Published in final edited form as:

A A Case Rep. 2017 April 01; 8(7): 182–185. doi:10.1213/XAA.0000000000000459.

Necrotizing Soft Tissue Infection or Sweet's Syndrome: Surgery vs No Surgery?

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Abstract

We report a case of Necrotizing Sweet's syndrome in a 24-year-old transsexual male who presented with recurrent myonecrosis of the neck/upper chest. Upon index admission, computer tomography revealed gas and fat stranding of the sternocleidomastoid and pectoralis major muscle -- findings 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 infiltration extending into the dermis and muscle necrosis, findings consistent with Necrotizing Sweet's syndrome. The initiation of IV corticosteroids, the gold standard treatment for Necrotizing Sweet's syndrome, lead to significant clinical improvement. When soft tissue infections do not respond to debridement and broad-spectrum antimicrobial coverage, perioperative care providers should consider Necrotizing Sweet's syndrome as an underlying cause. By facilitating the early diagnosis and appropriate management of unique conditions such as Necrotizing Sweet's syndrome anesthesiologists can not only play a

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Conflict of Interest: Sadeq A. Quraishi has received consulting fees from Lungpacer, Inc., Trevena, Inc., and Abbott Laboratories. In addition to this, Dr. Quraishi serves as an uncompensated Board member for both the Vitamin D Council and the C. Diff Foundation

Author Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Author Contributions: TMNO and SAQ contributed to the concept and design of the manuscript; TMNO, DDY, SRB and SAQ contributed to the acquisition and interpretation of the data; TMNO, SRB and SAQ drafted the manuscript; TMNO, SRB, DDY and SAQ revised the manuscript. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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

more visible role as leaders in the emerging Perioperative Surgical Home model, but also may prevent significant patient morbidity and reduce unnecessary utilization of healthcare resources.

Introduction

Sweet's 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 infiltrate of the dermis.^{1,2} Sweet's syndrome with necrosis of muscle and/or adipose tissue is rare, but has been recently reported as a sub-type of Sweet's syndrome known as Necrotizing Sweet's 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 first line treatment in the latter, this therapeutic intervention is essentially contraindicated in the former, as the patient's condition would worsen rather than improve.¹

The primary goal of this case report is to raise awareness of Necrotizing Sweet's syndrome so that perioperative specialists, such as anesthesiologists and intensivists can lead providers towards the most appropriate therapeutic regimen. The early recognition of Necrotizing Sweet's syndrome is essential in decreasing morbidity by circumventing unnecessary and potentially harmful surgical interventions, as is early dermatologic consultation.¹ Necrotizing Sweet's 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 fluid culture negative.

Case Presentation

Our patient was a 24 year-old transsexual, female-to-male, with a past medical history of testosterone-induced cystic acne and Hashimoto's thyroiditis who initially presented to a community hospital with a two-day history of increased sub-mental 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 9th post-discharge day, the patient was re-hospitalized for suspected recurrent NSTI.

On re-admission, the patient presented with fever, rigors, significant pain of the neck, as well as a monomorphous pustular rash of the upper back and shoulders. Computed tomography (CT) imaging demonstrated soft-tissue inflammation as well as gas in the sternocleidomastoid muscle and fat stranding of the pectoralis major muscle; all findings consistent with NSTI (Figure 1). Surgical exploration revealed extensive necrosis of the sternocleidomastoid fascia and surrounding tissue. No compelling causative organisms were

identified on Gram's stain, wound culture, acid-fast 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 CT imaging and observed findings during the operation, the patient was switched to IV daptomycin, meropenem, clindamycin, and fluconazole for broad-spectrum antimicrobial coverage.

Persistently negative tissue as well as body fluid 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 inflammation and abscess formation - results more consistent with Sweet's syndrome (Figure 2). These findings 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 (e.g. nosocomial gram-negative infection) was thought to outweigh the likelihood of Sweet's 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 prior to our patient's second admission. The patient was therefore scheduled to complete his four-week IV therapeutic regimen of daptomycin, meropenem, and fluconazole 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's stain and tissue cultures remained negative, which prompted reconsideration of a non-infectious cause for this patient's condition. Taking into account previous tissue samples that demonstrated extensive neutrophilic infiltration and myonecrosis, and symptoms that were refractory to both surgical intervention and extensive antimicrobial coverage, Necrotizing Sweet's Syndrome, a rare subtype of AFND, was deemed the most likely etiology for this patient's overall clinical picture. As such, IV corticosteroid (2mg/kg methylprednisolone) therapy was initiated, which provided decreased pain and erythema of the affected area within hours of the first 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 significant erythema and pain of the neck, upper chest and right shoulder while on 50mg of prednisone, which led to his fourth hospitalization. During this admission, the patient underwent additional incision and drainage procedures, and IV corticosteroid therapy (2mg/kg methylprednisolone) was re-initiated. Since Sweet's syndrome remained the leading diagnosis, it was recommended by Dermatology to minimize trauma (i.e. 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 Position Emission Tomography (PET) scan, soft tissue excisional

biopsies of the right neck, and diagnostic serum protein electrophoresis (SPEP) to rule out any underlying malignancy; the results of which were all unremarkable. The patient was eventually discharged to home three weeks after his fourth hospitalization on a 6-week prednisone taper, colchicine (1.5mg per day), and cyclosporine (3mg/kg per day). Although systemic corticosteroids are the gold standard therapy for Sweet's syndrome, colchicine and cyclosporine were used as adjuvant therapy,^{2,4} to decrease pathergy of the surgical sites.^{1,2}

Differential Diagnosis

Necrotizing soft tissue infection, 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's syndrome, first described in the 1960's⁵ is a dermatologic condition that has been linked to a variety of disease states. Reported through hundreds of case reports and case series, the evidence related to Sweet's syndrome is vast, and has been outlined in a comprehensive review by Cohen in 2003.² The major classifications of Sweet's syndrome are: idiopathic (classic), malignancy-associated and drug-induced. Idiopathic Sweet's is more common in women, typically manifests prior to 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 percent of patients with Sweet's syndrome, where symptomatology has been reported prior to an oncologic diagnosis, or during cancer resurgence.² Acute myelogenous leukemia is the most common cancer associated with Sweet's 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 (e.g. granulocyte-colony stimulating factor)¹ and antibiotics (e.g. 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 three-patient case series by Kroshinsky, et al.¹ Risk factors for Sweet's syndrome in these patients were hematologic malignancy and the administration of granulocyte colony-stimulating factor.¹ Despite these reported risk factors for Sweet's syndrome, two of the three patients were first treated for an NSTI with surgical debridement, and all three were treated with IV antibiotics despite repeat negative tissue cultures as well as Gram's staining.¹ The third patient in the series received no surgical intervention because of early diagnosis of Necrotizing Sweet's syndrome by Dermatology/Dermatopathology consultants.¹

Minimizing surgical intervention in individuals with Sweet's syndrome is imperative, given its association with pathergy.¹ Pathergy is a non-specific 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 three patients in the case series by Kroshinsky, et al. 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's thyroiditis, an autoimmune disorder that has been independently associated with classic Sweet's syndrome.^{6,7} A causative link between these two 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 (e.g. 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's syndrome.²

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

Awareness and early detection of Necrotizing Sweet's syndrome, an uncommon but clinically significant syndrome, is important since 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's syndrome, such as painful erythematous skin lesions, fever, and diffuse neutrophilic infiltrate of the dermis on histology. Though 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's syndrome typically requires close communication between perioperative physicians (i.e. 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's syndrome) during pre-operative consultation may help to establish a greater leadership role.

Acknowledgments

We thank Dr. Ivan A. Chebib for insightful discussions and for providing histological images for the manuscript.

Funding Disclosure: Tiffany M.N. Otero received support from the National Center for Advancing Translational Sciences, National Institutes of Health, Award Number TL1TR001062. D. Dante Yeh received support from the Nestle Foundation, Award Number 226280.

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Figure 1.

Axial and Coronal CT imaging of the neck with IV contrast: (A) 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. Histologic images of the deep neutrophilic inflammation involving subcutaneous tissue (A) and extension into skeletal muscle (B).