Septal Panniculitis as a Manifestation of Lyme Disease

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A 22-year-old woman presented with fever, chills, photophobia, and headaches, followed by a centrally clearing erythematous skin eruption, migratory polyarthralgias, conjunctivitis, and subsequently, tender, nodular skin lesions. Antibodies to Borrelia burgdorferi were consistent with acute Lyme disease. Skin biopsy revealed acute septal panniculitis. This dermatologic manifestation has not been previously described in Lyme disease.

Lyme disease, initially described by Steere et al [1] in 1977, is a multisystem disease, usually beginning in summer with a characteristic skin lesion, erythema chronicum migrans. The lesion is often associated with symptoms suggesting a viral-type illness, including myalgias, arthralgias, fatigue, headache, stiff neck, and lymphadenopathy. After several weeks to months, neurologic or cardiac abnormalities may develop. Subsequently, many patients have intermittent or chronic arthritis, which can be associated with destructive articular changes. In the last few years, it has been determined that the disease is caused by a spirochete, Borrelia burgdorferi [2], which has been successfully isolated from skin, blood, cerebrospinal fluid, and synovium of infected patients [3], and is transmitted by the bite of the Ixodes dammini or other related ticks. Antibiotic therapy, in particular with tetracycline for erythema chronicum migrans and the associated symptoms and high-dose intravenous penicillin for the later findings, appears to be highly effective [4].

Erythema chronicum migrans is the hallmark skin lesion of Lyme disease, serving as a distinctive clinical marker for the diagnosis. Typically, erythema chronicum migrans begins as a red macule or papule that expands centrifugally to form an annular lesion, often with central clearing, occasionally with an indurated center [1]. In its absence or when it presents in an atypical fashion, the diagnosis of Lyme disease may be difficult because of the nonspecific nature of the early manifestations.

We present herein a case of Lyme disease in which the skin manifestation was highly unusual, initially presenting with typical erythema chronicum migrans, but followed by multiple painful nodular lesions with histologic evidence of septal panniculitis.

CASE REPORT

A previously healthy 22-year-old white woman had acute pain over the dorsum of the left foot and swelling in the left popliteal fossa on August 20, 1984. The following day, she had fever to 38.5°C, chills, and for two days experienced photophobic headaches, along with nuchal rigidity. On August 24, raised, confluent erythema developed over her anterior chest, which cleared from the center and resolved completely in 24 hours. By August 26, she was experiencing severe, migratory polyarthralgias of the knees, left

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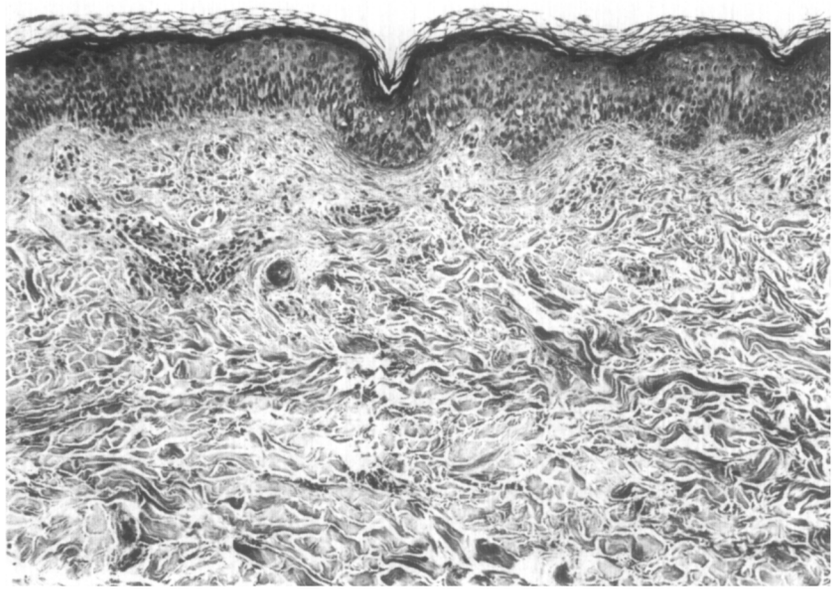

Figure 1. *Epidermis and superficial dermis. There is a sparse superficial perivascular lymphohistiocytic infiltrate. The overlying epidermis is normal (hematoxylin and eosin stain; original magnification × 500, reduced by 35 percent).*

elbow, and left wrist. She had one day of extreme nausea and crampy abdominal pains on August 28. She finally sought medical advice on August 30 because of persistent wrist and knee pain and the appearance of conjunctivitis of the right eye.

She denied any recent sore throat, diarrhea, vaginal discharge, or dysuria. There had been no sexual exposure to suggest venereal diseases. She had spent one week in Cape Cod, Massachusetts, and one week in eastern Long Island, New York in June 1984. She did not recall any insect bites or previous rashes.

On initial examination, she was febrile to 38.5°C; the skin was warm and flushed, without any rash; the left wrist and left knee were tender but demonstrated no swelling or loss of motion; nonexudative conjunctivitis of the right eye was present. Results of physical examination were otherwise normal.

Laboratory data included: leukocytes 6,500/mm^3, with 63 percent mature neutrophils, 3 percent band forms, 29 percent lymphocytes, 2 percent eosinophils; hemoglobin 12.8 g/dl, hematocrit 38.9 percent; platelets 289,000/mm^3; erythrocyte sedimentation rate (Westergren) 24 mm per hour; normal electrolytes, urea nitrogen, creatinine, muscle and liver enzymes, and results of urinalysis; negative results of serologic tests for hepatitis B virus, syphilis, rheumatoid factor, antinuclear antibodies, cryoglobulins, C-reactive protein, and streptozyme.

The patient began to receive tetracycline hydrochloride 500 mg every six hours for presumed Lyme disease. She was seen again after four days, reporting overall improvement, but still experiencing low-grade fevers and diffuse arthralgias. Naproxen 375 mg every 12 hours was added for symptomatic relief. Tetracycline was discontinued after two weeks.

On September 18, 1984, she again had fever, increasingly severe arthralgias, nausea, and headache. In addition, she had multiple erythematous, tender, indurated subcutaneous nodules distributed mostly over the calves, with occasional lesions on the thighs. Results of chest radiography were normal. The leukocyte count was 11,200/mm^3, with a normal differential; erythrocyte sedimentation rate was 43 mm per hour; C3 level was 213 mg/dl (normal, 70 to 176 mg/dl); C4 level was 77 mg/dl (normal, 16 to 45 mg/dl). Antibodies to B. burgdorferi, determined by indirect immunofluorescence, were reported to be present at a titer of 1:256.

Biopsy of a lesion from the right thigh was performed. The specimen consisted of full-thickness epidermis and dermis with a thin portion of superficial adipose tissue. The epidermis was histologically normal. In the dermis, there was a sparse superficial perivascular lymphohistiocytic infiltrate (**Figure 1**). The significant changes involved the subcutaneous adipose tissue, consisting of patchy lymphohistiocytic infiltrates surrounding small blood vessels and in the fibrous septums dividing fat lobules (**Figure 2**). Occasional neutrophils, plasma cells, and eosinophils were also present. There was no actual vasculitis in the form of vessel wall necrosis, but several small vessels were densely infiltrated by inflammatory cells (**Figure 3**). The few larger vessels included in the specimen were not involved. Multiple sections prepared with the Warthin-Starry silver stain were examined, but no spirochetes were identified. The biopsy results were interpreted as acute septal panniculitis.

Tetracycline 500 mg every six hours was reinstituted on September 21, after the serologic test results were reported. In addition, naproxen was increased to 500 mg every 12 hours. Within two days, she showed symptomatic improvement, and the nodular subcutaneous lesions resolved completely within five days. She completed a three-week course of tetracycline and has had no recurrence of any symptoms.

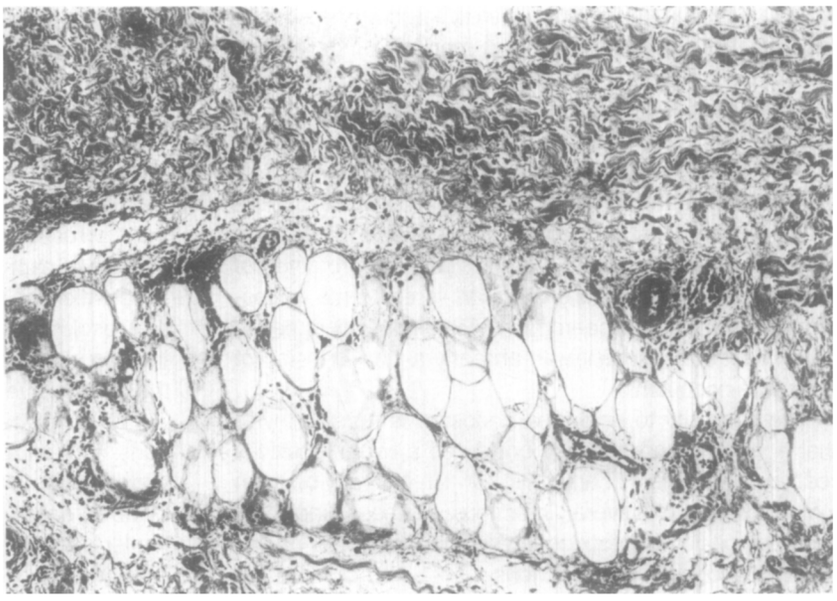

Figure 2. *Subcutaneous fat lobule and fibrous septums with perivascular and septal inflammation (hematoxylin and eosin stain; original magnification × 500, reduced by 35 percent).*

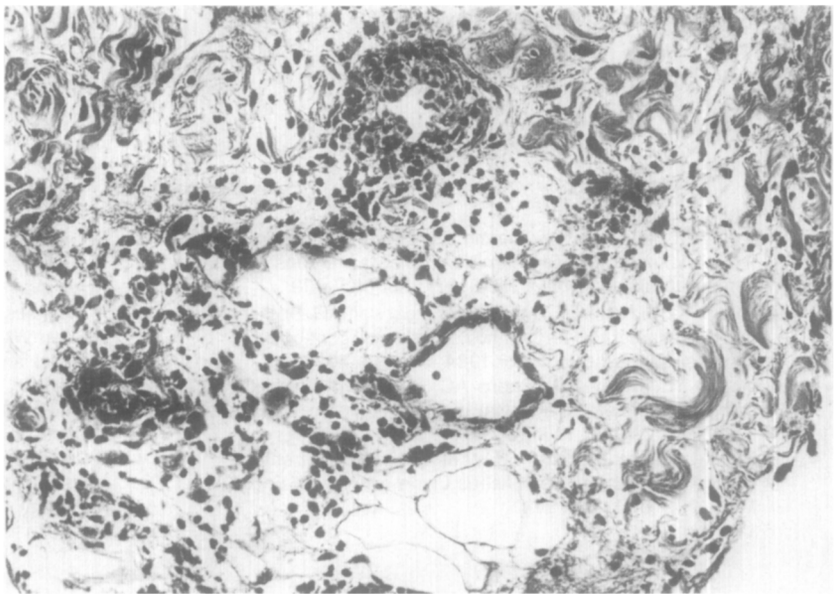

Figure 3. *Subcutaneous fat with dense perivascular inflammation involving small vessels (hematoxylin and eosin stain; original magnification × 1,285, reduced by 35 percent).*

COMMENTS

Erythema chronicum migrans usually presents as a red macule or papule at the site of the tick bite, which expands as an erythematous patch, or more frequently, as an annular lesion with partial clearing of the central region. It is usually flat, but can be raised at the center, periphery, or both. On occasion, the lesion may appear scaly or can become pustular, ulcerate, or crust over. About 25 percent of patients will have multiple lesions. Rarely, secondary lesions may be atypical in presentation, and manifest as localized or generalized urticaria, malar erythema, or a generalized macular eruption [5].

This patient presented with a skin eruption consistent with erythema chronicum migrans. However, the initial skin lesion was followed 25 days later by the development of tender, erythematous, subcutaneous lesions of her lower extremities, with histologic changes of septal panniculitis. This is the first case of panniculitis as skin manifestation of Lyme disease.

The typical histologic lesion of erythema chronicum migrans is a superficial and deep perivascular and interstitial infiltrate consisting mostly of lymphocytes [5]. The infiltrate may also include either plasma cells and eosinophils or occasionally both. The overlying epidermis is

typically unremarkable. Spirochetes have been identified with the Warthin-Starry stain in as many as 41 percent of the biopsy specimens from patients with Lyme disease.

To our knowledge, panniculitis has not been previously described in Lyme disease. Pathologically, inflammation of the subcutaneous adipose tissue may involve mainly the intralobular fibrous septums (septal panniculitis) or the fat lobules themselves (lobular panniculitis). Either form may occur with or without vasculitis [6]. The prototype of septal panniculitis without vasculitis is erythema nodosum. The histologic appearance of the biopsy specimen in our patient is consistent with an early and mild lesion of erythema nodosum.

The similarity to erythema nodosum is noteworthy in that erythema nodosum is considered a hypersensitivity reaction to a variety of antigenic stimuli, and may be seen in the course of several infectious diseases, including beta-hemolytic streptococcal, yersinial, and other bacterial, mycotic, and viral infections.

Although the patient's skin lesions developed after introduction of naproxen, a nonsteroidal anti-inflammatory drug, it is unlikely to be secondary to that medication. Cutaneous reactions to nonsteroidal agents are common and are usually manifest as maculopapular or morbilliform eruptions, urticaria, or erythema multiforme [7,8]. Although erythema nodosum has rarely been reported after aspirin administration [9], we are unaware of recorded cases of erythema nodosum or other types of panniculitis after administration of the other nonsteroidal agents. The disappearance of the skin lesions despite continuation of the medication further militates against these lesions being due to naproxen administration. Similarly, the lack of association of erythema nodosum with tetracycline and the resolution of the lesions while continuing antibiotic therapy suggest that tetracycline cannot be implicated as the provocative agent.

Had it not been for the description of a skin eruption consistent with erythema chronicum migrans preceding the development of the painful nodules, the diagnosis of Lyme disease would have been obscured. The finding of tender subcutaneous nodules in a patient with arthralgias/arthritis, gastrointestinal complaints, and constitutional symptoms is nonspecific and compatible with several diagnoses. As demonstrated by this case, Lyme disease must be considered in the differential diagnosis of panniculitis.

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