CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 22-2024: A 30-Year-Old Woman with Postpartum Fever, Abdominal Pain, and Skin Ulcers

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CME

PRESENTATION OF CASE

Dr. Molly Siegel (Obstetrics, Gynecology, and Reproductive Biology): A 30-year-old woman (gravida 1, para 1) was admitted to this hospital 6 days after the delivery of her baby because of fever and abdominal pain.

The patient had received routine prenatal care at another hospital. Laboratory test results obtained 6 months before this admission are shown in Table 1.

Six days before this admission, the patient went into labor at 35 weeks 3 days' gestation and was brought to the emergency department of this hospital. Laboratory test results are shown in Table 1. The result of testing for group B streptococcus colonization was not available; empirical treatment with vancomycin was administered. Spontaneous rupture of membranes occurred, resulting in clear, odorless fluid. Eight hours later, the patient vaginally delivered a male infant and an intact placenta. She had lost an estimated 300 ml of blood, and she had a second-degree perineal laceration, which was repaired. The baby was large for gestational age, weighing 3575 g. On the second postpartum day, the patient was discharged home.

During the subsequent 4 days, the patient pumped breast milk and visited her baby in the special care nursery of this hospital daily while he was being treated for prematurity and feeding difficulties. She had mild diffuse abdominal and pelvic cramping and vaginal bleeding with occasional clots. On the day of the current admission, fever and chills developed, and the patient returned to the emergency department of this hospital. Review of systems was notable for small, painful bumps in the inguinal area on both sides that had developed during pregnancy and had intermittently drained blood and pus. She also had leg swelling that had abated since childbirth.

On examination, the temporal temperature was 38.7°C and the blood pressure

125/80 mm Hg. The lungs were clear on auscultation, the breasts nontender, the uterine fundus mildly tender, and the legs mildly swollen. Tender, erythematous pustules that drained yellow, purulent fluid were present in the inguinal area on the right side; scarring was present in the inguinal area on the left side. The repaired perineal laceration was healing well. The white-cell count was 22,940 per microliter (reference range, 4500 to 11,000). Other laboratory test results are shown in Table 1. Blood and cervical cultures were obtained.

The patient had rosacea, acne, and hidradenitis suppurativa. Episodes of diverticulitis had occurred 5 years and 2 years before this admission, and an episode of epiploic appendagitis had occurred 10 weeks before this admission. She was taking prenatal vitamins, topical azelaic acid, and acetaminophen and ibuprofen as needed for abdominal pain. Amoxicillin and cephalexin had caused hives. She worked as an educator and lived with her husband and dog in a suburban area of New England. She did not vape or smoke cigarettes, drink alcohol, or use illicit drugs. Her father and paternal grandfather had arthritis that had been diagnosed in early adulthood, her brother had Crohn's disease, and another brother had neurofibromatosis. Her mother was healthy.

Dr. Rory L. Cochran: Computed tomography (CT) of the abdomen and pelvis, performed after the administration of intravenous contrast material, showed normal postpartum uterine enlargement, with mild adjacent fat stranding.

Dr. Siegel: Empirical treatment with gentamicin and clindamycin was started. The patient was admitted to the hospital with a presumptive diagnosis of endometritis. Fever, abdominal pain, and leukocytosis did not abate, and vancomycin was added on hospital day 3. A test dose of cefepime was administered on hospital day 4. When the patient did not have an allergic reaction to the test dose, gentamicin and clindamycin were stopped, and she was treated with vancomycin, cefepime, and metronidazole.

Dr. Melanie C. Kwan: On hospital day 6, an endometrial biopsy was performed. Pathological examination of the biopsy specimen revealed neutrophilic debris that included fragments of stroma with a dense neutrophilic infiltrate.

Dr. Cochran: Magnetic resonance imaging (MRI) and magnetic resonance angiography of the pelvis, performed before and after the administration of intravenous contrast material, showed mild ascites (Fig. 1A) and anasarca (Fig. 1B). No evidence of retained products of conception, fluid collections, or venous or arterial thromboses was observed. Four days later, magnetic resonance angiography of the pelvis revealed increased ascites and anasarca, as well as two new fluid collections: a peripherally enhancing left parametrial collection that measured 6.3 cm in largest dimension (Fig. 1C) and a collection located near the right uterocervical junction that measured 3.2 cm in largest dimension (Fig. 1D).

Dr. Siegel: Treatment with cefepime and metronidazole was stopped, vancomycin was continued, and meropenem was started because of ongoing fever. A percutaneous catheter was inserted into the left parametrial fluid collection, and 20 ml of purulent fluid was drained; cultures showed no growth.

On hospital day 11, abdominal pain increased, and shortness of breath developed. The oxygen saturation was 86% while the patient was breathing ambient air. Supplemental oxygen was administered through a nasal cannula at a rate of 2 liters per minute, and the oxygen saturation increased to 91%. The temporal temperature was 36.7°C, the blood pressure 109/58 mm Hg, the heart rate 112 beats per minute, and the respiratory rate 24 breaths per minute. The patient appeared tired and ill. Marked jugular venous distention was present. The heart sounds were tachycardic and regular, and the lungs were clear on auscultation. The abdomen was distended and diffusely tender on palpation, and the percutaneous catheter inserted along the midline of the pelvis had scant purulent drainage. Diffuse anasarca and symmetric 1+ ankle edema were present. Laboratory test results are shown in Table 1. Transthoracic echocardiography showed normal biventricular function; however, the right atrium and right ventricle were dilated, and the interventricular septum was flattened during diastole. The main pulmonary artery and its branches were also dilated.

Dr. Cochran: CT pulmonary angiography showed bibasilar subsegmental atelectasis and no pulmonary embolism. CT of the abdomen and pelvis revealed increased ascites and anasarca, new splenomegaly, new hepatomegaly with heterogeneous peripheral enhancement (Fig. 1E), and mild

Table 1. Laboratory Data.*

Variable	Reference Range, This Hospital†	6 Mo before This Admission	6 Days before This Admission	On This Admission	Hospital Day 11
Blood					
White-cell count (per μl)	4500–11,000	11,820	16,180	22,940	34,720
Differential count (per μl)					
Neutrophils	1800–7700	—	13,060	19,230	33,470
Lymphocytes	1000–4800	—	1650	1140	310
Monocytes	200–1200	—	1090	160	0
Eosinophils	0–900	—	170	360	620
Basophils	0–300	—	70	90	0
Hemoglobin (g/dl)	12.0–16.0	13.9	13.4	8.5	8.1
Hematocrit (%)	36.0–46.0	41.3	39.2	25.5	24.9
Platelet count (per μl)	150,000–400,000	406,000	358,000	456,000	590,000
Prothrombin time (sec)	11.5–14.5	—	—	—	18.2
Prothrombin-time international normalized ratio	0.9–1.1	—	—	—	1.5
Activated partial-thromboplastin time (sec)	22.0–36.0	—	—	—	35.4
D-dimer (ng/ml)	0–500	—	—	—	3392
Fibrinogen (mg/dl)	150–400	—	—	—	610
Erythrocyte sedimentation rate (mm/hr)	0–20	—	—	—	55
C-reactive protein (mg/dl)	0.0–0.8	—	—	—	132.0
Lactate dehydrogenase (U/liter)	110–210	—	—	—	202
Haptoglobin (mg/dl)	30–200	—	—	—	484
Sodium (mmol/liter)	135–145	—	—	141	144
Potassium (mmol/liter)	3.4–5.0	—	—	3.2	3.4
Chloride (mmol/liter)	98–108	—	—	103	107
Carbon dioxide (mmol/liter)	23–32	—	—	22	24
Urea nitrogen (mg/dl)	8–25	—	—	11	12
Creatinine (mg/dl)	0.60–1.50	—	—	0.51	0.73
Glucose (mg/dl)	70–110	—	—	126	113
Albumin (g/dl)	3.3–5.0	—	—	3.3	1.9
Total protein (g/dl)	6.0–8.3	—	—	6.1	4.9
Aspartate aminotransferase (U/liter)	9–32	—	—	17	24
Alanine aminotransferase (U/liter)	7–33	—	—	20	16
Alkaline phosphatase (U/liter)	30–100	—	—	393	670
Total bilirubin (mg/dl)	0.0–1.0	—	—	0.2	1.0
γ-Glutamyltransferase (U/liter)	5–36	—	—	—	102
Lactic acid (mmol/liter)	0.5–2.0	—	—	0.8	1.3
N-terminal pro–B-type natriuretic peptide (pg/ml)	0–450	—	—	—	9006
Rubella	Nonimmune	Nonimmune	—	—	—
Syphilis	Negative	Negative	—	—	—
Hepatitis B virus surface antigen	Negative	Negative	—	—	—
Human immunodeficiency virus	Negative	Negative	—	—	—

Table 1. (Continued.)

Variable	Reference Range, This Hospital†	6 Mo before This Admission	6 Days before This Admission	On This Admission	Hospital Day 11
Urine					
Color	Yellow	—	—	Yellow	—
Clarity	Clear	—	—	Clear	—
pH	6.0	—	—	5.5	—
Specific gravity	1.012	—	—	1.015	—
Glucose	Negative	—	—	Negative	—
Ketones	Negative	—	—	Trace	—
Leukocyte esterase	Negative	—	—	1+	—
Nitrite	Negative	—	—	Negative	—
Blood	Negative	—	—	1+	—
Protein	Negative	—	—	Negative	—
Erythrocytes (per high-power field)	0–2	—	—	3–5	—
Leukocytes (per high-power field)	0–9	—	—	<10	—
Cervical swab					
Gonorrhea	Negative	Negative	—	Negative	—
Chlamydia	Negative	Negative	—	Negative	—

* 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 glucose to millimoles per liter, multiply by 0.05551. To convert the values for bilirubin to micromoles per liter, multiply by 17.1. To convert the values for lactic acid to milligrams per deciliter, divide by 0.1110.

† 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.

periportal edema. The percutaneously drained left parametrial fluid collection had resolved; the fluid collection at the right uterocervical junction remained unchanged. Results of liver-function tests were abnormal, and magnetic resonance cholangiopancreatography revealed multiple new intrahepatic fluid collections, which were hyperintense on T2-weighted imaging (Fig. 1F).

Dr. Daniela Kroshinsky: The next day, new edematous, violaceous, friable plaques developed on the left upper arm at the site where a previous peripheral intravenous catheter had been inserted. A new erythematous-to-violaceous bulla on the left abdominal wall also developed. The plaques located on the left arm subsequently ulcerated (Fig. 2A), as did new skin lesions located in the right inguinal crease and on the mons pubis. During the next 2 days, the bulla located on the left abdominal wall also began to ulcerate, and another similar lesion formed around the site where the percutaneous drainage catheter had been inserted. The ulcers involving the left upper arm, right inguinal crease, and mons pubis increased in area and depth, and a new ulcer formed in the left inguinal crease.

Dr. Siegel: Treatment with intravenous furosemide was administered. Vancomycin was stopped, meropenem was continued, and daptomycin and micafungin were started.

A diagnostic test was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Joseph F. Merola: This previously healthy 30-year-old woman was admitted to the hospital 6 days postpartum because of fever and abdominal pain, which were early symptoms of a complex and evolving process. In constructing a differential diagnosis, I will consider pregnancy-related infections and other infections. Given that the drained intraabdominal fluid collection was sterile and the response to broad-spectrum antimicrobial therapy was poor, I will also consider noninfectious causes of her syndrome. I suspect that the

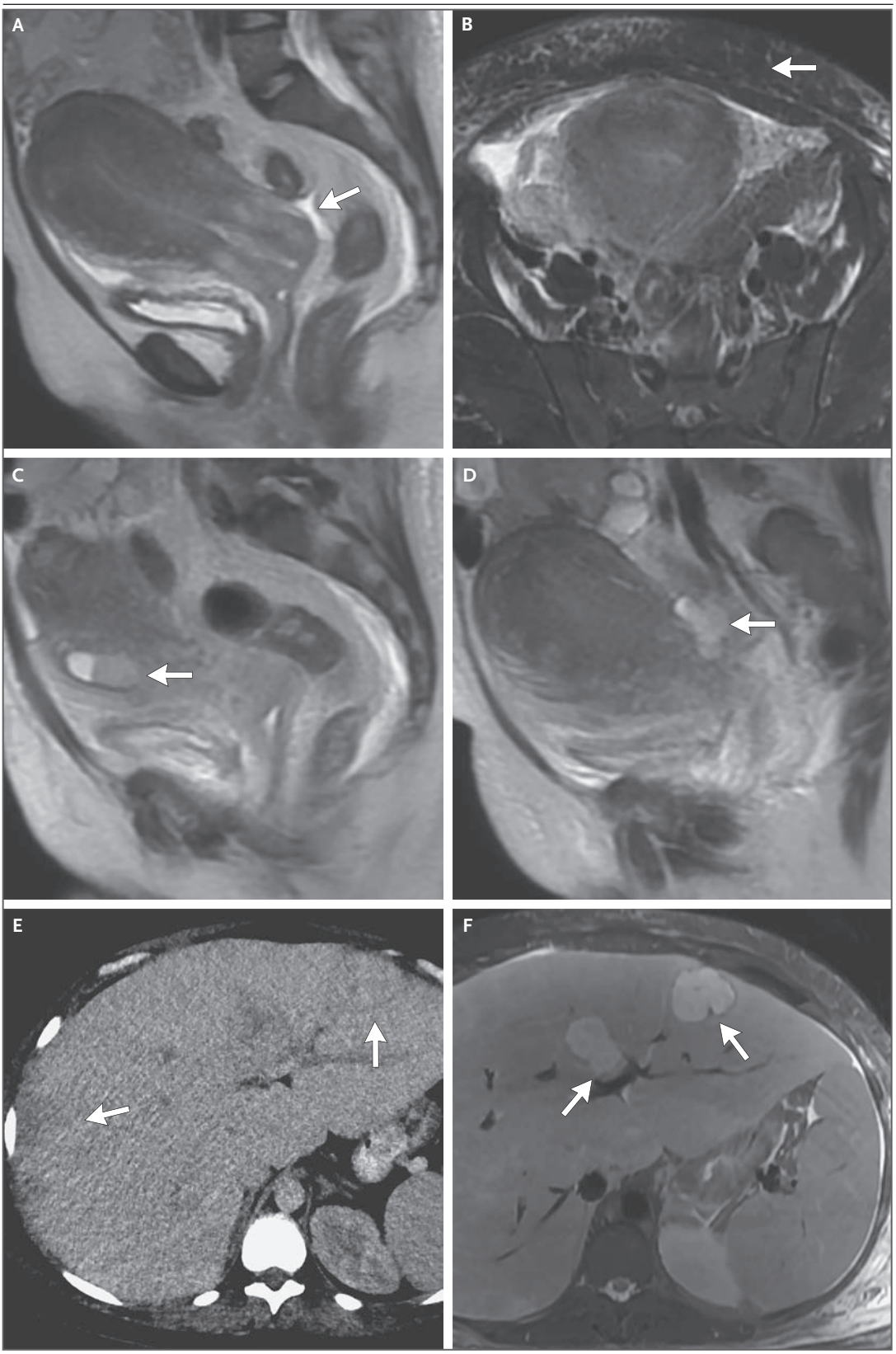

Figure 1 (facing page). Imaging Studies of the Abdomen and Pelvis.

MRI of the pelvis was performed. A T2-weighted sagittal image (Panel A) shows small-volume ascites (arrow). A fat-saturated T2-weighted axial image (Panel B) shows body-wall edema (arrow), as well as ascites. A T2-weighted sagittal image of the left side of the pelvis (Panel C) shows a layering left parametrial fluid collection (arrow). A T2-weighted sagittal image of the right side of the pelvis (Panel D) shows a fluid collection at the right uterocervical junction (arrow). CT of the abdomen and pelvis was also performed. A contrast-enhanced axial image (Panel E) shows diffuse enlargement of the liver with heterogeneous peripheral enhancement (arrows). Magnetic resonance cholangiopancreatography was performed. A fat-saturated T2-weighted axial image (Panel F) shows multiple hyperintense intrahepatic fluid collections (arrows).

patient's history of hidradenitis suppurativa, epiploic appendagitis, moderate peripartum leukocytosis, and preterm labor and her family history of early arthritis and inflammatory bowel disease may be important clues in this case. Finally, I will consider systemic inflammatory disease with skin manifestations.

COMMON POSTPARTUM INFECTIONS

In the early postpartum period, the development of fever, leukocytosis, and neutrophilia is most likely to be a response to infection. In this patient, the abdominal pain and history of diverticulitis could suggest an intraabdominal infection. The elevated alkaline phosphatase and γ-glutamyltransferase levels could suggest a hepatobiliary source. The patient is also at risk for mastitis, wound infection, cystitis, and pyelonephritis. However, her history and findings on physical examination, laboratory testing of blood and urine, and imaging studies are not consistent with any of these common infections.

The most likely cause of fever, leukocytosis, and abdominal pain in the early postpartum period is a gynecologic infection such as endometritis. Pyometra is a rare cause of these manifestations. Although endometritis is usually a clinical diagnosis, the lack of response to antimicrobial therapy makes this diagnosis unlikely. However, an endometrial biopsy specimen showed predominantly neutrophilic debris with a dense neutrophilic infiltrate. These histopathological findings do not allow us to rule out a diagnosis of endometritis.

OTHER CAUSES OF POSTPARTUM FEVER

Despite the administration of empirical broad-spectrum antimicrobial therapy, new intraabdominal fluid collections, tachycardia, tachypnea, and hypoxemia developed. Cultures of blood, genital skin, endometrial tissue, and intraabdominal fluid samples were negative. However, atypical and disseminated infections, such as fungal and mycobacterial infections, should be considered. The patient is not known to be immunocompromised and does not have apparent risk factors for these infections.

Noninfectious causes — such as phlebitis, venous thromboembolism, drug fever, hypersensitivity reactions, and cancer — should also be considered. However, these diagnoses are unlikely on the basis of the history and examination findings, and they are not associated with abdominal pain. An inflammatory or autoimmune disease is possible; I will consider these later.

The patient had early skin manifestations, including tender, erythematous pustules in the right inguinal area and scarring in the left inguinal area. Symptoms of hidradenitis suppurativa worsen during the postpartum period in 20 to 60% of cases,[1] and the skin manifestations seen in this patient could be consistent with a flare or infection of lesions associated with hidradenitis suppurativa. Drainage of yellow, purulent fluid in the context of fever increases the likelihood of infected hidradenitis suppurativa–associated lesions as well as other skin diseases (e.g., folliculitis and furunculosis), other typical or atypical skin infections, and sexually transmitted infections (e.g., granuloma inguinale). Although these diseases can cause fever, they are not associated with abdominal pain.

SYSTEMIC DISEASES WITH SKIN MANIFESTATIONS

As this patient's hospital course progressed, signs of systemic disease emerged: ascites, anasarca, hepatosplenomegaly, laboratory evidence of early disseminated intravascular coagulation, and possible right heart failure with associated pulmonary hypertension. These findings could be clinical signs of an evolving dysregulated systemic inflammatory process. Although infection had been an appropriate initial consideration, the negative cultures and the progression of disease despite multiple lines of antimicrobial therapy suggest the possibility of inflammatory and autoimmune processes.

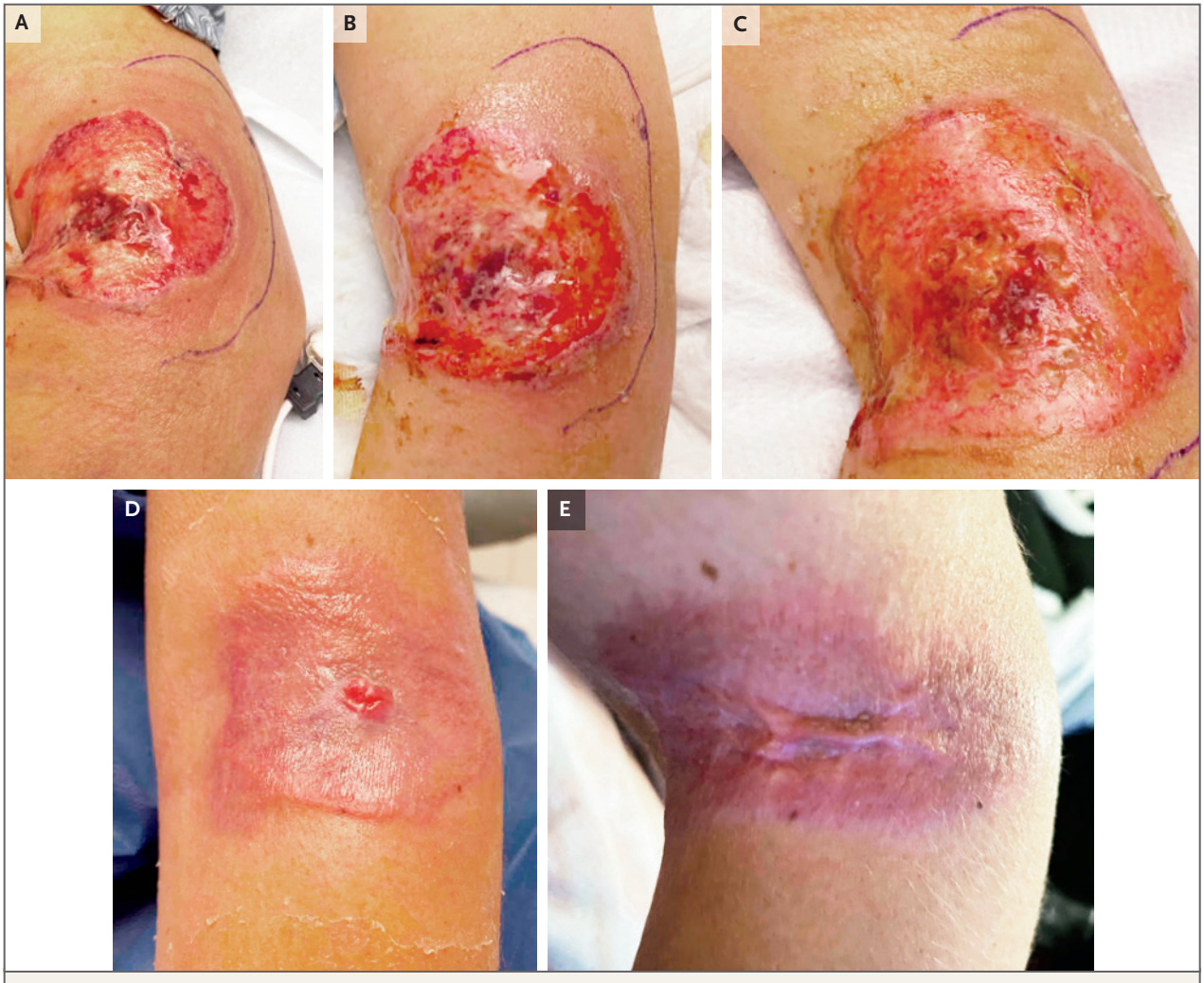

Figure 2. Clinical Photographs of the Lesion on the Left Upper Arm before and after Treatment.

Before treatment (Panel A), the lesion on the left upper arm is an edematous ulcer with a rolled, violaceous, friable border and surrounding erythema and edema. On day 2 of the glucocorticoid course (Panel B), the lesion is a shallow, well-demarcated ulcer with a reduced violaceous border and greatly diminished surrounding inflammation. On day 3 of the glucocorticoid course (Panel C), the lesion is a well-demarcated, clean-based erosion with central ulceration and early marginal reepithelialization. On day 24 of the glucocorticoid course (Panel D), the lesion has nearly complete reepithelialization, with a small area of central hypergranulation. Two months after completion of the glucocorticoid course (Panel E), the lesion is a pink patch with a central linear plaque; the appearance is consistent with a hypertrophic scar.

INFLAMMATORY AND AUTOIMMUNE PROCESSES

Autoinflammatory syndromes such as PAPA syndrome (pyogenic arthritis, pyoderma gangrenosum, and acne) and PASH syndrome (pyoderma gangrenosum, acne, and hidradenitis suppurativa) can be considered. PAPA syndrome would typically develop earlier than the process seen in this patient, but the condition has incomplete genetic penetrance, and testing for the gene that encodes proline–serine–threonine phosphatase–interacting protein 1 (*PSTPIP1*) should be considered. The patient has a family history of early arthritis, but she does not have features of inflammatory arthritis, so the diagnosis of PAPA syndrome is unlikely. PASH syndrome is possible, but no genetic testing for this condition is available.

The differential diagnosis associated with the morphologic features observed in this case — bullous and necrotic skin lesions and violaceous ulcerated plaques with scalloped, undermined

borders — includes inflammatory causes (e.g., neutrophilic dermatoses), uncommon infections (e.g., ecthyma gangrenosum and deep fungal and mycobacterial infections), necrotizing vaculitides, and vasculopathic conditions. The presence of microscopic hematuria, markedly elevated levels of inflammatory markers, and a pulmonary process with hypoxemia makes systemic vasculitis possible; however, the skin lesions are not consistent with vasculitis, and no evidence of vasculitis was identified on endometrial biopsy.

PATHERGY

It is notable that bullous, necrotic, and ulcerating skin lesions occurred at sites of previous minor trauma, including sites where a peripheral intravenous catheter and a percutaneous catheter had been inserted. This phenomenon is known as pathergy. The presence of pathergy-related ulcers narrows the differential diagnosis to neutrophilic dermatoses, which include pyoderma gangrenosum, cutaneous Crohn's disease, Behçet's disease, variants of Sweet's syndrome, and other neutrophilic autoinflammatory syndromes. This patient has a family history of Crohn's disease. In addition, the risk of inflammatory bowel disease is increased among patients with hidradenitis suppurativa,[2] and the involvement of the inguinal creases is reminiscent of the "knifelike" ulcers described in patients with cutaneous Crohn's disease. However, she does not have bloody diarrhea, and imaging studies did not show inflammation of the gastrointestinal tract. Therefore, a diagnosis of inflammatory bowel disease is unlikely, although future workup, including colonoscopy, should be considered.

I favor the diagnosis of systemic Sweet's syndrome with extracutaneous manifestations. This acute febrile neutrophilic dermatosis with pathergy can be associated with pregnancy. This patient's fever, leukocytosis, elevated levels of inflammatory markers, pregnancy-associated disease, and possible pulmonary features are consistent with this diagnosis.[3,4] Although Sweet's syndrome has diagnostic criteria, the diagnosis largely relies on ruling out other causes, which can present both diagnostic and therapeutic challenges. I would recommend a skin biopsy to establish the diagnosis of Sweet's syndrome. In addition, a trial of glucocorticoids is both diagnostic and therapeutic in a patient with Sweet's syndrome.

DR. JOSEPH F. MEROLA'S DIAGNOSIS

Sweet's syndrome.

PATHOLOGICAL DISCUSSION

Dr. Kwan: A punch biopsy of skin from the edge of a nonhealing ulcer on the left upper arm was performed. Histopathological examination revealed a dense inflammatory infiltrate throughout the biopsy specimen (Fig. 3A) with epidermal ulceration and erosion (Fig. 3B). No papillary dermal edema or vasculitis was seen. The dermal inflammatory infiltrate was composed of neutrophils; other inflammatory cells, such as lymphocytes, histiocytes, and plasma cells, were not observed (Fig. 3C). An infectious cause was considered because of the dense neutrophilic infiltrate; however, special staining for microorganisms (bacteria, fungi, and acid-fast bacilli) was negative, and concurrent tissue cultures showed no growth. Taken together, the findings are consistent with Sweet's syndrome, pyoderma gangrenosum, or another neutrophilic dermatosis.

Sweet's syndrome, initially described as acute febrile neutrophilic dermatosis,[5] can be associated with various conditions, including pregnancy.[6-9] On histopathological examination, Sweet's syndrome is characterized by a dense, diffuse dermal neutrophilic infiltrate that can extend into the subcutis, mimicking the appearance of an abscess.[10] Vasculitis is not typically seen in patients with Sweet's syndrome[9,11] but has been reported.[12,13] Other inflammatory cells, such as lymphocytes and eosinophils, may be present.[9,10] Another diagnostic consideration is pyoderma gangrenosum, which characteristically manifests as an ulcerative lesion undermined by a purulent exudate.[11] In patients with pyoderma gangrenosum, a prototypical but nonspecific lymphocytic or leukocytoclastic vasculitis at the edge of the ulcer can be detected, a feature that is not characteristic of Sweet's syndrome.[9,10] Pyoderma gangrenosum is often associated with a mixed inflammatory infiltrate with plasma cells and eosinophils.[10] Both pyoderma gangrenosum and Sweet's syndrome can have extracutaneous manifestations and show considerable histopathological overlap. This patient's biopsy specimen had features of both Sweet's syndrome and pyoderma gangrenosum but did not have evidence of vas-

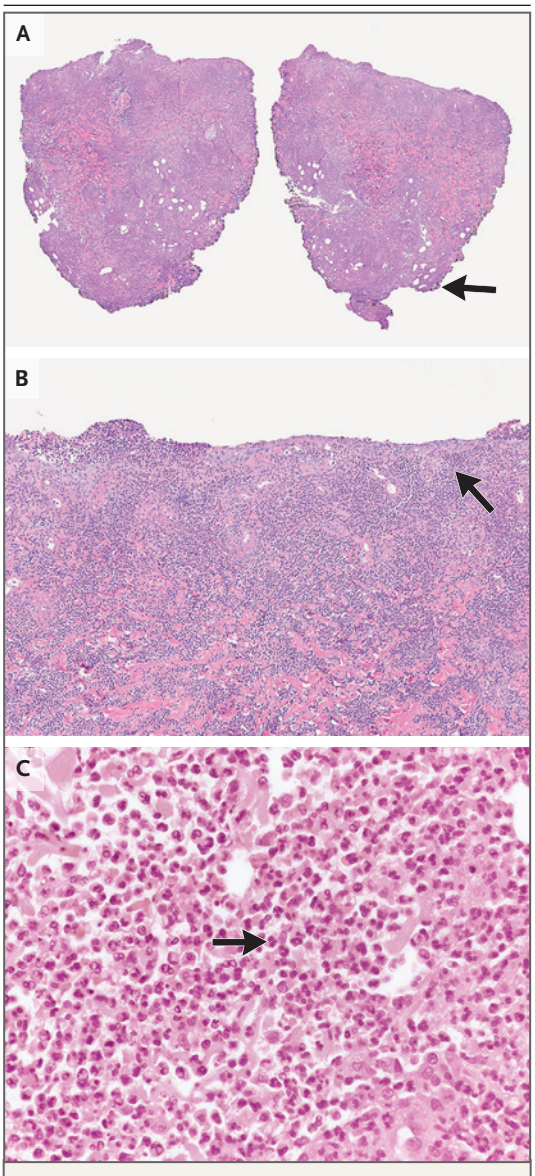

Figure 3. Skin-Biopsy Specimen.

Hematoxylin and eosin staining of sections of the skin-biopsy specimen shows a dense inflammatory infiltrate that extends into the subcutis (Panel A, arrow). The skin surface has ulceration and erosion (Panel B, arrow). At high magnification, the inflammatory infiltrate is shown to be composed of neutrophils (Panel C, arrow), without conspicuous lymphocytes, histiocytes, or plasma cells.

culitis or mixed inflammatory cells, which makes Sweet's syndrome the most likely histopathological diagnosis.

PATHOLOGICAL DIAGNOSIS

Sweet's syndrome.

DISCUSSION OF MANAGEMENT

Dr. Kroshinsky: Neutrophilic dermatoses are conditions characterized by cutaneous neutrophilic infiltration without an infectious cause, with possible involvement of other organs. Many skin diseases broadly fall under this category, but in practice, the term is largely used to refer to Sweet's syndrome, pyoderma gangrenosum, Behçet's disease, bowel-associated dermatosis–arthritis syndrome, and rheumatoid neutrophilic dermatitis. Sweet's syndrome, which is considered to be a hypersensitivity reaction to a predisposing factor, can occur in all age groups, but it usually occurs in patients 30 to 60 years of age and has a predilection for women. Up to 30% of cases are associated with cancer (particularly hematologic cancers, such as acute myeloid leukemia and myelodysplasia), 25% of cases with a triggering infection (mainly in children), 10% of cases with drug exposure (particularly exposure to granulocyte colony-stimulating factor, all-trans retinoic acid, or bortezomib), and rare cases with inflammatory bowel disease, connective-tissue diseases, or pregnancy.[14,15]

The skin lesions that occur in patients with Sweet's syndrome are typically tender, edematous, erythematous-to-violaceous papules and plaques that enlarge and can take on a pseudovesicular, pseudopustular, targetoid, cellulitic, panniculitic, or ulcerative phenotype. Although the lesions favor the head and neck, they can arise anywhere on the body and are associated with fever in up to 80% of cases.[14] The diagnosis of Sweet's syndrome is based on the presence of two major and two minor criteria (Table 2).[16] Systemic features frequently arise, including arthralgias, arthritis, myalgias, ocular involvement, alveolitis, multifocal sterile osteomyelitis, or mesangial glomerulonephritis. In rare cases, myositis, aseptic meningitis, encephalitis, sensorineural hearing loss, hepatitis, pancreatitis, ileitis, colitis, myocardial infiltration, aortitis, or another systemic manifestation occurs.[17,18] Patients with Sweet's syndrome may have symptoms of sepsis and have

no response to broad-spectrum antimicrobial therapy, as in this case.[14] A variant of Sweet's syndrome involving necrotizing neutrophilic dermatosis that mimics necrotizing fasciitis has been described, and patients with this variant have rapidly progressive deep-tissue infiltration, inflammation, and necrosis.[8,19]

Another feature unique to neutrophilic dermatoses is the phenomenon of pathergy, which is a nonspecific inflammatory response to intradermal trauma that manifests as papules, plaques, pustules, or ulceration. Pathergy can occur with minor trauma, such as that caused by the insertion of a peripheral intravenous catheter or percutaneous catheter. Pathergy may not develop in all cases of neutrophilic dermatosis, but when it is present, it is highly suggestive of this diagnosis. The induction of pathergy was once used as a clinical test for Behçet's disease; an 18-gauge needle was inserted through the dermis at an angle, and lesions would develop within 48 hours. Recognition of pathergy is of critical importance, particularly in cases of necrotizing neutrophilic dermatosis, because débridement can result in a catastrophic cycle of expansion and further surgical intervention.[8,19]

Sweet's syndrome usually resolves spontaneously over a period of weeks to months, with recurrences arising in 30 to 50% of cases. Recurrences occur most commonly in the context of an underlying hematologic cancer.[14] Effective therapies are available for the treatment of Sweet's syndrome. Systemic glucocorticoids are the most common initial treatment. The dramatic response of lesions and symptoms within 48 hours after the initiation of glucocorticoid treatment is considered to be both diagnostic and therapeutic.[16,20] Other first-line options include dapsone, potassium iodide, and colchicine. Reports have suggested that cyclosporine, thalidomide, intravenous immune globulin G, infliximab, adalimumab, anakinra, tocilizumab, baricitinib, and other agents may be effective as well.[21-28]

Dr. Malavika Prabhu: Pregnancy-associated Sweet's syndrome is rare,[8,29-31] accounting for 2% of all cases of Sweet's syndrome[15]; it is also probably underrecognized because the initial presentation overlaps with that of infections. For example, in this patient, the moderate leukocytosis that had occurred during pregnancy could have been an early manifestation of Sweet's syndrome. In pregnant patients, treatment depends on the severity of the clinical condition and may involve either close observation or high-dose glucocorticoid therapy, which is safe during pregnancy when indicated; alternative treatment options that are safe during pregnancy include tumor necrosis factor α inhibitors, cyclosporine, and other agents.[26,32]

Table 2. Diagnostic Criteria for Sweet's Syndrome.*

Criterion	Present in This Patient
Major criteria (both required)	
Abrupt onset of typical cutaneous lesions	Yes
Consistent histopathological findings	Yes
Minor criteria (≥2 required)	
Association with underlying condition or exposure	No
Fever and constitutional signs and symptoms	Yes
Leukocytosis	Yes
Rapid response to systemic glucocorticoids	Yes (later revealed)

* Data are from Su and Liu.[16]

In total, 31 cases of pregnancy-associated Sweet's syndrome have been reported.[15] Of the 28 cases with outcomes reported for the patient, 20 resolved with systemic glucocorticoid therapy, 7 with close observation, and 1 with dapsone therapy. Of the 26 cases with outcomes reported for the fetus, 25 were associated with the delivery of healthy infants (including three who were premature) and 1 was associated with fetal loss. Two cases had no discussion of fetal outcomes. Eight patients had Sweet's syndrome during more than one pregnancy.[33]

Pregnancy-associated Sweet's syndrome recurs with a subsequent pregnancy in a minority of cases, but the overall perinatal outcome is favorable.[33] Timely identification and management of Sweet's syndrome can prevent progression to extracutaneous involvement and organ injury. This patient was counseled that another pregnancy, if desired, could be pursued with close clinical monitoring for early signs of recurrent Sweet's syndrome during pregnancy and in the postpartum period.

The patient is at risk for recurrent spontaneous preterm labor in a future pregnancy. Al-

though the underlying mechanism of her spontaneous preterm labor is unclear, possible theories include the uterine overdistention associated with a fetus that is large for gestational age, as well as the inflammatory milieu of Sweet's syndrome driving the onset of labor. An interval between pregnancies of at least 18 months is associated with a decreased risk of recurrent prematurity. Close clinical surveillance for symptoms of preterm labor would also be recommended during pregnancy.

FOLLOW-UP

Dr. Kroshinsky: Treatment with intravenous methylprednisolone was started, and within 12 hours after the initiation of glucocorticoid treatment, the abdominal pain, shortness of breath, and hypoxemia markedly abated, as did inflammation of the skin lesions (Fig. 2B). Treatment with oral nifedipine was also started for systemic hypertension. After 3 days of high-dose glucocorticoid therapy, empirical antibiotic therapy was discontinued, and the largest ulcer began to reepithelialize (Fig. 2C). After 5 days of glucocorticoid therapy, the white-cell count — which had peaked at 49,990 per microliter the day before the initiation of glucocorticoid treatment — was 15,960 per microliter, and the patient was discharged home.

At home, the patient completed a tapering course of oral prednisone over a 3-week period and a tapering course of nifedipine over a 2-week period. Three weeks after discharge, the largest ulcer had nearly healed (Fig. 2D). Six weeks after discharge, the results of repeat transthoracic echocardiography were normal.

PATIENT PERSPECTIVE

The Patient: Being readmitted a week after having my baby was not how I envisioned my start to motherhood. Thankfully, during my hospitalization, I was close to my baby, who was still in the special care nursery. It's hard to remember my moments with him on the days I began to get really sick. As almost 2 weeks went by, I was getting worse, not better, with no diagnosis, which was both frustrating and very scary. My family never lost hope. Even on the days when I wasn't sure what was going to happen next, they were confident that I was going to be OK because of the care I was receiving. I did struggle both physically and mentally for a while, even after I was discharged from the hospital, but I can say that almost 10 months later, I am back to my normal self. The baby and I are both healthy, and that's really all we can ask for.

FINAL DIAGNOSIS

Sweet's syndrome.

This case was presented at Medicine Grand Rounds.

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

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