

# Recurrent Leg Cellulitis: Pathogenesis, Treatment, And Prevention

Robert P. Pierce, M.D., and Allen J. Daugird, M.D.

Recurrent cellulitis can develop in a variety of settings. Recurrent febrile episodes associated with arm or leg infections, sometimes described as erysipelatosus, have been noted for years to occur in the setting of filarial, postoperative, or idiopathic chronic lymphedema.<sup>1</sup> More recently, recurrent cellulitis has been described as a late complication of coronary artery bypass venectomy,<sup>2-8</sup> pelvic surgery, such as vulvectomy with lymphadenectomy<sup>9</sup> or hysterectomy with lymphadenectomy,<sup>10</sup> or of pelvic irradiation after hysterectomy.<sup>11,12</sup> The cause of recurrent cellulitis has not been precisely defined but appears to be multifactorial, involving mechanical, infectious, and immune-mediated factors. We present a case of a woman with recurrent cellulitis of the legs and briefly review the literature concerning the pathogenesis, treatment, and prevention of this perplexing problem.

## Case Report

A 78-year-old obese, hypertensive woman was admitted to the hospital after 2½ days of redness, swelling, and pain in the right leg. She reported a history of "phlebitis" in her legs in the distant past. Fifteen years before admission to our hospital, she was admitted to another facility with swelling, pain, eczematous changes, and blebs of the left leg. She was discharged 1 month later, her condition diagnosed as "cellulitis superimposed over old postphlebotic leg." Six years before admission to our hospital she was again treated for cellulitis, this time in the right leg. Streaking suggestive of lymphangitis, redness, small blisters, and right lower extremity edema (2 to 3+) were noted at the time of that admission. She developed bullous lesions during the hospitalization, but she gradually improved with antibiotic

therapy. Subsequently, she developed chronic bilateral lower leg edema before her first hospitalization at our institution.

Upon admission, she denied fever, chills, nausea, vomiting, shortness of breath, or chest pain. She reported bilateral tubal ligation and ovarian cyst removal more than 20 years ago. Five years ago she had a radical mastectomy for adenocarcinoma of the breast but had negative lymph nodes and underwent no further treatment. There was no history of cellulitis of the right arm after the mastectomy. She denied any other pelvic surgery, leg surgery, or abdominal or pelvic irradiation.

On examination, her temperature was 37.4°C (99.32°F), blood pressure 144/84 mmHg, pulse 80 beats per minute, and respirations 24/minute. She was an obese woman in no acute distress. Her head, eyes, ears, throat, heart, lungs, and abdomen were normal. There was pitting edema (3+) in the legs bilaterally and marked erythema, warmth, and tenderness of the right calf. The circumference 15 cm below the patella measured 54 cm on the right, 38 cm on the left. There were no vesicles, bullae, ulcers, or erythematous streaks. Absent were any fissures, maceration, or other changes suggestive of tinea pedis. The white cell count was  $13.8 \times 10^9/L$  (13,800/mm<sup>3</sup>) with a differential showing 0.83 segmented neutrophils and 0.05 band forms.

She was given heparin and cefazolin intravenously. A venogram showed no deep venous thrombosis but was suggestive of previous thrombophlebitis involving the lesser saphenous and anterior tibial veins with multiple incompetent communicators. On the 2nd hospital day, the patient's temperature rose to 38.7°C (101.7°F), but her fever quickly dropped, and she remained afebrile for the remainder of the hospitalization. The leg redness and warmth gradually resolved but the edema remained. She was discharged on the 8th hospital day to complete an additional week of oral cephalixin therapy.

Sixteen weeks later she had the first of five readmissions for cellulitis of the legs. These hos-

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From the Department of Family and Community Medicine, University of Missouri, Columbia. Address reprint requests to Robert P. Pierce, M.D., MA303 Medical Sciences Building, University of Missouri Hospital and Clinics, One Hospital Drive, Columbia, MO 65212.

pitalizations occurred during the next 15 months. Four of the episodes occurred in the right leg, one in the left. The interval between episodes averaged 11 weeks (range 6 to 18 weeks). Her symptoms typically appeared during a 2-day time period. On two occasions she had symptoms suggesting systemic toxicity. Her temperature upon admission averaged 38.6°C (101.5°F) (range 37.6°C [99.7°F] to 39.8°C [103.6°F]), and leukocyte counts averaged  $11.4 \times 10^9/L$  (11,400/mm<sup>3</sup>) (range 7.1 to  $14.5 \times 10^9/L$ ). A left shift was generally present. Tinea pedis was noted on only one hospitalization. At that time, topical miconazole cream was applied, and her dermatophytosis resolved. Treatment with the topical antifungal agent was continued daily, but she nonetheless developed recurrent cellulitis 6 weeks later. Attempts to reduce her chronic edema mechanically with compression stockings were also unsuccessful.

After the sixth hospitalization she was prescribed a prophylactic daily oral dose of 1 g of penicillin V potassium. Although her marked leg edema has remained unchanged, she has had no recurrences of cellulitis in 48 weeks of treatment.

### Discussion

The role of impaired venous drainage in the pathogenesis of recurrent cellulitis is suggested by the presence of the disease in patients who have had saphenous venectomy during coronary artery bypass grafting.<sup>3,4</sup> Impaired lymphatic drainage may be even more important in the pathogenesis of recurrent cellulitis, as the protein-rich lymphatic fluid serves as an excellent culture medium for bacteria. Mechanical disruption of lymphatic flow from lymph node resections or radiation therapy may be the process that increases the likelihood of recurrent cellulitis after these procedures. Filarial processes destroy lymphatic channels and increase likelihood of cellulitis episodes.<sup>13</sup> Although less well described, bacterial processes, such as a single episode of cellulitis or lymphangitis, may destroy lymphatic channels through direct toxic effects. The subsequent disruption of normal lymphatic flow may predispose some patients, such as the one we describe, without surgical risk factors or a history of radiation, to recurrent cellulitis.<sup>3,13</sup>

Bacterial pathogens in patients with recurrent cellulitis have proved difficult to recover.<sup>4,10</sup> In

seven reports of more than 80 episodes of cellulitis in 31 venectomy patients, cultures were obtained during acute episodes from skin 6 times and from blood 28 times.<sup>2,8</sup> Only 7 times were pathogens isolated, 3 times from skin and 4 times from blood.<sup>2,6</sup> When a causative organism is isolated from tissue, it is most often nongroup A  $\beta$ -hemolytic streptococcus (groups B, C, and G).<sup>2,9,11,12</sup> Staphylococcus has also been implicated, though to a much lesser degree.<sup>1,5</sup> In many instances, no portal of entry for these pathogens is identified. In other cases, breaks in the skin barrier resulting from dermatophytosis may be the portal of entry, as tinea pedis infections have been found in a significant number of patients with recurrent cellulitis.<sup>2,5,6,14</sup>

There is indirect evidence that host immune responses also play a role in the development of some patients' recurrent cellulitis. There are case reports of patients with recurrent cellulitis who improve without antimicrobial therapy.<sup>3,9</sup> Older reports describe immediate local reactions to intradermal injection of trichophytin extract in patients with recurrent erysipelas-like reactions and fungal infections of the feet.<sup>14,15</sup> The role of tinea pedis therefore may not only be to provide a portal of entry for streptococcal or other organisms through breaks in the skin, but also to stimulate a dermatophytid immune response. Immune responses to bacterial exotoxins have been implicated in the pathogenesis of recurrent cellulitis as well. Older reports describe patients with recurrent erysipelas who develop an erysipelas-like reaction in the area of their recurrences following the injection of sterile streptococcal filtrates at a distant site.<sup>16</sup> In more recent animal studies, streptococcal exotoxins produced erythematous, edematous skin reactions once an animal was sensitized.<sup>17</sup> Furthermore, streptococcal exotoxin appears to enhance hypersensitivity reaction to other antigens, such as PPD,<sup>17</sup> leading one author to speculate that the pathogenesis of recurrent cellulitis may involve streptococcal exotoxin-enhanced hypersensitivity to fungal antigens.<sup>2</sup> Finally there is indirect evidence that impaired vascular drainage can result in increased local concentrations of allergen to which a host may be sensitized, increasing the allergic response in the area of poor drainage.<sup>18</sup>

The clinical manifestations described in each of the various series of recurrent cellulitis are simi-

lar. Chronic lymphedema is not always present, but there is typically some evidence or history of venous or lymphatic compromise. Patients generally present with high fever, systemic toxicity, and leukocytosis. Although not seen in our patient, there can be a delay of up to 24 hours before the arm or leg shows typical findings of cellulitis.<sup>8,9</sup> Local erythema can start in the area of a preexisting extremity or abdominal surgical scar, or the erythema, as in this case, can arise without any other preceding skin lesions. The extremity generally has erythema, swelling, and tenderness typical of any cellulitis, but some authors have noted a uniquely fat, irregular, nonindurated and well-demarcated border to the erythema.<sup>2,12</sup> Most series do not report any subsequent desquamation.

The treatment of an acute attack of recurrent cellulitis is essentially that of any cellulitis. Once the recurrent pattern is recognized and the acute episode is controlled, treatment is directed at cellulitis prevention. In several reports,<sup>2,5,6</sup> control of patients' tinea pedis resulted in control of their cellulitis recurrences. Our patient had clinically evident tinea pedis on only one occasion, however, and its control did not prevent recurrence of her disease. Penicillin did yield clinical improvement in our patient. When given orally or as a monthly injection, penicillin has been shown in one other case report and in two case series to be effective in preventing disease recurrences<sup>9-11</sup> and, therefore, should be considered in patients with recurrent leg cellulitis.

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