Sweet syndrome following routine orthopedic surgeries: A case series of 7 patients with surgical rechallenges

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INTRODUCTION

Sweet syndrome (SS), or acute febrile neutrophilic dermatosis, is characterized by the abrupt onset of edematous, erythematous to violaceous plaques, fever, leukocytosis, and dense neutrophilic infiltrate on histopathology. Patients experience rapid resolution of symptoms following initiation of systemic corticosteroids and have no evidence of causative infection.[1] SS additionally demonstrates pathergy, a nonspecific inflammatory response to skin trauma, including venipuncture and skin biopsy. These 7 cases highlight the importance of early recognition of SS in avoiding interventions that may lead to progression of disease, reducing unnecessary antibiotic use, and initiating effective treatment.

METHODS

A retrospective chart review of 7 patients who developed SS following an orthopedic surgery at a tertiary care medical center between January 1, 2014 and December 31, 2022 was conducted.

Abbreviations used:

IV: intravenous
SS: Sweet syndrome

CASE SERIES

Case 1

A 68-year-old woman presented 1 week after right total hip replacement with significant bloody drainage from the surgical site. She was admitted for incision and drainage of a suspected wound hematoma or necrotizing fasciitis. Empiric antibiotics were initiated, and wound culture was negative for microorganisms. Two days later, she underwent explantation.

Despite broad antibiotic coverage, edematous, violaceous plaques developed around the incision site (Fig 1), neutrophilic leukocytosis of 30 × 1000/mm^3, and daily fevers. Dermatology was consulted, and given concern for SS, punch biopsy was performed, demonstrating dense neutrophilic infiltrate with superficial edema (Fig 2). Pathergy at venipuncture sites was noted. The patient was treated with intravenous

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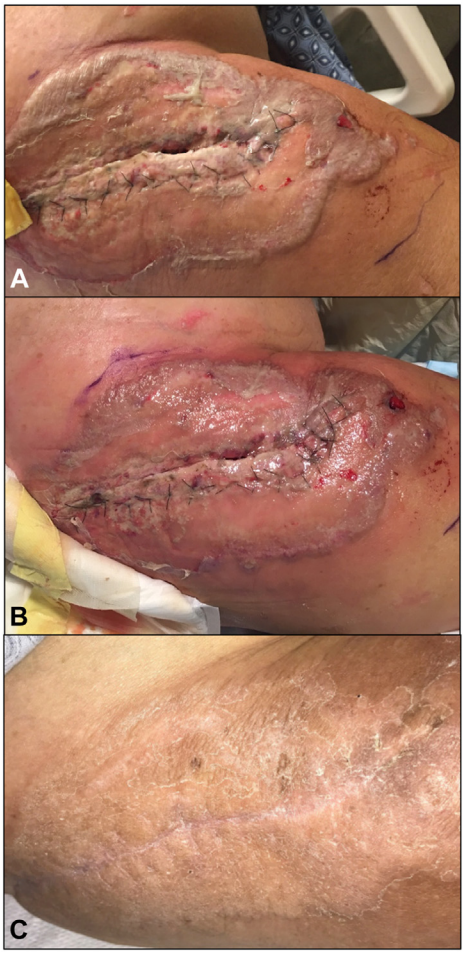

Fig 1. Case 1. **A,** Clinical image 1 week postoperatively of the right total arthroplasty incision site with violaceous edema and pseudobullous borders. **B,** Four hours after steroid administration. **C,** Well-healed surgical site after 1 month of dapsone 100 mg daily.

(IV) methylprednisolone 1 mg/kg daily, resulting in dramatic improvement of her skin, fevers, and leukocytosis. Workup for underlying hematologic malignancy and inflammatory bowel disease was negative.

One month later, her wound dehisced and required revision surgery. She was to start cyclosporine 3 mg/kg divided twice daily 3 days before surgery for prophylaxis but only took 2 doses preoperatively. She developed a flare of her SS 1 day postoperatively and was started on prednisone 0.5 mg/kg daily in conjunction with cyclosporine, leading to resolution of her clinical disease (Fig 1, *C*). Two weeks after discontinuation of cyclosporine and prednisone taper, her surgical wound became more erythematous and edematous. Dapsone 100 mg was added, resulting in resolution of disease.

Two years later, she was started on cyclosporine 150 mg twice daily and IV methylprednisolone 48 mg

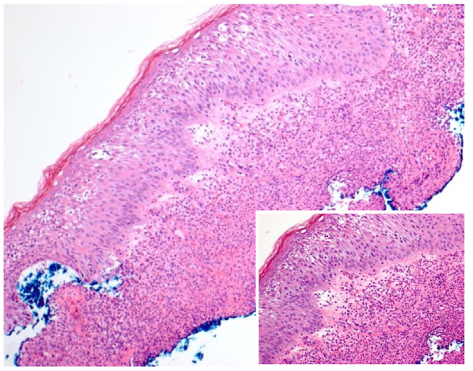

Fig 2. Case 1. Dense dermal infiltrate of neutrophils and significant edema of the dermis (inset: ×40 magnification).

daily in anticipation of her second revision surgery, which she tolerated with no SS recurrence.

Four years after her initial SS episode, she required spinal surgery and initiated prophylaxis with prednisone 60 mg taper starting 2 days prior to surgery and IV methylprednisolone 60 mg the day prior to and day of surgery. She did not develop any recurrence of SS following the procedure.

Case 2

A 75-year-old man with history of myelodysplastic syndrome presented 5 days following a right total knee arthroplasty with persistent fevers and purulent drainage along with superficial sloughing at the surgical site. Despite negative wound cultures and antibiotic coverage, he continued to spike fevers to 102 °F and had leukocytosis of 12.73 × 1000/mm^3. Dermatology was consulted.

Skin examination was notable for an exquisitely painful surgical wound on his right knee. Repeat wound cultures were negative. No biopsy was taken due to the assessment that the blistering was superficial. With consistent wound care, the patient's fevers, skin lesions, and knee pain resolved over 4 weeks.

Three years after the initial episode, a similar wound complication developed with persistent fevers after right femoral artery access during a cardiac catheterization. He had not received any prophylaxis prior to the procedure. Dermatology was consulted, and punch biopsy confirmed a diagnosis of SS. Treatment with systemic corticosteroids and dapsone 100 mg daily led to rapid resolution of erythema and pain. Two months later, he received IV methylprednisolone as prophylaxis prior to his transcatheter aortic valve replacement. The procedure was successful, and he did not experience any recurrence of SS.

Table I. Summary of Sweet syndrome after orthopedic surgeries

Case	Age (y)/ sex	Surgery	SS risk factors	Empiric antibiotics	Infectious stains	Clinical presentation	Treatment	Outcome
1	68F	Right total hip replacement	None	Yes	Negative	Fevers, leukocytosis, tender, violaceous plaque surrounding incision site	IV MP 1 mg/kg daily Prednisone 0.5 mg/kg daily CSA 3 mg/kg divided twice daily Dapsone 100 mg daily	Improved with IV MP and prednisone taper
2	75M	Right total knee arthroplasty	MDS	Yes	Negative	Fevers, leukocytosis, purulent drainage, superficial sloughing	Wound care	Improved with consistent wound care
3	38F	Left carpal tunnel release	None	Yes	Negative	Fevers, leukocytosis, erythema and edema	IV MP 48 mg daily Prednisone 60 mg taper	Improved with systemic corticosteroids
4	18F	ACL repair	None	Yes	Negative	Fevers, leukocytosis, violaceous plaque, worsened with debridement	Prednisone 1 mg/kg daily Anakinra 200 mg daily CSA 2 mg/kg twice daily	Improved with prednisone and anakinra
5	51M	Right meniscus repair	None	Yes	Negative	Fevers, leukocytosis, ulcer with undermined gunmetal borders	IV MP 1 mg/kg daily CSA 3 mg/kg divided twice daily	Improved with IV MP and CSA
6	76M	Right total knee arthroplasty	MM, prior SS	Yes	Negative	Fevers, leukocytosis, hypotension	IV MP 65 mg daily CSA 3 mg/kg twice daily	Improved with IV MP and CSA
7	73M	Left total hip replacement	CLL, prior SS	Yes	Negative	Fevers, erythematous edematous and warm plaque at incision site, violaceous nodules at IV site	IV MP 80 mg daily Prednisone 100 mg taper CSA 200 mg twice daily	Improved with IV MP, prednisone, and CSA

ACL, Anterior cruciate ligament; *CLL*, chronic lymphocytic leukemia; *CSA*, cyclosporine; *F*, female; *IV*, intravenous; *M*, male; *MDS*, myelodysplastic syndrome; *MM*, multiple myeloma; *MP*, methylprednisolone; *SS*, Sweet syndrome.

Table II. Procedures and outcomes following postsurgical Sweet syndrome diagnosis

Case	Total number of procedures following SS diagnosis	Prophylaxis?	Procedure	Time after initial SS episode	SS recurrence?
1	3	Incomplete CSA	Revision right total hip replacement	1 mo	Flare, improved with prednisone and CSA, resolved with adjunct dapsone
		MP and CSA	Second revision right total hip replacement	2 y	No
		MP and prednisone	Spinal surgery	4 y	No
2	2	None	Cardiac catheterization	3 y	Yes, responded to IV MP and dapsone
		MP	Transcatheter aortic valve replacement	3 y	No
3	3	Prednisone	Split thickness skin graft	1 mo	No
		None	Electromyography	3 mo	No
		MP and prednisone	Anterior cervical discectomy and fusion	5 mo	No
4	1	CSA	Left knee arthroscopy and synovectomy	10 mo	No
5	1	None	Split thickness skin graft	1 y	No
6	2	CSA	Right total knee arthroplasty	5 y	No
		None	Repeat exploration of knee	5 y	Flare, resolved with IV MP and CSA
7	1	None	Left total hip replacement	12 y	Yes, responded to IV MP

CSA, Cyclosporine; *IV*, intravenous; *MP*, methylprednisolone; *SS*, Sweet syndrome; *TAVR*, transcatheter aortic valve replacement.

Case 3

A 38-year-old healthy woman presented 6 days following left carpal tunnel release for severe edema and erythema of the left hand and wrist. She additionally had fevers, leukocytosis of 22 × 1000/mm^3, and lack of clinical improvement following multiple broad-spectrum antibiotics and surgical debridement. Wound and blood cultures were negative. Dermatology was consulted, and the patient was diagnosed with necrotizing SS. She improved with prednisone 60 mg daily. One month later, her prednisone taper was extended in anticipation of her split thickness skin graft, with prednisone 20 mg daily given 3 days prior followed by a 14 day taper afterward. She tolerated the procedure with no SS recurrence.

Three months following the initial episode, she underwent electromyography without medication prophylaxis and did not develop any SS recurrence.

Five months following the initial episode, she underwent C4-C5 anterior cervical discectomy and fusion with prednisone 60 mg daily starting 3 days before surgery, IV methylprednisolone the day of, and prednisone taper afterward. She did not experience any SS recurrence.

Cases 4 to 7

Cases 4 to 7 of SS occurring in patients following an orthopedic surgery are summarized in Table I. Outcomes of procedures in patients 4 to 7 with prior diagnosis of SS are summarized in Table II.

DISCUSSION

Patients with SS may present following an infection (most commonly upper portion of the respiratory tract and gastrointestinal tract) or with associated malignancy, inflammatory bowel disease, recent drug exposure, and/or pregnancy; however, idiopathic cases can also occur.[2,3] With regard to surgical procedures, SS has been described in the setting of varicose vein surgery,[4] spinal surgery,[5] pneumonectomy,[6] and coronary artery bypass grafting.[7] SS arising after orthopedic surgeries is rare; reported cases include development of SS 11 years after undergoing bilateral total knee arthroplasty,[8] 3 weeks after a right tibial osteotomy,[9] and necrotizing SS 2 days after elective right partial palmar fasciectomy.[10]

Erythema and edema at the surgical site along with lack of clinical response to antibiotics and/or surgical debridement should prompt evaluation for SS. A higher level of suspicion should be considered in patients entering procedures with hematologic malignancies, although spontaneous occurrences in patients without SS risk factors are not infrequent.

Postoperative SS may have a similar clinical presentation to conditions of infectious (cellulitis and prosthesis infection) and inflammatory (hematoma and thrombophlebitis) etiology, and necrotizing SS may mimic necrotizing fasciitis.[11] Misdiagnosis can delay treatment and result in inappropriate interventions.

While considered the gold standard of therapy for SS, systemic corticosteroid use perioperatively may raise concerns of delayed wound healing or prosthetic joint infection.[12] Thus, steroid-sparing agents such as cyclosporine can help successfully bridge patients given its rapid onset of action and lack of inhibition on wound healing.[13] Avoidance of skin instrumentation and surgical intervention is essential to prevent pathergy and progression of disease.

Importantly, our cases highlight that with a multidisciplinary approach and prophylactic immunosuppression prior to and immediately following the procedure, patients with prior history of postsurgical SS are able to safely undergo future surgeries. With cyclosporine and/or systemic corticosteroids as prophylaxis, the 6 patients in our case series who required future surgeries successfully tolerated their procedures and had no recurrence of SS. Of the 4 cases who experienced SS flare or recurrence following surgery, all either received no or incomplete prophylaxis. Two patients (cases 3 and 5) underwent successful procedures without receiving prophylaxis, demonstrating the variability of outcomes that can occur even among individuals.

CONCLUSION

SS should be considered in the setting of a suspected postoperative wound infection failing to improve with broad antibiotic coverage. Early clinical recognition of SS after an orthopedic surgery is important in minimizing morbidity, as repeated surgical intervention may cause progression of disease. A history of SS does not preclude future surgical procedures, and patients can be safely managed with prophylactic immunosuppression. Close coordination between dermatologists and surgeons with consideration of individual patient risk factors is necessary to determine best practices for the management of surgical rechallenge.

Conflicts of interest

None disclosed.

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