EJCRIM
European Journal
of Case Reports
in Internal Medicine

SWEET SYNDROME PRESENTING WITH FEATURES OF CELLULITIS SHORTLY AFTER FEMORAL ANGIOPLASTY

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Received: 13/06/2024
Accepted: 26/08/2024
Published: 24/09/2024

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Informed consent was obtained for the purpose of this report. Prior to engaging in any data collection or analysis, a comprehensive and transparent discussion was conducted with the individual involved, ensuring their complete understanding of the nature, objectives and potential implications of the report.

How to cite this article: Wang Q, Sinclair J, Amaravadi A, Arioride O. Sweet syndrome presenting with features of cellulitis shortly after femoral angioplasty. *EJCRIM* 2024;**11**:doi:10.12890/2024_004670

ABSTRACT

Neutrophilic dermatosis, or Sweet syndrome, is a cutaneous disorder caused by neutrophilic infiltration in the upper dermis. It has been associated with medications, infections and malignancies but to date it has not been associated with femoral arterial angioplasty or stenting. We present the case of a 75-year-old female who, after angioplasty and stent placement of the right superficial femoral artery, developed right heel pain with ulceration that did not respond to broad antibiotics. She underwent incision and drainage twice without improvement; both times produced negative cultures. She then underwent a punch biopsy by dermatology, which was consistent with acute spongiotic and other neutrophilic dermatoses. She was started on prednisone with immediate improvement of her symptoms. She was discharged to a rehabilitation centre with a prednisone taper and antibiotics. This report highlights the importance of maintaining Sweet syndrome on the differential for cellulitis as it is a rare mimicry of other infectious and non-infectious aetiologies, which are common in the perioperative space. Early treatment is crucial to improve symptoms, outcomes, healthcare cost and potentially the length of stay.

KEYWORDS

Sweet syndrome, neutrophilic dermatosis, angioplasty, autoinflammation

LEARNING POINTS

- Sweet syndrome, a rare skin condition related to neutrophil infiltration, may be triggered by angioplasty.
- Sweet syndrome is easily misdiagnosed as infectious conditions such as cellulitis.

INTRODUCTION

Neutrophilic dermatosis, or Sweet syndrome, classically presents as a tender papule, plaque and/or nodules with systemic fever and neutrophilia[1]. It was first described by Dr Robert Douglas Sweet in 1964[2]. It has been associated with a wide range of medications and malignancies including solid tumours and haematologic malignancies[3]. There have also been sporadic cases of tattoo-associated Sweet syndrome reported[4,5]. However, to date no association has been found between femoral arterial angioplasty and Sweet syndrome.

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CASE DESCRIPTION

A 75-year-old female had a past medical history of right superior femoral artery stenosis, coronary artery disease status post percutaneous intervention on aspirin and clopidogrel. She presented to the emergency department for pain of the right lower leg, worse on the right heel, that started one day after right superior femoral artery angioplasty with stenting.

On presentation, she was initially afebrile; blood pressure was 90/45. The physical examination was notable only for right heel erythema *(Fig. 1)* with tenderness on palpation. Laboratory tests revealed a white blood cell count of 12.1, and blood cultures were negative. A computed tomography scan of the heel showed no evidence of gas or abscess; magnetic resonance imaging (MRI) was obtained and showed no evidence of abscess or osteomyelitis. She was diagnosed with right heel cellulitis and reperfusion injury from her recent angioplasty and was started on broad-spectrum antibiotics. She received multiple doses of narcotic and non-narcotic pain medications without improvement of her pain. On hospital day 1 she developed several episodes of fever above 38°C. On hospital day 7 the lesion developed into a large pus-filled bulla *(Fig. 2)*. She was evaluated by vascular surgery and an incision and drainage was done, with negative cultures. She was eventually admitted to the intensive care unit (ICU) after several hypotensive episodes for closer observation. The patient had another incision and drainage on hospital day 12 for failure to improve despite broad antibiotics. After the wound was debrided, the ulcer worsened. Her white blood cell counts steadily increased despite the negative cultures.

Dermatology was consulted due to uncertainty of the diagnosis and biopsied the lesion, which showed epidermal hyperplasia, hyperkeratosis, spongiosis and multiple large intraepidermal vesicles filled with fluid, and a mild number of neutrophils. The dermis was compacted with sheets of neutrophils from superficial dermal to the deep edge of the biopsy that obscured the normal dermal structures. There was superficial dermal red blood cell extravasation, and prominent and reactive vascular endothelial multiple tissue levels were examined. No bacteria colonies or fungal organisms were seen. The findings are consistent with acute spongiotic and neutrophilic dermatosis *(Fig. 3)*.

The patient was started on prednisone 50 mg daily with immediate improvement of her symptoms. A repeated MRI showed posterior inferior calcaneus hyperintensity, which could be reactive or postsurgical changes. Early osteomyelitis could not be ruled out and antibiotics were continued. She was discharged to a rehabilitation centre on antibiotics and a prednisone taper, to follow up with dermatology and as an infectious disease outpatient.

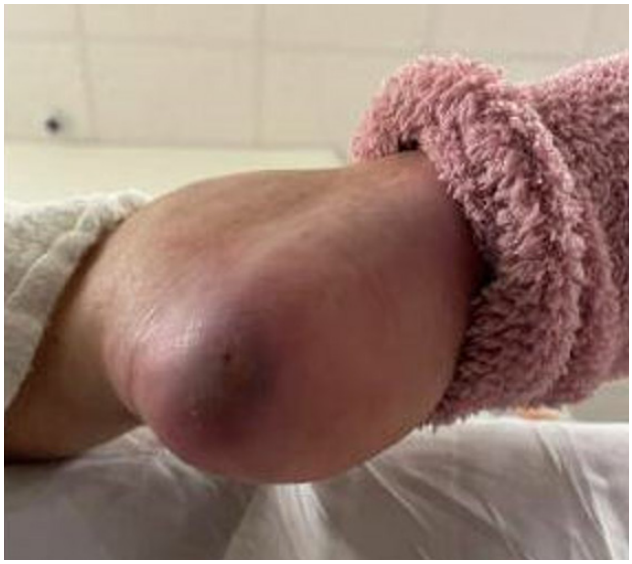

Figure 1. Right heel skin lesion on admission, without associated ulceration.

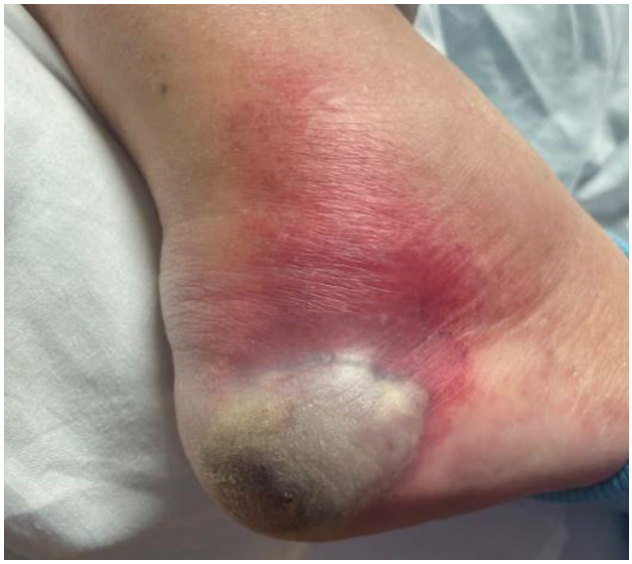

Figure 2. The lesion developed into a large bulla filled with pus.

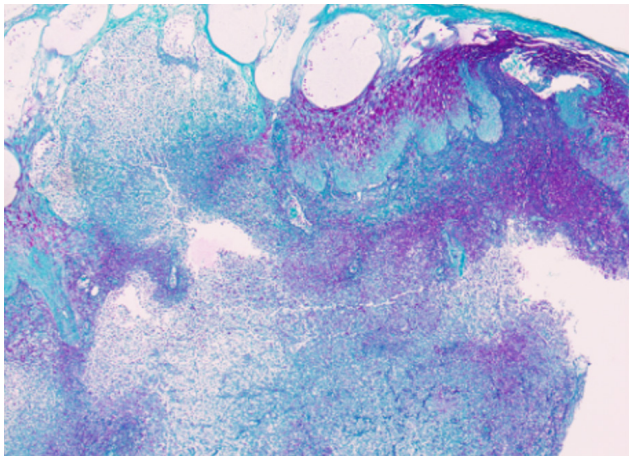

Figure 3. Diffusely intense dermal neutrophilic infiltrates.

DISCUSSION

The pathophysiology of Sweet syndrome is not yet fully established but it is believed to be multifactorial. One of the leading hypotheses is a trigger-induced hypersensitivity reaction, which could be bacterial, vital or tumour antigens[6]; circulating cytokines are also believed to play a role[6]. These triggers, infection, tumour antigens and exogenous therapies cause up-regulation of inflammatory cytokines including

granulocyte colony-stimulating factor (G-CSF), tumour necrosis factor α (TNF-α) and interleukin-1 (IL-1), all of which lead to neutrophilic maturation and proliferation. Dermal localisation results from activated lymphocyte endothelial adhesion and tissue extravasation due to increased lymphocytic cytokines[6]. Although this is the first report of angioplasty-associated Sweet syndrome, it is important to keep it on the differential in the perioperative phase given the high rates of cellulitis and its potential for mimicry. There have been sporadic cases of tattoo-associated Sweet syndrome which may share some pathways in common. Kluger et al. reported the first case of tattoo-associated Sweet syndrome[5]. They reported a patient who developed Sweet syndrome at the same location of a tattoo applied five days prior, which was confirmed by skin biopsy; the patient's symptoms responded well to steroids. It was believed that the Sweet syndrome was either related to or co-existed with the tattoo. One hypothesis is that the local inflammation caused by the tattoo attracted neutrophils activated by the cascade of Sweet syndrome to the tattoo region[5].

Angioplasty and stent placement are an invasive procedure, which we believe was an exogenic trigger by inducing endothelial injury. The calculated Naranjo score is 5, suggesting probable adverse reaction to angioplasty[7]. The local inflammation and cytokines activation this induced can attract neutrophils, which cause further damage of skin and soft tissue. Given the patient's lack of pain relief for two weeks despite broad-spectrum antibiotics, incision and drainage, opiate and non-opiate pain medications but significant improvement after prednisone suggests autoinflammation was the major cause of the pain and skin lesion.

Her repeated MRI showed possible early osteomyelitis, so she was continued with antibiotics for six weeks. We are unsure if the infection happened prior to, or after Sweet syndrome, if the infection has led to Sweet syndrome or vice versa. One hypothesis is, there was a cellulitis with reperfusion injury initially, which further dysregulated immune mediators and triggered Sweet syndrome, which then caused more skin and soft tissue necrosis and damage, and precipitated worsening of the infection. The incision and drainage procedures that the patient underwent also caused more neutrophil proliferation and worsened her symptoms. To break the loop, the steroids reduced the autoinflammation, which led to skin ulcer healing, which helped the antibiotics treating the infection.

While sharing a lot of features with infectious conditions, it is hard to recognise Sweet syndrome due to its rarity. It can mimic infectious conditions such as cellulitis. But when patients are not responding to treatment of cellulitis then we should be alerted to other potential diagnoses. Von den Driesch proposed the modified criteria of Sweet syndrome in 1994[8] and Nofal et al. proposed two sets of revised diagnostic criteria for Sweet syndrome in 2017 to simplify the diagnosis and avoid misdiagnosis[9] *(Table 1)*. The first set is constant features, which must be presented for a definite diagnosis, and the second set is variable features, which show the varying presentations of Sweet syndrome and can help avoid misdiagnosis[9]. Pyoderma gangrenosum is another differential diagnosis that could have a similar presentation to Sweet syndrome, and early biopsy would reveal the final diagnosis and guide treatment as early as possible.

Constant features
Clinical: Abrupt onset of painful or tender erythematous papules, plaques or nodules
Histopathological: Dense dermal neutrophilic infiltrate
Variable features
Clinical: 1. Fever >38°C 2. Atypical skin lesions (including haemorrhagic blisters, pustular lesions, cellulitis-like lesions)
Histopathological: 1. Presence or absence of leukocytoclastic vasculitis 2. Subcutaneous variant 3. Histiocytoid variant 4. Xanthomatous variant 5. Cryptococcosis variant
Laboratory: 1. Elevated ESR 2. Elevated C-reactive protein levels 3. Leukocytosis 4. Neutrophilia 5. Anaemia

Table 1. Revised diagnosis criteria by Nofal et al. 2017[8].

Regarding management, this patient responded well to steroids, which is believed to be the mainstay treatment of Sweet syndrome. Compared with malignancy-associated Sweet syndrome, non-malignant Sweet syndrome usually responds better with steroids[10]. Other treatments included immunomodulators and biologics[10].

In summary, Sweet syndrome is a rare autoinflammatory painful skin lesion with neutrophilic infiltrates. It can be induced by local skin inflammation after invasive procedures. It is something we should keep in mind as providers when patients are not responding to treatment for infectious conditions. Early biopsy is the key, and steroid is the mainstay of the management.

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