, the Otolaryngology-Head and Neck Surgery service was consulted and the patient underwent therapeutic incision and drainage procedures of the affect area. Following these therapeutic interventions, the patient initially demonstrated symptomatic improvements over the course of his 9-day hospitalization. He was then discharged home to complete an antibiotic course of intravenous (IV) piperacillin/tazobactam (× 7 days) followed by oral amoxicillin/clavulanate (× 14 days), as well as oral doxycycline (× 21 days). Despite this broad antimicrobial coverage, on the ninth postdischarge day, the patient was rehospitalized for suspected recurrent NSTI.

On readmission, the patient presented with fever, rigors, signi cant pain of the neck, and a monomorphous pustular rash of the upper back and shoulders. Computed tomography imaging demonstrated soft tissue in ammation as well as gas in the sternocleidomastoid muscle and fat stranding of the pectoralis major muscle; all ndings consistent with NSTI (Figure 1). Surgical exploration revealed extensive necrosis of the sternocleidomastoid fascia and surrounding tissue. No compelling causative organisms were identi ed on Gram stain, wound culture, acid-fast

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smear, or mycobacterial culture from tissue samples and blood cultures obtained from the procedure; only very rare Candida albicans were isolated from a specimen from the upper right chest. However, in light of the strong clinical suspicion for NSTI based on computed tomography imaging and observed ndings during the operation, the patient was switched to IV daptomycin, meropenem, clindamycin, and uconazole for broad-spectrum antimicrobial coverage.

Persistently negative tissue as well as body uid cultures and the atypical rash present on his second admission prompted dermatologic consultation to rule out pyoderma gangrenosum. Pathology samples taken from previous debridement surgeries demonstrated subcutaneous, skeletal muscle as well as fat necrosis, with extensive neutrophilic in ammation and abscess formation—results more consistent with Sweet syndrome (Figure 2). These ndings were sent to the dermatopathology consultant service; however, after a discussion with the primary surgical team and all other consulting services, the possibility of an infectious etiology (eg, nosocomial Gram-negative infection) was thought to outweigh the likelihood of Sweet syndrome, especially given the uncharacteristic rapid progression of skin and muscle necrosis. Moreover, an underlying infection could not be ruled out, considering the administration of extensive antimicrobials before our patient's second admission. The patient was therefore scheduled to complete his 4-week IV therapeutic regimen of daptomycin, meropenem, and uconazole at the time of discharge with visiting nurse assistance.

Despite extensive treatment with broad-spectrum IV antimicrobials, the patient returned yet again with recurrent erythema, pain, and muscle necrosis of the neck as well as upper chest. The resurgent symptoms led to the patient's third admission. During this hospitalization, necrotic tissue was debrided and again evaluated for a causative organism. Gram stain and tissue cultures remained negative, which prompted for reconsideration of a noninfectious cause for this patient's condition. Taking into account the previous tissue samples that demonstrated extensive neutrophilic ltration and myonecrosis, and symptoms that were refractory to both surgical intervention and extensive antimicrobial coverage, necrotizing Sweet syndrome, a rare subtype of AFND, was deemed the most likely etiology for this patient's overall clinical picture. As such, IV corticosteroid (2 mg/kg methylprednisolone) therapy was initiated, which provided decreased pain and erythema of the affected area within hours of the rst dose. After his third hospitalization, the patient was discharged home on a 2-week oral prednisone taper with visiting nurse services to assist with wound care.

Unfortunately, 14 days after discharge, the patient began to re-experience signi cant erythema and pain of the neck, upper chest, and right shoulder while on 50 mg of prednisone, which led to his fourth hospitalization. During this

Figure 1. Axial and coronal CT imaging of the neck with IV contrast. Axial and coronal views revealed small foci of air anterior to the right sternocleidomastoid muscle (A) and extensive subcutaneous fat stranding from the right mandible interiorly to the mid thorax (B).

Figure 2. Histological images of the deep neutrophilic in ammation involving subcutaneous tissue (A) and extension into skeletal muscle (B).

admission, the patient underwent additional incision and drainage procedures, and IV corticosteroid therapy (2 mg/kg methylprednisolone) was reinitiated. Because Sweet syndrome remained the leading diagnosis, it was recommended by dermatology to minimize trauma (ie, surgical debridements) because of the risk of pathergy associated with necrotizing AFND. [1]

Given the strong association between AFND and solid-organ tumors/hematologic cancers, our patient underwent a positron emission tomography scan, soft tissue excisional biopsies of the right neck, and diagnostic serum protein electrophoresis to rule out any underlying malignancy; the results of which were all unremarkable. The patient was eventually discharged to home 3 weeks after his fourth hospitalization on a 6-week prednisone taper, colchicine (1.5 mg/day), and cyclosporine (3 mg/kg/day). Although systemic corticosteroids are the gold-standard therapy for Sweet syndrome, colchicine and cyclosporine were used as adjuvant therapy[2,4] to decrease pathergy of the surgical sites.[1,2]

DIFFERENTIAL DIAGNOSIS

NSTI, cellulitis, pyoderma gangrenosum, pityrosporum folliculitis

OUTCOME AND FOLLOW UP

One month following his fourth hospitalization, the patient continued to improve clinically without further incident of the affected areas.

DISCUSSION

Sweet syndrome, first described in the 1960s,[5] is a dermatologic condition that has been linked to a variety of disease states. As reported through hundreds of case reports and case series, the evidence related to Sweet syndrome is vast and has been outlined in a comprehensive review by Cohen and Kurzrock. [2] The major classifications of Sweet syndrome are idiopathic (classic), malignancy associated, and drug induced. Idiopathic Sweet is more common in women, typically manifests before an upper respiratory tract infection, and is associated with underlying inflammatory bowel disease, autoimmune disorders, recent vaccination, and pregnancy.[2] The malignancy subtype is found in approximately 20% of patients with Sweet syndrome, where symptomatology has been reported before an oncologic diagnosis or during cancer resurgence.[2] Acute myelogenous leukemia is the most common cancer associated with Sweet syndrome, but solid tumors of the breast, genitourinary tract, and gastrointestinal tract have also been reported with AFND. [2] Finally, drug-induced AFND has been reported after the initiation of a variety of medications, the most common being colony-stimulating factors (eg, granulocyte-colony stimulating factor)[1] and antibiotics (eg, trimethoprim–sulfamethoxazole). [2]

However, a subtype of AFND with evidence of fat and muscle necrosis, as seen in our patient, was only recently identified in a 3-patient case series by Kroshinsky et al.[1] Risk factors for Sweet syndrome in these patients were hematologic malignancy and the administration of granulocyte colony-stimulating factor. [1] Despite these reported risk factors for Sweet syndrome, 2 of the 3 patients were first treated for an NSTI with surgical debridement, and all 3 were treated with IV antibiotics despite repeated negative tissue cultures as well as Gram staining.[1] The third patient in the series received no surgical intervention because of the early diagnosis of necrotizing Sweet syndrome by dermatology/dermatopathology consultants. [1]

Minimizing surgical intervention in individuals with Sweet syndrome is imperative, given its association with pathergy.[1] Pathergy is a nonspecific inflammatory response to intradermal trauma, characterized by deep perivascular mixed inflammatory cell infiltrate with neutrophils on histopathology.[1] Even minor trauma can elucidate this reaction; thus, avoiding surgical procedures is vital in preventing further inflammatory damage. Much like our patient, all 3 patients in the case series by Kroshinsky et al[1] had culture-negative samples, continued to deteriorate clinically while on antimicrobials alone, and clinically improved after the initiation of systemic corticosteroids. [2]

Unlike the patients presented in the previously mentioned case series,[1] our patient did not have an underlying malignancy. However, our patient did possess clinically relevant features that have been reported to induce AFND. Specifically, our patient had a history of Hashimoto thyroiditis, an autoimmune disorder that has been independently associated with classic Sweet syndrome.[6,7] A causative link between these 2 conditions remains to be determined.[6,7] However, both conditions appearing in the same individual are theorized to result from a hypersensitivity reaction to an eliciting antigen, where the possible antigenic trigger is diverse (eg, bacterial, viral, or tumor antigen). [6,7] Moreover, our patient's testosterone-induced cystic acne was being

treated with minocycline, a medication that has been attributed to the development of drug-induced Sweet syndrome. [2]

Androgen-induced acne is a common side effect of testosterone treatment.[8,9] A 2-patient case series by Turrion-Merino et al[9] was among the first to report that transsexual men may require continuous oral isotretinoin (30 mg per day) after developing severe inflammatory acne with scarring secondary to therapeutic androgen therapy. The clinical side effects of testosterone treatment were also reported by Wierckx et al[8] in a cohort of 50 transsexual men. On prospective analysis, testosterone-induced facial acne was present in more than 82% of patients after 6 months of continuous androgen therapy.[8] Because of the high prevalence of severe acne after testosterone therapy, hypervigilant dermatologic care at the initiation of androgen treatment is paramount. Sexual minorities, particularly individuals with gender identity disorders, have unique needs, of which care providers should be aware.[9] Furthermore, despite increased recognition of gender identity disorder over the past decade, there remains a paucity of literature that investigates the serious dermatologic issues related to androgen therapy in transsexual men.[10]

Awareness and early detection of necrotizing Sweet syndrome, an uncommon but clinically significant syndrome, are important, as repeated surgical intervention may trigger an exacerbation of the inflammatory process and ultimately lead to additional resections and increased morbidity. [1] Care providers should be aware of the major associations and clinical hallmarks exhibited by Sweet syndrome, such as painful erythematous skin lesions, fever, and diffuse neutrophilic infiltrate of the dermis on histology. Although the necrotizing subtype of AFND is particularly rare, this inflammatory condition should be considered in the differential diagnosis of NSTIs, a common and emergent surgical problem, given the similarities found on imaging and presentation. Diagnosis of necrotizing Sweet syndrome typically requires close communication among perioperative physicians (ie, anesthesiologists, intensivists, and surgeons), as well as consultation by dermatology and/or dermatopathology. Moreover, as anesthesiologists work to define their position in the emerging perioperative home model, the ability to recognize and facilitate appropriate management of unique care situations (such as necrotizing Sweet syndrome) during preoperative consultation may help to establish a greater leadership role.

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REFERENCES

1. Kroshinsky D, Alloo A, Rothschild B, et al. Necrotizing Sweet syndrome: a new variant of neutrophilic dermatosis mimicking necrotizing fasciitis. J Am Acad Dermatol. 2012;67:945–954.
2. Cohen PR, Kurzrock R. Sweet's syndrome revisited: a review of disease concepts. Int J Dermatol. 2003;42:761–778.
3. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis. 2014;59:147–159.
4. Maillard H, Leclech C, Peria P, Avenel-Audran M, Verret JL. Colchicine for Sweet's syndrome. A study of 20 cases. Br J Dermatol. 1999;140:565–566.
5. Sweet RD. An acute febrile neutrophilic dermatosis. Br J Dermatol. 1964;76:349–356.
6. Francisco CR, Patal PC, Cubillan EA, Isip-Tan IT. Sweet's syndrome associated with Hashimoto's thyroiditis. BMJ Case Rep. 2011. doi: 10.1136/bcr.02.2011.3921.
7. Medeiros S, Santos R, Carneiro V, Estrela F. Sweet syndrome associated with Hashimoto thyroiditis. Dermatol Online J. 2008;14:10.
8. Wierckx K, Van de Peer F, Verhaeghe E, et al. Short- and long-term clinical skin effects of testosterone treatment in trans men. J Sex Med. 2014;11:222–229.
9. Turrion-Merino L, Urech-Garcia-de-la-Vega M, Miguel-Gomez L, Harto-Castano A, Jaen-Olasolo P. Severe acne in female-to-male transgender patients. JAMA Dermatology. 2015;151:1260–1261.
10. Katz KA, Furnish TJ. Dermatology-related epidemiologic and clinical concerns of men who have sex with men, women who have sex with women, and transgender individuals. Arch Dermatol. 2005;141:1303–1310.