CASE REPORT

Mimicker of necrotising fasciitis with systemic inflammatory response syndrome: recurrent necrotising Sweet's syndrome associated with chronic myelogenous leukaemia

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SUMMARY

A 73-year-old man presented with severe right upper quadrant abdominal pain, overlying erythema, hypotension and fever. CT scan revealed fasciitis and myositis of the right rectus abdominis muscle with subcutaneous inflammation involving the fasciae and muscle. Laboratory studies showed extreme leucocytosis. The combination of his symptoms, CT findings and laboratory results suggested necrotising fasciitis with systemic inflammatory response syndrome. Subsequent negative cultures on skin and muscle biopsy led to a diagnosis of necrotising neutrophilic panniculitis. Recurrent episodes of fever, and abdominal and buttocks pain at various sites, suggested an underlying haematological condition. Bone marrow biopsy and genetic analysis revealed chronic myelogenous leukaemia. The patient's symptoms of Sweet's syndrome resolved with glucocorticoid treatment and did not recur after starting treatment with a tyrosine kinase inhibitor.

BACKGROUND

Hypotension and fever due to necrotising Sweet's syndrome (also called Sweet syndrome) can easily be misdiagnosed as sepsis with necrotising fasciitis. This case serves as a reminder that recurrent episodes of Sweet's syndrome should raise suspicion for an underlying condition such as a haematological malignancy. A tyrosine kinase inhibitor was used for the treatment of this patient's chronic myelogenous leukaemia (CML) and did not result in any recurrent episodes of Sweet's syndrome.

CASE PRESENTATION

A 73-year-old man presented to the emergency department, with fever (39°C) and severe right upper quadrant (RUQ) abdominal pain that had gradually worsened over 4 days. The pain was dull, exacerbated by movement, and had become so severe that he had difficulty getting up from bed. He denied nausea, vomiting, diarrhoea, constipation or trauma.

His history was pertinent for squamous cell carcinoma of the lung (stage IIB), which was in complete remission. He had undergone right middle lobectomy 2 years previously and had received adjuvant chemotherapy. He took amlodipine and valsartan for hypertension. He had no known allergies. He was widowed, lived alone and was

physically active. He was a social drinker and had stopped smoking at age 71 years.

On examination, he appeared sick but well oriented. His blood pressure was 90/50 mm Hg, heart rate 130 bpm, temperature 39.4°C, respiratory rate 20 breaths/min and oxygen saturation (on room air) 95%. Examination of the heart and lungs was unremarkable. The abdominal wall was warm and with overlying erythema ([figure 1A](#)). The abdomen was soft and distended, with normal bowel sounds. There was severe tenderness and guarding to palpation of the RUQ, but no rebound and no hepatomegaly. Murphy's sign was negative and there was no tenderness at McBurney's point.

INVESTIGATIONS

Laboratory studies showed an elevated white blood cell (WBC) count of 32 300/μL with a left shift. Lactate dehydrogenase was 805 IU/L (normal range 107–220), creatine phosphokinase (CPK) was 590 IU/L (normal range 51–207) and C reactive protein (CRP) was 30.05 mg/dL (normal range <0.40; [table 1](#)). Renal function tests and liver enzymes were unremarkable. Amylase and lipase levels were normal.

CT scan of the abdomen revealed fasciitis and myositis of the right rectus abdominis. There was no evidence of pancreatitis ([figure 1B](#)). The patient was admitted for suspected necrotising fasciitis, and intravenous fluids with antibiotics (clindamycin and aztreonam) were administered. Fever and rigours persisted for 5 days. Blood and urine cultures were sterile. Gram stain of fluid aspirated from the abdominal wall demonstrated scant neutrophils and no organisms. Skin and muscle biopsies showed severe deep neutrophilic panniculitis and mild myositis with necrosis ([figure 2](#)). Cultures from the fat and muscle biopsy remained negative. The fever, abdominal pain and leucocytosis gradually improved following treatment with non-steroidal anti-inflammatory agents. The patient was discharged home on the 17th hospital day.

One week after discharge, the patient returned to the hospital, again with fever and abdominal pain, but this time on the left side. On examination, his blood pressure was 100/60 mm Hg, heart rate 120 bpm, respiratory rate 20 breaths/min and temperature 39.6°C. He had severe tenderness and guarding to palpation of the left lower abdominal wall, with overlying erythema. Laboratory studies

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Figure 1 (A) Physical examination of erythematous right upper quadrant abdominal wall. (B) CT scan of myositis of right rectus abdominis.

showed a WBC count of 18 300/ μ L. He was readmitted to the hospital. Skin and muscle biopsies of the tender left abdominal wall revealed findings similar to those of the first muscle biopsy—deep neutrophilic panniculitis and myositis. Repeat blood cultures and cultures of the biopsied tissue were again sterile. Upper gastrointestinal endoscopy, colonoscopy and CT scan showed no evidence of intra-abdominal malignancy. Measurements of C3 and C4 were within normal limits and autoantibody results (antinuclear, antiSSA/Ro, antiSSB/La, antiJo1 and antineutrophil cytoplasmic antibody) were negative. Prednisolone 30 mg (0.5 mg/kg/day) improved his symptoms and was tapered to 5 mg/day. He was discharged home on the 14th hospital day.

Two months after the second episode, the patient again returned to the hospital, this time with fever (38.4°C) and right buttock pain. He was alert and oriented, but with profound hypotension (systolic blood pressure 46 mm Hg and heart rate 100 bpm). Laboratory studies showed a WBC of 88 900/ μ L, CPK of 1294 IU/L and CRP of 24.01 mg/dL.

DIFFERENTIAL DIAGNOSIS

Sweet's syndrome related to infection, inflammatory bowel disease, autoimmune conditions, pancreatitis, α 1-antitrypsin deficiency or drugs (G-CSF or tyrosine kinase inhibitor) were unlikely based on clinical presentation, laboratory data and negative cultures. Extreme leucocytosis in association with recurrent systemic inflammatory reactions and deep necrotising panniculitis suggested necrotising Sweet's syndrome, possibly due to an underlying myeloproliferative disease. The diagnosis

of CML was made after marrow examination revealed granulocytic proliferation with maturation (figure 3A) and karyotype t(9;22) Philadelphia chromosome with trisomy 8 (figure 3B).

TREATMENT

The first-line treatment for Sweet's syndrome is systemic glucocorticoids and is usually characterised by a rapid and dramatic response. Colchicine or dapsone can be used as alternative therapies or as steroid sparing agents. Our patient was treated with prednisolone 30 mg/day (0.5 mg/kg/day) and the fever promptly resolved within 48 h. The tyrosine kinase inhibitor, nilotinib (300 mg twice daily), was added for the treatment of his CML. Although a few cases of drug-induced Sweet's syndrome triggered by tyrosine kinase inhibitor dasatinib have been reported, our case suggested that haematological malignancy-associated Sweet's syndrome did not recur with treatment with nilotinib.

OUTCOME AND FOLLOW-UP

Three months later, the prednisolone was tapered off and the patient's CML went into complete cytogenetic response (defined by the absence of the Philadelphia chromosome in metaphase by fluorescent in situ hybridisation study). He has had no recurrences of necrotising Sweet's syndrome during the ensuing 4 years.

DISCUSSION

Sweet's syndrome is an eponym for acute febrile neutrophilic dermatosis without vasculitis. It is characterised by clinical findings that include fever, tender erythematous skin lesions

Table 1 Laboratory data

Variable	Reference range	On admission	Day 17	2nd episode	3rd episode
Haemoglobin (mg/dL)	13.5–17.5	13.8	11.6	10.5	11.5
White cell count (/ μ L)	4800–8500	32 300	8100	18 300	88 900
Differential count (%)					
Promyelocytes	0	0	0	0	8
Myelocytes	0	2	0	0	17
Metamyelocytes	0–0.5	7	2	1	14
Stab neutrophils	1–9	18	4	18	38
Segmented neutrophils	40–65	46	41	48	13
Lymphocytes	20–50	9	28	7	3
Basophils	0–1.5	0	4	1	0
Platelet count (/ μ L)	130 000–370 000	137 000	236 000	210 000	155 000
Lactate dehydrogenase (IU/L)	107–220	805		298	1397
Creatine kinase (IU/L)	51–207	590		64	1294
C reactive protein (mg/dL)	<0.40	30.05	0.34	9.97	24.41

Figure 2 Histology of the skin and muscle. Images of H&E-stained sections at high-power magnification ($\times 400$) are shown: (A) severe neutrophilic panniculitis; (B) myositis with necrosis without organisms or vasculitis.

(papules, nodules or plaques), leucocytosis and elevated inflammatory markers, along with pathological features consistent with diffuse neutrophilic infiltrate in the dermis. Sweet's syndrome is clinically classified into three groups: classical (or idiopathic), malignancy-associated and drug-induced. A variant of Sweet's syndrome, subcutaneous Sweet's syndrome, involves mainly subcutaneous fat rather than the dermis, and its pathology demonstrates neutrophilic panniculitis. Necrotising Sweet's syndrome manifests with deeper necrotic soft tissue involvement of the fascia and muscles, and mimics necrotising fasciitis.¹ In this case, abrupt onset of fever, tender erythematous skin/muscle lesion, extreme leucocytosis and neutrophilic infiltrates in fat tissue suggested a clinical entity consistent with subcutaneous Sweet's syndrome.

There have been several case reports of subcutaneous Sweet's syndrome associated with haematological conditions, most commonly with myeloproliferative disorders. Chan and colleagues described 16 cases of Sweet's syndrome with erythematous tender nodules showing necrotising panniculitis. Six of these were associated with acute myelogenous leukaemia and 10 were related to myelodysplastic syndrome (MDS).² Necrotising panniculitis in multiple myeloma is rare, occurring in only 1 out of 2357 patients who have the disease.³ Two cases of CML have been reported in which the tyrosine kinase inhibitor dasatinib appeared to trigger recurrent subcutaneous Sweet's syndrome.^{4,5} In our case, however, recurrent Sweet's syndrome had occurred before the treatment of CML and did not recur after starting nilotinib.

Fujimura *et al*⁶ reported cases of two patients who presented with periodic fever and erythema nodosum associated with MDS and trisomy 8, where one patient showed markedly elevated CPK. Trisomy 8 is frequently found in myelodysplastic/

myeloproliferative neoplasm,⁷ and an increasing number of cases with fever and erythema nodosum in trisomy 8 have been described.⁶ Chen *et al*⁸ reported that genes for inflammatory cytokines such as TGF- β were upregulated in patients with MDS and trisomy 8. Trisomy 8 may be a predisposing factor to develop periodic fever and erythema nodosum in haematological malignancy.

Sweet's syndrome with shock is uncommon. A case of Sweet's syndrome in a 30-year-old woman who presented with abdominal wall necrosis and shock after delivery was described by de Moya *et al*.⁹ The pathology of the uterus revealed necrotising panniculitis and myonecrosis, consistent with necrotising Sweet's syndrome. Six cases of systemic inflammatory response syndrome (SIRS) have been reported in patients with Sweet's syndrome and three had underlying haematological dyscrasias.^{9–12} All six cases developed acute onset of Sweet's syndrome with extracutaneous involvement, and three were fatal. Each case had sterile cultures and a negative response to antibiotics, but rapid improvement with glucocorticoids suggested SIRS secondary to Sweet syndrome (table 2).

Neutrophilic infiltration in the skin and deeper tissues is accompanied by increased proinflammatory cytokines.¹³ The systemic response to these cytokines might produce a clinical presentation of Sweet's syndrome that looks similar to sepsis or SIRS. Involvement of fasciae and muscle in necrotising Sweet's syndrome resembles necrotising soft tissue infection, and the extreme inflammatory response leads to fever and hypotension. Similar to the patients in these cases, our patient presented with hypotension, recurrent necrotising panniculitis and sterile blood cultures, but also similar to these patients, our patient likewise experienced rapid improvement of his condition with glucocorticoids.

Figure 3 Bone marrow examination results. (A) Images of H&E-stained sections are shown. At lesser magnification ($\times 100$), granulocytic proliferation with maturation. (B) The karyotype was t(9;22) Philadelphia chromosome with trisomy 8.

Table 2 Characteristics of patients with Sweet's syndrome and systemic inflammatory response syndrome

Reference	Age, years	Sex	Presentation	Associated conditions	Treatment	Outcome
6	30	F	Necrotising SS	Upper respiratory infection and pregnancy	Prednisolone: 120 mg/day, cyclosporine	Improved
7	53	F	Classical SS	Pyelonephritis	Prednisolone: 60 mg/day	
8	76	M	Classical SS	MDS	Prednisolone: 1 mg/kg/day and 5-azacitadine	Fatal
9	7	F	Subcutaneous SS	MDS after autologous bone marrow transplant for treatment of acute myelogenous leukaemia, and G-CSF	Methylprednisolone: 1 mg/kg/day	Improved
10	44	F	Subcutaneous SS	MDS after chemotherapy for aggressive B-cell lymphoma	Prednisolone: 30 mg/day, hydroxyurea, colchicine, potassium iodide and intravenous immunoglobulin	Fatal
Current case	73	M	Necrotising SS	Chronic myelogenous leukaemia	Prednisolone 30 mg/day, nilotinib	Improved

F, female; G-CSF, granulocyte-colony stimulating factor; M, male; MDS, myelodysplastic syndrome; SS, Sweet's syndrome.

In summary, we presented a case of recurrent subcutaneous panniculitis with underlying CML mimicking necrotising fasciitis, which promptly responded to steroid treatment.

Learning points

- Involvement of fasciae and muscle in necrotising Sweet's syndrome may mimic necrotising fasciitis and soft tissue infection. Blood cultures and tissue biopsy are crucial to differentiate these conditions.
- Necrotising Sweet's syndrome can cause a systemic inflammatory response and needs to be distinguished from sepsis.
- Recurrent Sweet's syndrome may be associated with underlying haematological disease.
- Treatment for haematological malignancies may prevent recurrence of Sweet's syndrome.

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Competing interests None declared.

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