Granulomatous panniculitis caused by *Candida albicans*: A case presenting with multiple leg ulcers

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A 61-year-old woman had rapidly enlarging ulcers on both legs and three draining subcutaneous nodules on the left thigh. Findings of skin biopsy specimens revealed granulomatous panniculitis with a large number of blastospores and pseudohyphae. *Candida albicans* was cultured from the ulcers, the nodules, the mouth, the esophagus and gastric juice, feces, and urine. The ulcers healed after 5 months of therapy with itraconazole. Predisposing factors were diabetes mellitus, dysfunction of the hypothalamic-pituitary system, hypochromic anemia, and prior treatment with a broad-spectrum antibiotic. In contrast to three other reported cases of *Candida* panniculitis, our patient had not undergone immunosuppressive therapy. (J AM ACAD DERMATOL 1993;28:315-7.)

*Candida* species are common human commensal organisms, but local or systemic factors may lead to tissue invasion. This report describes a woman who had leg ulcers caused by *Candida albicans*.

**CASE REPORT**

A 61-year-old woman had heart failure and diabetes mellitus for approximately 1 year. Small ulcers developed on her left ankle and the base of her left thumb. She was treated with angiotensin-converting enzyme inhibitors and a broad-spectrum antibiotic (bacampicillin). Despite treatment the ulcers grew larger, and new ones developed on both legs.

Examination revealed multiple ulcers of various sizes on her legs and ankles (Fig. 1). The edges were irregular and partly undermined, and their floors were covered with a purulent acid serosanguinous exudate. Some ulcers extended to the fascia. The tissue between the ulcers was indurated, and deep-seated nodules were palpable. She had three subcutaneous nodules on the medial left thigh, one of which drained a seropurulent exudate.

Livedo reticularis was noticed on both lower extremities. Doppler ultrasound examination revealed no evidence of a circulatory disturbance. The regional lymph nodes were not enlarged.

Sections of a nonulcerated skin nodule on the left thigh showed interstitial dermal edema and hemorrhage in the papillary and reticular layer and lack of pilosebaceous units. A sparse mononuclear infiltrate was observed around dermal blood vessels.

The most prominent feature was a noncaseating granulomatous infiltrate with predominant lobular and focal septal involvement. In the upper portion of the subcutaneous fat an irregular confluent infiltrate that consisted of...
histiocytes and epithelioid cells was seen either between fat cells or replacing them. Foci of roundish epithelioid cells were found in the deeper part of the subcutis. Findings of periodic acid-Schiff and Grocott-Gomori methenamine-silver nitrate stains revealed a large number of round or ovoid budding bodies and plentiful cigar-shaped bodies that demonstrated pseudohyphae and blastospores characteristic of Candida organisms (Fig. 2). Within the granulomatous areas a variable degree of mononuclear infiltrate with predominance of plasma cells and few lymphocytes was observed.

Pseudomonas aeruginosa and streptococci were isolated from the surface of the ulcers. C. albicans was cultured from the undermined edges of the ulcers and the nodule on the left thigh. C. albicans was also cultured from the biopsy specimens, the mouth, the esophagus, gastric juice, feces, and urine.

Candida antigen could not be detected in serum (latex test). Candida antibody titers were 1:160 to 1:320 (hemagglutination inhibition test; normal to slightly increased). Tests of delayed-type skin reactivity showed responses to Streptococcus and Proteus antigens and tuberculin but not to trichophytin or candidin. Serum levels of IgG and IgM were slightly decreased. Antibodies against human immunodeficiency virus could not be detected (enzyme-linked immunosorbent assay). Results of flow cytometric analysis of blood lymphocytes showed increased activated T cells (HLA-DR+), natural killer cells, and T-suppressor cells. The helper/suppressor cell ratio was 1:1.1.

Hematologic examination showed hypochromic microcytic anemia with decreased levels of serum iron but normal iron-binding capacity and levels of serum ferritin. A reactive leukocytosis of 11,000 cells/µl with neutrophilia of 83% and toxic granulation of neutrophils were noted.

Endocrinologic examination showed decreased basal serum thyroid-stimulating hormone concentration, low free triiodothyronine, and normal free thyroxine. Response to thyrotropin-releasing hormone stimulation was reduced. Thyroid ultrasonography did not show pathologic findings. Plasma cortisol levels were normal, but plasma adrenocorticotropic hormone levels were decreased. X-ray film of the lateral skull showed a normal sella. In addition, the patient had diabetes mellitus.

Oral itraconazole (Sporanox), 200 mg/day, was given for 3 weeks; the dosage was then reduced to 100 mg/day. Nystatin was administered orally. After 2 weeks of treatment C. albicans could no longer be grown from the mouth, urine, or feces. Five months later most of ulcers had healed with depressed scars.

**DISCUSSION**

Most cases of infectious panniculitis appear as inflamed subcutaneous nodules on the lower extremities. Other sites include the shoulders, arms, fingers, abdominal wall, and gluteal region. Clinically, these lesions resemble erythema nodosum or an abscess.

Gram-negative and gram-positive bacteria, atypical mycobacteria, Actinomyces and Nocardia species, and various fungi can infect the subcutaneous adipose tissue. Infectious panniculitis may result from either inoculation of the pathogen into the subcutaneous tissue or hematogenous dissemination.

To the best of our knowledge, only three cases of
Granulomatous panniculitis caused by Candida albicans

Panniculitis caused by Candida species have been published. In a series of 15 cases of infectious panniculitis, Patterson et al. described two immunocompromised patients who had panniculitis of the lower extremities caused by Candida species. Galimberti et al. described a 68-year-old woman who had three deep ulcers on the leg resulting from C. albicans–induced panniculitis. There was, however, no evidence of systemic candidiasis. The patient was given methylprednisone and gold for pemphigus vulgaris. Additional risk factors were steroid-induced diabetes and refractory anemia of unknown origin. Histologically, the ulcers were deeply infiltrated with spores and pseudohyphae. The diagnosis of Candida-induced panniculitis was confirmed by culture.

In our patient subcutaneous nodules preceded the ulcerative process, which suggested hematogenic spread of Candida. However, cutaneous and visceral lesions of disseminated candidiasis are characteristically suppurative, in contrast with our histopathologic findings and those in the three other reported cases in which Candida was demonstrated within subcutaneous epithelioid cell granulomas. Despite some predisposing factors for disseminated candidiasis, the cause for this unusual inflammatory response to Candida in our patient remains speculative.

Although inoculation is the usual mode of infection in subcutaneous mycoses such as sporotrichosis or chromomycosis, we do not believe that inoculation led to ulcerative panniculitis in our patient, because yeasts were also cultured from her gastrointestinal and urinary tract.

When C. albicans is present in high concentrations in the gastrointestinal tract, it can migrate across the intact endothelium by a process known as persorption. This phenomenon was first described in 1963 by Volkheimer. Self-experimentation by Krause et al. demonstrated that in a healthy person, ingestion of 10¹² cells of C. albicans was followed by a transient toxic reaction and positive urine and blood cultures within hours. Symptoms of fungemia were observed as many as 9 hours after ingestion. Persorption of yeasts from the intestine is considered the most important mode of infection in Candida sepsis and candidal abscesses of the kidney, central nervous system, or other sites.

Our patient had no history of Candida sepsis or an indwelling catheter that could have served as portal of entry. Thus infection from persorption appears to be most likely.

Known predisposing factors for candidiasis include diabetes mellitus, endocrine disorders, and iron deficiency. Our patient had these conditions plus prior treatment with a broad-spectrum antibiotic. In contrast to the patients described by Patterson et al. and Galimberti et al., our patient did not receive immunosuppressive therapy.

The nature of the immunodeficiency in our patient remains unclear. Slightly decreased serum levels of IgG and IgM can be attributed to severe heart failure in the left side of the heart and pneumonia and to Candida infection itself. Antibody titers to C. albicans were low but detectable. Results of skin testing showed normal response to Streptococcus, Proteus antigens, and tuberculin, which suggested normal T cell–mediated immunity. There was, however, no reaction to candidin and trichophytin.

REFERENCES