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Case 28-2012: A 30-Year-Old Woman with Shock and Abdominal-Wall Necrosis after Cesarean Section

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PRESENTATION OF CASE

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N Engl J Med 2012;367:1046-57.

DOI: 10.1056/NEJMcpc1208146

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Dr. Trevin C. Lau (Obstetrics and Gynecology): A 30-year-old woman presented with shock and abdominal-wall necrosis after a cesarean section.

The previously well primigravida had undergone cesarean section at 36.4 weeks' gestation after 34 hours of labor, because of suspected chorioamnionitis (abdominal pain and an elevated white-cell count), fetal tachycardia, and a prolonged deceleration on a fetal heart-rate tracing during labor augmented by oxytocin.

The patient had received routine prenatal care. A urine culture 6.5 months before admission had grown group B streptococcus. One week before admission, sinus congestion occurred transiently, without fever, nausea, vomiting, diarrhea, or dysuria. Medications on admission included prenatal vitamins, iron, and acetaminophen. The patient had no known allergies. She lived with her husband and worked in health care. She owned a dog and a cat; her husband changed the litter. She did not drink alcohol, smoke, or use illicit drugs. She had traveled to Europe and Mexico. Her father had died of heart disease at 59 years of age, and a sister had had two spontaneous miscarriages.

Laboratory-test results are shown in Table 1. Urinalysis was normal. Ampicillin and gentamicin were given before and during delivery. A male infant weighing 3230 g was delivered; the 1-minute and 5-minute Apgar scores were 8 and 9, respectively. The placenta weighed 480 g (60th percentile for gestational age), and pathological examination revealed no gross abnormalities; there was marked acute inflammation of the decidua basalis (a maternal tissue), with neutrophils, eosinophils, abscess formation, and necrosis, but there was no acute chorioamnionitis and there were no microorganisms.

Approximately 10 hours post partum, the temperature rose to 38.4°C and the white-cell count was elevated. The administration of clindamycin was begun. On the fourth hospital day, 37 hours post partum, dyspnea developed; the blood pressure was 90/50 mm Hg and the pulse 130 to 139 beats per minute. During the next 13 hours, the systolic blood pressure decreased to 70 to 79 mm Hg and remained low despite

fluid resuscitation; the temperature was 38.1°C and the respiratory rate 22 breaths per minute. On examination, the patient appeared ill. Crackles in both lung bases and a systolic murmur (grade 2/6) were heard. The abdomen was distended and soft, with few bowel sounds and tenderness over the surgical incision, which appeared clean and dry, without erythema. The extremities were cool, with 2+ edema. Levels of blood glucose, phosphorus, and lactic acid were normal, as were tests of coagulation; other test results are shown in Table 1. An electrocardiogram showed a sinus rhythm at 129 beats per minute, with low-voltage QRS waves and nonspecific ST-segment abnormalities. The patient was transferred to the surgical intensive care unit.

Computed tomography (CT) of the chest and legs, performed according to a protocol for the assessment of pulmonary embolism, revealed no evidence of pulmonary embolism or deep venous thrombosis. Transthoracic echocardiography revealed diffuse hypokinesis of both ventricles, a left ventricular ejection fraction of 38%, mild mitral and pulmonary insufficiency, moderate tricuspid insufficiency, and no thrombus or valvular vegetations. Ultrasonography of the abdomen showed a small amount of ascites and a right pleural effusion. CT of the abdomen without the administration of contrast material showed a small volume of ascites, subcutaneous emphysema, a postpartum uterus, mild ileus without obstruction, and trace pleural effusions bilaterally, without evidence of abscess. Cultures of the blood, urine, and placenta obtained during the first 2 days were sterile; repeated blood and urine cultures remained sterile. Testing of a nasal swab for methicillin-resistant *Staphylococcus aureus* (MRSA) was negative. The administration of imipenem-cilastatin, vancomycin, and dalteparin was begun, clindamycin was continued, and the other antibiotic agents were stopped.

During the next several days, the patient was afebrile, and the left ventricular ejection fraction increased to 57%. Drainage was noted from the incision, which was débrided and packed on the fifth day; the underlying tissue appeared well perfused and viable, and the fascia was intact. On the eighth day, a rash developed. Imipenem-cilastatin and clindamycin were stopped, and the administration of aztreonam and metronidazole was begun.

On the 12th hospital day, the temperature rose to 39.6°C; the blood pressure was 122/52 mm Hg,

the pulse 138 beats per minute, and the respiratory rate normal. There was mild tenderness of the abdominal incision and 3+ pitting edema to the thighs. Serosanguineous fluid drained from the incision, but underlying tissue appeared viable, without purulent drainage. Cultures remained sterile. The administration of vancomycin, aztreonam, and metronidazole was stopped. On the 13th day, fever persisted; there was induration of the abdominal wall, without erythema. Laboratory-test results are shown in Table 1. Packed red cells were transfused. CT of the abdomen and pelvis after the administration of contrast material revealed low-density material in the endometrial cavity, irregular enhancing tissue at the margin of the endometrial canal, fluid in the rectovaginal pouch with enhancing peritoneum, persistent subcutaneous emphysema and tissue changes at the level of the lower rectus abdominis muscles, and an anastomotic appearance of the colon.

Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and abdominal-wall débridement were performed; clindamycin and doxycycline were administered preoperatively. Pathological examination of the tissues showed endomyometritis, with neutrophils and eosinophils, necrosis, and abscesses; serositis involving the anterior uterine peritoneal surface and both fallopian tubes; and acute and chronic inflammation, with abscesses and necrosis, of the skin and skeletal muscle. No organisms were seen, and cultures were sterile. A 10-day course of clindamycin, vancomycin, and imipenem-cilastatin was begun. Wound débridement was performed intermittently.

On the 18th day, testing for the 1849G→T (V617F) mutation in JAK2 (the Janus kinase gene) was negative. Abdominal-wound reconstruction and partial closure were performed. On the 25th day, the administration of metronidazole, doxycycline, and a combination of piperacillin and tazobactam was begun, and other antibiotics were discontinued. Testing for antineutrophil cytoplasmic antibodies (ANCA) and antibodies to proteinase 3 and myeloperoxidase was negative. Blood levels of lipase and amylase were normal; other test results are shown in Table 1. Intravenous immune globulin was given (two doses, 7 days apart). The white-cell count gradually decreased (Table 1). During the next 4 weeks, the wound was irrigated and débrided, the biologic mesh (used in the abdominal-wound reconstruction) was re-

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Admission	7 Hr after Admission	4th Day	13th Day	18th Day	22nd Day	25th Day	36th Day	2 Mo after Admission
Hematocrit (%)	36.0–46.0 (women)	36.5	35.5	30.1	23.8	27.3	30.7	21.6	21.8	20.3
Hemoglobin (g/dl)	12.0–16.0 (women)	12.8	12.4	10.8	7.9	9.2	10.3	7.1	7.3	6.3
White-cell count (per mm ³)	4500–11,000	28,800	37,700	39,500	63,400	40,700	55,700	89,300	17,300	42,600
Differential count (%)										
Neutrophils	40–70	93	92	62	83	73	91		72	
Band forms	0–10			31	8	4				
Lymphocytes	22–44	4	4	2	4	2	4		19	
Monocytes	4–11	3	4	4	3	11	4		6	
Eosinophils	0–8	0	0	0	0	3	1		2	
Basophils	0–3	0	0	0	0	0	0		1	
Metamyelocytes	0			1	2	3				
Myelocytes	0					4				
Platelet count (per mm ³)	150,000–400,000	255,000	214,000	200,000	447,000	1,300,000	911,000	809,000	868,000	508,000
Haptoglobin (mg/dl)	16–199				304			348		
Fibrinogen (mg/dl)	150–400				500					
Erythrocyte sedimentation rate (mm/hr)	0–17									73
Sodium (mmol/liter)	135–145			134	136	134	138	139	137	129
Potassium (mmol/liter)	3.4–4.8			3.4	3.4	4.0	3.1	3.7	3.5	4.1
Chloride (mmol/liter)	100–108			98	102	102	102	106	102	93
Carbon dioxide (mmol/liter)	23.0–31.9			26.3	24.1	24.1	23.9	21.1	26.8	24.5
Urea nitrogen (mg/dl)	8–25			11	10	13	4	19	12	11
Creatinine (mg/dl)	0.60–1.50			1.00	0.97	0.63	0.68	3.62	1.15	0.89
Estimated glomerular filtration rate (ml/min/1.73 m ²)				>60	>60	>60	>60	16	55	>60
Bilirubin (mg/dl)										
Total	0.0–1.0			0.5		1.2	4.7	6.8	1.6	
Direct	0.0–0.4			0.3		0.6	3.3	4.8	0.6	
Protein (g/dl)										
Total	6.0–8.3			4.1		4.2	4.8	4.3	5.7	4.5
Albumin	3.3–5.0			1.7		1.8	2.1	2.1	2.9	
Globulin	2.3–4.1			2.4		2.4	2.7	2.2	2.8	
Calcium (mg/dl)	8.5–10.5			7.6	7.6	7.1	7.2	7.6	8.1	8.8

Alkaline phosphatase (U/liter)	30–100	128	121	229	216	111
Aspartate aminotransferase (U/liter)	9–32	37	67	140	17	11
Alanine aminotransferase (U/liter)	7–30	17	32	132	12	8
Lactate dehydrogenase (U/liter)	110–210	301			333	176
Immunoglobulins (mg/dl)						
IgA	69–309				86	60
IgG	614–1295				304	506
IgM	53–334				32	49
M component (by immunofixation)					0.06, IgG kappa	0.06, IgG kappa
C3 (mg/dl)	86–184					40
C4 (mg/dl)	16–38					13

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for bilirubin to micromoles per liter, multiply by 17.1. To convert the values for calcium to millimoles per liter, multiply by 0.250.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

moved, and split-thickness skin grafts from donor sites on the thighs were applied to a tissue bed overlying the bowel.

Two months after admission, as the patient's discharge from the hospital was being planned, purulent drainage developed at the edges of the skin graft, with erythema at the margins, and leukocytosis recurred (Table 1). Wound exploration revealed focal myonecrosis and necrosis of the edges of the skin graft, which were débrided.

Consultations with the immunology and dermatology services were obtained. The patient reported recurrent sinusitis and acute otitis media before the age of 5 years. She had had no rashes or difficulty with wound healing. There was no history of allergy or immunodeficiency in first-degree relatives. On examination, the edges of the abdominal wound were red and indurated. There were several superficial pustules (3 to 4 mm in diameter) on an edematous and erythematous base over the donor site of the skin graft on the right anterior thigh and multiple scattered hemorrhagic crusts on both skin-graft donor sites. The remainder of the examination was unchanged. Test results are shown in Table 1.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Marc A. de Moya: All discussants are aware of the diagnosis in this case. This patient had what appeared to be a necrotizing soft-tissue infection after cesarean section. The four tenets of care for necrotizing infections are early detection, aggressive débridement, adequate antibiotic therapy, and physiological support. CT can be useful when evaluating a necrotizing soft-tissue infection, with sensitivity and a negative predictive value of virtually 100%.¹ May we review the imaging studies?

Dr. Anuradha S. Shenoy-Bhangle: On the 13th hospital day, CT of the abdomen and pelvis after the administration of intravenous contrast material revealed an enlarged postpartum uterus with an endometrial cavity that was distended with fluid (Fig. 1A). The anterior endomyometrial junction was irregular, with heterogeneous enhancement (Fig. 1B). Ascites and an enhancing peritoneal lining were seen. These findings were consistent with endometritis, pyometra, or both.²

Dr. de Moya: Management of necrotizing soft-tissue infections with antibiotics alone is associated with mortality rates approaching almost

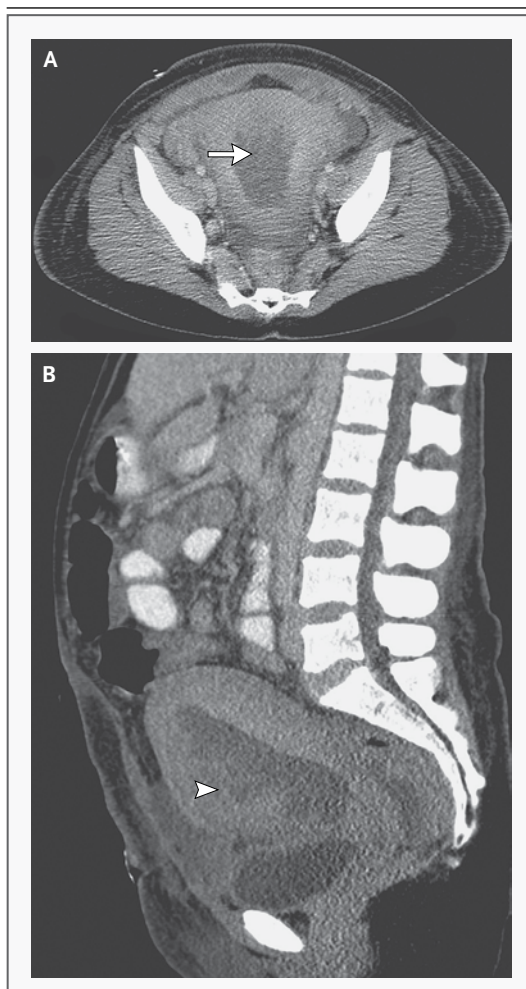


Figure 1. CT of the Abdomen and Pelvis with the Administration of Contrast Material.

Panel A shows an enlarged postpartum uterus with an endometrial cavity that is distended with fluid (arrow). Panel B shows an irregular, heterogeneously enhancing endomyometrial junction (arrowhead).

100%. Early surgical exploration is associated with lower mortality rates (20 to 50%).^{3,4} Nonetheless, the mortality in severe cases such as this one approaches 60%, and the illness can leave patients severely debilitated. Intraoperative “second-look” procedures should be performed within 12 to 24 hours after débridement, to ensure surgical control of infection.

This patient was taken to the operating room urgently and was found to have a nonviable uterus and myonecrosis with purulence in the rectus sheath. The lower third of the rectus muscle and sheath were removed. The wound was débrided and left open, and a temporary vacuum-assisted

dressing was applied; there were plans for serial explorations and débridements. It was unusual to find no evidence of bacteria in a patient with such a severe necrotizing process.

Serial débridements were performed as the myonecrosis continued to progress. The myonecrosis eventually slowed and stopped. During this process, we wondered whether the patient had an immunologic deficiency; consultations were obtained from hematology and immunology, and the patient was found to have a low blood IgG level. She received two doses of intravenous immune globulin, with a decrease in the degree of leukocytosis to 8900 cells per cubic millimeter.

Once the necrosis stopped, we performed a partial reconstruction of the abdominal wall with the use of a biologic mesh to prevent further lateral fascial retraction, followed by a split-thickness skin graft with excellent graft growth during the following week. However, as her discharge day approached, leukocytosis returned and the graft began to appear necrotic. We consulted the infectious disease, immunology, and dermatology services.

Dr. Gregory K. Robbins: The infectious disease service’s initial differential diagnosis included recurrence of necrotizing soft-tissue infection, local wound infection in an immunologically impaired host, and pelvic abscess.

NECROTIZING SOFT-TISSUE INFECTION

Necrotizing soft-tissue infection (also known as necrotizing fasciitis)⁵ is a rare but well-known postpartum complication that has been discussed previously.⁶ Most such infections either are polymicrobial (type I), typically in immunocompromised and postsurgical patients, or are due to a single bacterial pathogen (type II). Type II necrotizing soft-tissue infection usually involves group A streptococcus, but increasingly, MRSA, group B streptococcus, klebsiella, or other bacteria are involved, most likely because of the emergence of new virulence factors.⁷ Necrotizing soft-tissue infection involving clostridium species (type III) also occurs, as do other unclassified types of infection, such as those involving *Vibrio vulnificus*. Pathological features include necrosis of fascia and other soft tissues, thrombosis, numerous bacteria, and a paucity of inflammatory cells.

Signs and symptoms of necrotizing soft-tissue infection, many of which this patient had, include fever, tachycardia, hypotension, erythema

with induration that extends beyond the involved area, pain disproportionate to appearance, bullae, crepitus, subcutaneous gas, ecchymosis, and skin discoloration and necrosis. A diagnosis that is made on the basis of clinical features has low sensitivity. Laboratory findings are nonspecific but commonly include an elevated white-cell count and a low serum sodium level. Prediction rules based on laboratory findings have been proposed but have undergone limited prospective validation and were not used in this case.^{5,8}

This case had several atypical features. The initial presentation was unusual, since postpartum necrotizing soft-tissue infection typically occurs within the first few days after delivery,^{4,9} whereas it occurred 12 days post partum in this patient; no organisms were identified by pathological examination, stains, or cultures (although this could have been a reflection of early antibiotic therapy); and marked acute inflammation was seen on pathological examination. In addition, most patients improve dramatically within 24 to 48 hours after débridement, but this patient had persistent leukocytosis and fevers. Finally, most relapses of necrotizing soft-tissue infection occur hours or days after débridement, and late relapses, as seen in this case, are extremely rare.

Nonetheless, in view of clear indicators for necrotizing soft-tissue infection, a rising temperature, a high white-cell count, increasing discharge, erythema, expanding induration, and pain out of proportion to examination, we concurred with plans for emergency surgical exploration and recommended additional input from the dermatology and immunology services.

Dr. Johnson T. Wong: The immunology service was consulted to address the poor wound healing in this patient. A unifying diagnosis must explain the extensive necrosis and inflammation in the clinical context of pregnancy and a recent viral syndrome, the intermittent high temperatures, and the laboratory findings of leukocytosis and hypogammaglobulinemia. We considered localized vascular insufficiency, neutrophilic dermatoses, and other autoimmune processes or immunodeficiency.

VASCULAR COMPROMISE

Vascular compromise may be due to thrombosis, vasculitis, or other damage to the blood vessels that is triggered by infection, trauma, atherosclerosis, or immune-mediated inflammation. Pathological examination of the uterus confirmed the

presence of thromboemboli in uterine vessels and hemorrhage in the wall, with marked eosinophilia. Among the vasculitides, pathergy (necrosis of tissues at sites of surgery or minor trauma) and extracutaneous involvement are characteristic of Behçet's disease. However, the absence of the typical mucocutaneous lesions and the absence of vasculitis in the necrotic tissues do not support this diagnosis. ANCA-associated vasculitides can be ruled out by the negative ANCA assay and the absence of vasculitis.

HYPOGAMMAGLOBULINEMIA

Early in this patient's admission, total IgG and IgM levels were low, with an IgG kappa M component and a low-to-normal IgA level. The low albumin level raised the possibility that the immunoglobulins might have been lost, perhaps into the necrotic tissues. Another explanation is decreased immunoglobulin synthesis due to poor nutrition and severe illness. Alternatively, hypogammaglobulinemia could be due to a primary immunodeficiency, such as common variable immunodeficiency (CVID). The patient had a childhood history of sinusitis and otitis media but no history of recurrent infections to suggest CVID. The diagnosis of CVID in patients with decreased levels of immunoglobulins is made only after other causes of hypogammaglobulinemia (e.g., thymoma, lymphoma, protein-losing enteropathy, proteinuria, malnutrition, and the use of immunosuppressive drugs) have been ruled out. This patient had no evidence of thymoma or lymphoma on CT. Other primary immunodeficiencies affecting neutrophil function, such as chronic granulomatous disease, seemed unlikely in view of the absence of a history of skin and other infections and her adult presentation. She received two infusions of intravenous immune globulin, with a decrease in the white-cell count, suggesting that it may have provided some benefit.

NEUTROPHILIC DERMATOSES

Pathergy associated with a neutrophilic dermatosis could account for the massive necrosis in this patient, because the affected organs and tissues had been traumatized by either the cesarean section or by pregnancy. Pathergy could explain the involvement of anatomically adjacent but developmentally distinct tissues and organs with different vascular supplies. Among the neutrophilic dermatoses, this case best fits Sweet's syndrome, which may be associated with a preceding upper respiratory

infection or with pregnancy, as well as with eosinophilic infiltrates. In neutrophilic dermatoses, the infiltration of the various inflammatory cells and their released cytokines may affect the function of the vascular supply, with thrombosis and hemorrhage often described, as they were in this case. A search of the literature revealed a few case reports of Sweet's syndrome in patients with such immunodeficiency disorders as CVID.¹⁰⁻¹²

SUMMARY

We recommended review of the patient's previous pathological specimens for evidence of neutrophilic infiltrates or localized vascular insufficiency. We also recommended immunologic evaluation, including assessment of T-cell subsets and repeated testing for immunoglobulin levels after the patient had recovered from the acute illness, as well as treatment with systemic glucocorticoids if cultures remained negative and her condition did not improve.

Dr. Daniela Kroshinsky: In view of this patient's clinical picture, the dermatologic differential diagnosis was limited to necrotizing (myonecrotic) Sweet's syndrome.¹³

SWEET'S SYNDROME

Sweet's syndrome (acute febrile neutrophilic dermatosis), is characterized by the presence of two major findings, both of which were seen in this patient: the abrupt onset of erythematous-to-violaceous, edematous cutaneous lesions, and the histopathological finding of superficial dermal edema and a dense dermal neutrophilic infiltrate. At least two of four minor criteria must also be present for the diagnosis. These include a high fever and leukocytosis, both of which this patient had; the other two criteria are a rapid response to glucocorticoids and an associated underlying condition or exposure.¹⁴ Associated conditions include cancer, especially hematologic cancers, which are the most common conditions associated with Sweet's syndrome in adults; infections, particularly upper respiratory and gastrointestinal infections but also infection with the human immunodeficiency virus; medications, especially granulocyte colony-stimulating factor and all-*trans* retinoic acid, although many others have been reported; inflammatory bowel diseases; and pregnancy.^{15,16} This patient had two potential triggers for Sweet's syndrome: an upper respiratory infection and pregnancy.

On examination of this patient, we saw distinctive edematous, erythematous plaques with very superficial purulence (Fig. 2A) on her thigh over the graft donor sites. Sweet's syndrome is distinguished from other neutrophilic dermatoses (Behçet's disease, pyoderma gangrenosum, and bowel-associated dermatosis–arthritis syndrome) by the appearance of cutaneous lesions and the presence of systemic symptoms, as well as extracutaneous involvement, including arthritis, arthralgias, myalgias, aseptic meningitis, ocular involvement, and on rare occasions, neutrophilic infiltration of the lungs, bones, kidneys, muscles, or pancreas.^{17,18} The lesions in this patient were consistent with the lesions in patients with Sweet's syndrome and, together with the systemic symptoms and extracutaneous involvement, strongly support this diagnosis.

There are many reports of Sweet's syndrome in pregnancy, all occurring in patients in the first or second trimester, in contrast to our patient's presentation, and most occurring in primigravid patients.^{15,16} Delivery typically results in resolution. A few patients had postpartum flares or recurrent Sweet's syndrome in conjunction with subsequent pregnancies. Involvement of the lungs, kidneys, and mucocutaneous surfaces developed in one patient, which improved after delivery of the baby and treatment with prednisone.¹⁹ The inflammatory process leading to necrosis of the skin and soft tissues adjacent to this patient's surgical wound, without a microbial source or response to treatment with antibiotics and with expansion on débridement, is characteristic of pathergy, which is an important clinical finding in neutrophilic dermatoses. Pathergy may occur at vascular puncture sites and limits the differential diagnosis to the category of neutrophilic dermatoses. Avoiding further débridement is critical if this patient actually has Sweet's syndrome, since the repeated trauma exacerbates the condition.

In summary, the appearance of the lesions on the thighs, high temperatures, leukocytosis with neutrophilia, pathergy of surgical and graft sites, and inflammatory neutrophilic infiltrates on pathological examination of the tissues all suggest Sweet's syndrome in this case. The process extended to the deep tissues, causing soft-tissue and muscle necrosis and mimicking a necrotizing soft-tissue infection, a condition we have called necrotizing Sweet's syndrome.¹³ It is important to

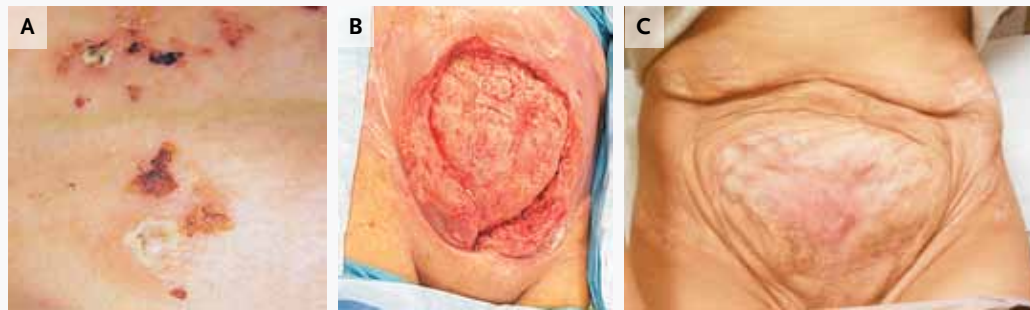


Figure 2. Clinical Photographs of the Patient.

Two months after admission, the skin-graft donor site on the right leg (Panel A) had edematous, erythematous plaques with superficial purulence, findings typical of Sweet's syndrome. After the administration of high-dose prednisone was begun, the abdominal graft became necrotic (Panel B, courtesy of Brian Rothschild, M.D.). Five months after the patient was discharged from the hospital, the skin was completely healed (Panel C, courtesy of Melissa Hull, M.D.).

rule out an associated condition, such as a hematologic cancer.

To rule out atypical infections, we obtained a biopsy specimen from a thigh lesion for histologic examination and culture. We also asked our colleagues in dermatopathology to review the previous surgical specimens to see if there were features consistent with Sweet's syndrome.

CLINICAL DIAGNOSIS

Necrotizing soft-tissue infection.

DRS. WONG AND KROSHINSKY'S DIAGNOSIS

Sweet's syndrome with extracutaneous involvement and soft-tissue and muscle necrosis.

PATHOLOGICAL DISCUSSION

Dr. Devon C. Gimbel: The placenta was initially examined because of an elevated maternal white-cell count during labor. There was no chorioamnionitis or fetal inflammatory reaction. Instead, a striking acute inflammation, with neutrophils, eosinophils, and abscess formation, was noted in the decidua basalis, with adjacent zones of necrosis (Fig. 3). The inflammation was unusual in that it was limited to the maternal surface of the placenta and did not involve the placental parenchyma. Staining for organisms (bacteria, fungi, and acid-fast bacilli) was negative.

The uterus and rectus muscle were initially examined because of concern about infection. Gross examination revealed necrosis involving almost the entire anterior half of the uterus. Microscopical examination (Fig. 4A, 4B, and 4C) revealed large areas of abscess formation with intact and fragmented neutrophils and eosinophils. The myometrial smooth muscle and the rectus skeletal muscle showed extensive acute inflammation with multiple foci of myonecrosis. Staining for bacteria and fungi was negative.

Review of the skin-biopsy specimen (Fig. 4D and 4E) showed an intact epidermis. There was papillary dermal edema and a superficial and a mid-dermal inflammatory infiltrate composed predominantly of mature neutrophils and eosinophils. Staining and cultures for organisms were negative.

Histologic features common to all the specimens included a dense inflammatory infiltrate composed of neutrophils and eosinophils, abscess formation, and tissue necrosis in the extracutaneous specimens. Although the first consideration was an infectious process, particularly pyogenic bacteria, sterile tissue sent from the operating room was always culture-negative, and no organisms were seen on histologic sections.

Neutrophilic dermatoses are characterized histologically by a sterile neutrophilic infiltrate, which can be very dense and may be associated with extensive tissue damage.²⁰ Although neutrophilic dermatoses are usually confined to the skin, ex-

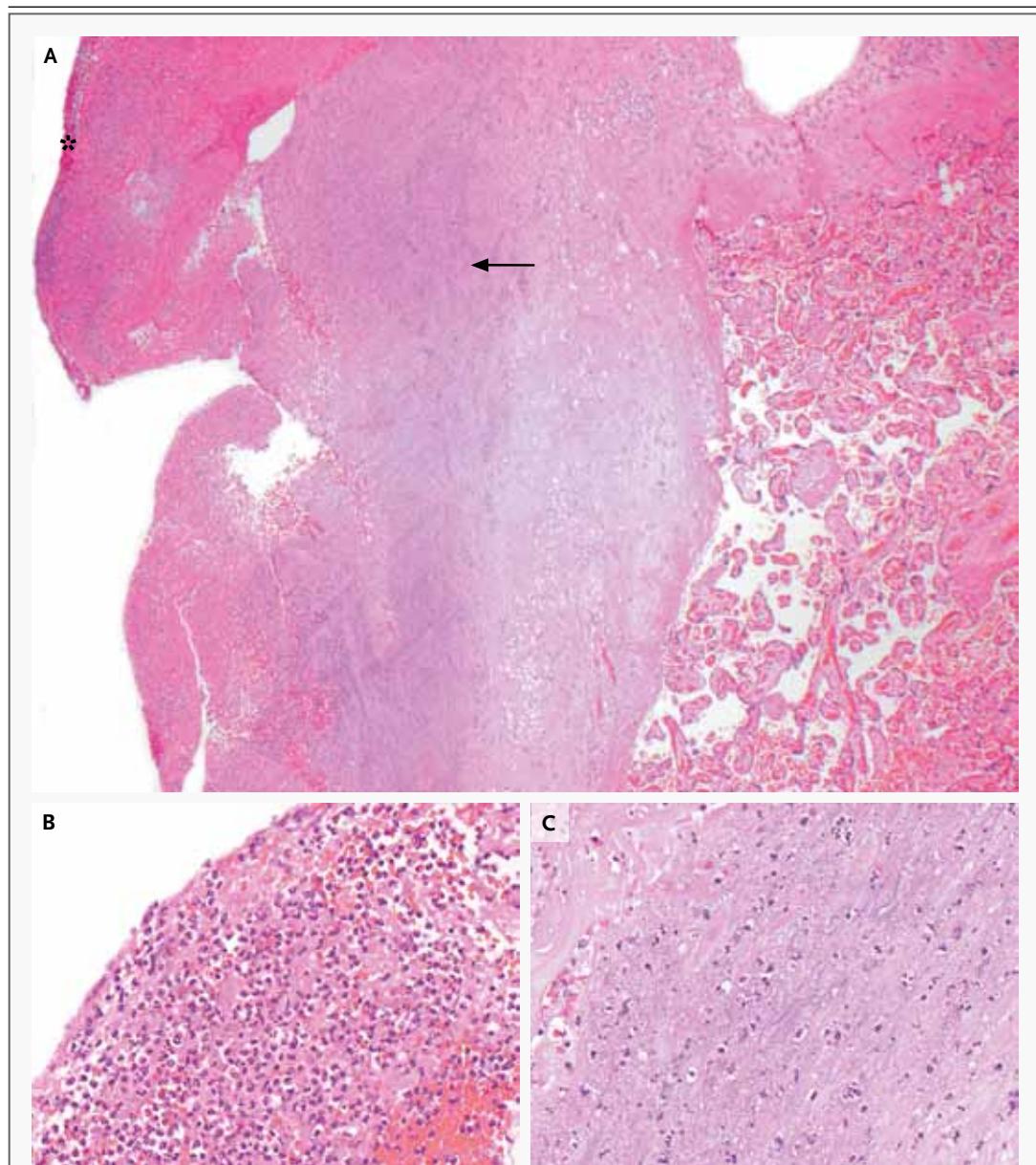


Figure 3. Pathological Features of the Placenta (Hematoxylin and Eosin).

A representative section of the placenta shows acute inflammation, with abscess formation in the decidua basalis (Panel A, asterisk; and Panel B) and adjacent zones of necrosis (Panel A, arrow; and Panel C).

tracutaneous involvement has been reported in nearly every organ of the body.^{17,18}

The absence of epidermal ulceration and of vasculitis, as well as the clinical appearance of this patient's skin lesions, argue against pyoderma gangrenosum and are features consistent with Sweet's syndrome. The findings in the placenta, uterus, and rectus muscle were consistent

with Sweet's syndrome with extracutaneous involvement.

DISCUSSION OF MANAGEMENT

Dr. Kroshinsky: Sweet's syndrome tends to resolve spontaneously over a period of weeks to months, particularly if the underlying trigger is treated or

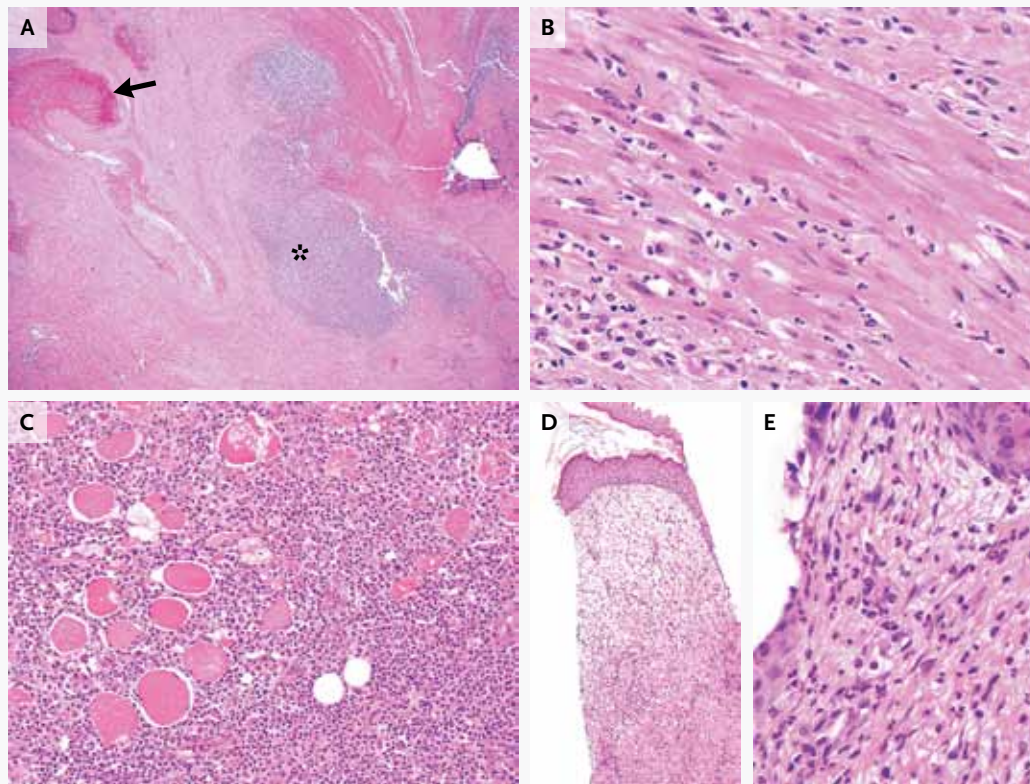


Figure 4. Pathological Features of the Uterus, Soft Tissues, and Skin (Hematoxylin and Eosin).

In Panel A, large areas of abscess formation (asterisk) and adjacent thrombosed blood vessels (arrow) involve the anterior uterus. The myometrial smooth muscle (Panel B) and the rectus skeletal muscle (Panel C) show extensive acute inflammation, with multiple foci of myonecrosis. In Panel D, a punch-biopsy specimen of the skin shows an intact epidermis with no ulceration, with papillary dermal edema, and with a superficial and a mid-dermal inflammatory infiltrate. The dermal inflammatory infiltrate is composed predominantly of mature neutrophils (Panel E).

removed. Recurrences occur in about 30% of cases and in up to 50% of cases associated with a hematologic cancer.²¹ Antibiotics are not effective unless the trigger is a bacterial infection. The administration of high-dose prednisone (usually 1 to 2 mg per kilogram of body weight per day) is the first-line treatment and is also a diagnostic test; it leads to improvement in clinical features and laboratory abnormalities within 24 to 48 hours. Once the patient has stabilized, the dose is tapered over a period of several weeks. Other agents that are effective include dapsone, cyclosporine, potassium iodide, colchicine, allopurinol, and thalidomide. Intravenous immune globulin has been used mainly in pediatric cases associated with immunodeficiency and may have been transiently effective in this patient.

Treatment with high-dose glucocorticoids can

cause delayed wound healing and infections, particularly when patients have underlying immunosuppression or wounds that have been débrided. The administration of cyclosporine can be added in patients who have wounds that require grafting, to prevent graft loss.¹³ Cyclosporine produces a rapid response, has few side effects for short courses, and in studies in animals produces less impairment of wound healing than do glucocorticoids.²² In this patient, with large skin grafts and hypogammaglobulinemia, I recommended initial treatment with both cyclosporine and prednisone.

The patient was treated with 120 mg of prednisone daily, rapidly tapered to 60 mg. Fevers and leukocytosis improved, but pathergy at the wound sites persisted, with graft failure (Fig. 2B). The administration of cyclosporine was begun after

10 days of treatment with prednisone, and prednisone was gradually tapered.

Dr. Georgios Kasotakis (Surgery): A repeat skin graft was performed. The lower half of the rectus muscle and sheath were reexcised because of recurrent myonecrosis. The graft was successful and the patient was discharged home after 12 weeks of hospitalization. She will require reconstructive plastic surgery of the abdominal wall (Fig. 2C).

Dr. Sarita U. Patil (Allergy and Immunology): The administration of immunosuppressive agents was tapered and discontinued 6 weeks after discharge, with no recurrence of the skin lesions. One month later, the patient was seen in the allergy and immunology clinic for evaluation of hypogammaglobulinemia. There were continued low levels of IgG, IgA, and IgM; protective tetanus, diphtheria, and pneumococcal antibody titers; and a new IgG lambda M component of 0.03 g per deciliter. Flow cytometry of blood revealed normal T-cell subsets, with 5% CD19+ B cells.

We thought that persistent hypogammaglobulinemia in this patient with recent immunosuppression was most likely secondary to her illness and immunosuppressive medications; the differential diagnoses included monoclonal gammopathy and CVID, although specific antibody titers are typically low in cases of CVID. Since there was no evidence of recurrent severe infections or infections with unusual organisms, we elected to repeat the evaluation later. One year after the patient's admission, levels of all immunoglobulins are normal and there is no M component. Thus, there is no evidence of an immunodeficiency disorder. The patient feels well, is fully active and able to care for her child, and is awaiting plastic surgical reconstruction of the abdominal wall.

Dr. Nancy Lee Harris (Pathology): As a pathologist, I wonder if it would have been possible to make this diagnosis sooner or to consider it in the future when we see necrotizing soft-tissue lesions without evidence of infection.

Dr. Drucilla J. Roberts (Pathology): This placenta was very unusual. I have never before seen an abscess on the maternal side of the placenta. We discussed the case with the patient's caregivers, and clinical suspicion of infection was so high that we didn't seriously consider alternative diagnoses. Since the findings were not consistent with a typical ascending infection of the placenta, and since there were numerous eosinophils, I wondered about a parasitic infection.

Dr. Gímbel: For dermatopathologists, Sweet's syndrome is always considered when there is a dense neutrophilic cutaneous infiltrate in a febrile patient with sterile cultures. For general pathologists, this diagnosis would seldom be considered, for two reasons. First, Sweet's syndrome rarely presents with such extensive extracutaneous manifestations, and to my knowledge, there have been no reports of placental involvement. Second, the skin manifestations in this patient appeared after other organ involvement, which is unusual. I think the lesson for pathologists is to be aware that Sweet's syndrome, although it is primarily a disorder of the skin, can affect other organs, so in a case with a dense neutrophilic infiltrate and no evidence of infection, consider this diagnosis.

ANATOMICAL DIAGNOSIS

Sweet's syndrome, with extensive necrotizing extracutaneous involvement (soft tissue, skeletal muscle, uterus, and placenta).

This case was discussed at the Obstetrics and Gynecology Grand Rounds.

Dr. Robbins reports receiving royalties from Wolters Kluwer for UpToDate. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Drs. Drucilla Roberts, Michael Greene, Georgios Kasotakis, Lyn Duncan, Sarita Patil, Jennifer Moore, Anjali Kaimal, and Alyssa Letourneau for assistance with the case history and the organization of the conference.

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