Case Report

Small Vessel Vasculitis in a Patient with Botryomycosis

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ABSTRACT. We describe a 53 year-old woman with primary biliary cirrhosis presenting with left ankle swelling and a purpuric rash. The skin biopsy of the rash revealed a small vessel vasculitis and a botryomycosis with Splendore-Hoeppeli phenomenon. Botryomycosis is an uncommon histologic finding of a chronic suppurative bacterial infection whereby bacteria form aggregates, which are surrounded by an eosinophilic matrix. With guidance from the skin biopsy findings, the patient was appropriately treated with antibiotics, resulting in complete resolution of symptoms. (J Rheumatol 2006;33:2545–7)

Key Indexing Terms:
VASCULITIS BOTRYOMYCOSIS

Active vasculitis is potentially life-threatening and fatal, therefore early recognition and treatment are crucial. Therapy can vary based on the cause of vasculitis: any available clues should be used to help clarify the diagnosis. We describe a case of small-vessel vasculitis whereby a comprehensive clinical evaluation and skin biopsy results were instrumental in diagnosis and treatment.

CASE REPORT

A 53-year-old woman with primary biliary cirrhosis (PBC) status post-liver transplant (1997) presented with a 3-day history of a progressive nonpruritic rash on her left lower extremity and a dull ache in her left ankle that rendered it unable to bear weight.

Her dermatologic history included chronic bilateral pretibial hyperkeratotic plaques, diagnosed as an atypical form of psoriasis based on prior skin biopsies, and an acute episode of bilateral lower extremity cellulitis (2000) that resolved with antibiotic therapy.

Other history included chronic renal insufficiency secondary to cyclosporine therapy (baseline creatinine 1.9), chronic cough attributed to postnasal drip and gastroesophageal reflux, restless leg syndrome, peripheral neuropathy attributed to diabetes mellitus, coronary artery disease, myocardial infarction, atrial fibrillation (prophylactically started on coumadin), Bell's palsy, parotid gland hyperplasia, and gout (not crystal proven).

She denied any fevers, night sweats, recent travel, insect bites, hemoptysis, abdominal pain, or exposure to new medications. She had xerostomia and xerophthalmia that improved after transplant.

Her medications included cyclosporine, mycophenolate mofetil, pravastatin, allopurinol, quinine sulfate, metoprolol, clopidogrel, warfarin, omega-3 vitamins, fenofibrate, aspirin, magnesium oxide, and omeprazole.

On examination, her vital signs were stable and she appeared well. Pertinent positive findings included a 2/6 systolic cardiac murmur, as well as edema, erythema, and warmth periarticular to the left ankle extending to the mid-calf, with a moderate effusion in the tibiotalar joint. Subtalar and tibiotalar ranges of motion were normal but uncomfortable. She had multiple painless, nonblanching, erythematous, papular lesions overlying the left ankle with a few scattered lesions spreading to the mid-calf. She also had bilateral pretibial, painless, hyperkeratotic lesions, 2 on the left lower extremity and one on the right. The left proximal lesion measured 2.8×2.5 cm, the left distal lesion 0.5×0.5 cm, and the right lesion 4.5×5.0 cm. She had decreased light touch sensation in a stocking-glove pattern of her bilateral lower extremities, more pronounced on the right. Abnormal laboratory values on initial evaluation (Table 1) included a blood urea nitrogen 31 mg/dl (normal 6–24 mg/dl), creatinine 2.2 mg/dl (0.4–1.3 mg/dl), erythrocyte sedimentation rate 44 (0–30 mm/h), C-reactive protein 55.50 (0.05–4.90 mg/l), partial prothrombin time 39.3 s (23–34 s) with an international normalized ratio of 2.4 (0.9–1.1). The rest of her laboratory results including complete blood count, liver function tests, and urinalysis were normal.

We aspirated 3 ml of clear yellow synovial fluid from the left tibiotalar joint, with a cell count of 68/ml and a negative Gram stain. These results suggested a sympathetic effusion; however, because of a persistent concern for an infectious etiology of the rash, we requested a dermatology consultation for a skin biopsy, drew blood cultures and administered intravenous cefazolin to account for Gram-positive organisms likely to cause soft-tissue infections. We also discontinued allopurinol in the event that this was a drug-induced vas-

Table 1. Laboratory values at initial presentation.

Variable (normal range)	Laboratory Value
Blood urea nitrogen, mg/dl (6–24)	31
Creatinine, mg/dl (0.4–1.3)	2.2
White blood cell count, K/μl (4–11)	9.7
Hemoglobin, g/dl (11–15)	11
Hematocrit (32–45%)	36.6
Platelets, K/μl (150–400)	244
Differential, %	
Neutrophils	69
Lymphocytes	19
Monocytes	9
Eosinophils	2
Basophils	1
Erythrocyte sedimentation rate, mm/h (0–30)	44
C-reactive protein, mg/l (0.05–4.90)	55.50
Prothrombin time, s (10.5–13)	23.6
International normalized ratio (0.9–1.1)	2.4
Partial prothrombin time, s (23–34)	39.3

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culitis. We tested for antineutrophil cytoplasmic antibody (ANCA), serum cryoglobulins, serum and urine protein electrophoresis (SPEP, UPEP), anti-SSA (Ro), anti-SSB (La), and antinuclear antibody (ANA).

Early in the clinical course, results from the skin biopsy of a small region with acute-onset papular lesions obtained from the left lower extremity became available (Figures 1 and 2). Findings were consistent with a small-vessel vasculitis, with histologic demonstration of an inflammatory infiltrate and erythrocyte extravasation around capillaries and arterioles. Further, one botryomycosis with Splendore-Hoeppli phenomenon was identified. Immunofluorescence staining was negative. Tissue culture (broth only) from the skin biopsy grew *Propionobacterium acnes*. All remaining laboratory examinations including blood cultures, ANA, ANCA, serum cryoglobulins, SPEP, UPEP, anti-SSA, and anti-SSB were negative.

Clinically, the patient's rash and ankle swelling resolved after receiving antibiotics and discontinuing allopurinol for 9 days. Her creatinine and peripheral neuropathy remained stable. Systemic corticosteroids were not initiated. No valvular lesions were seen on transthoracic echocardiogram.

DISCUSSION

The rapid response to antibiotics, growth of *P. acnes* from the skin biopsy, and presence of botryomycosis on histology indicated a diagnosis of infection-related small-vessel vasculitis. To our knowledge, this is the first reported case of botryomycosis occurring in the setting of an infection-related small-vessel vasculitis.

Despite its name, botryomycosis is not a fungal infection.

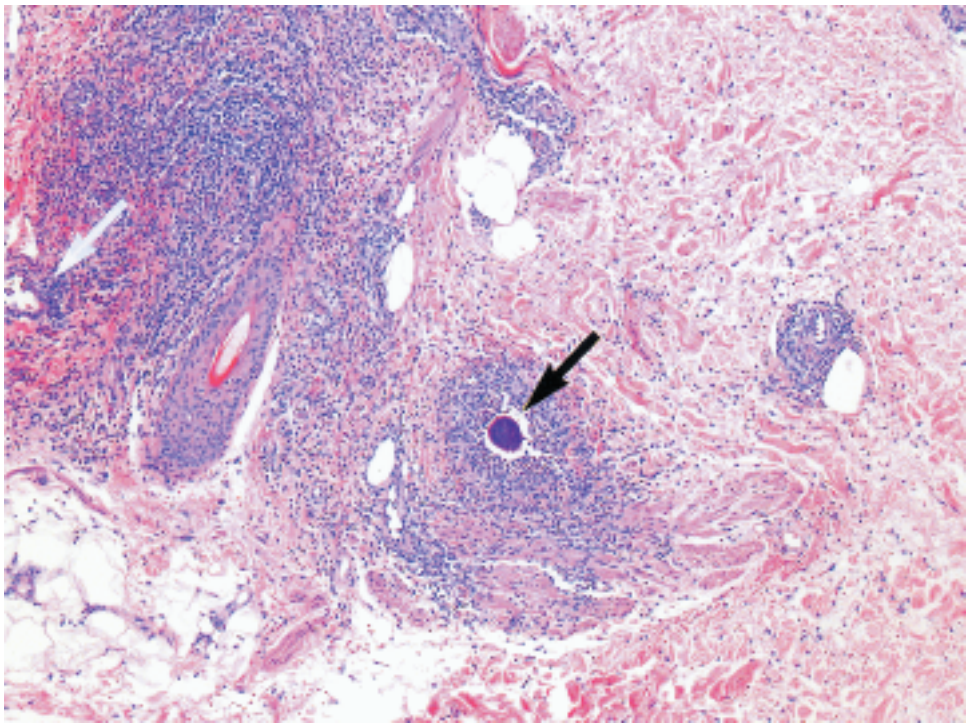
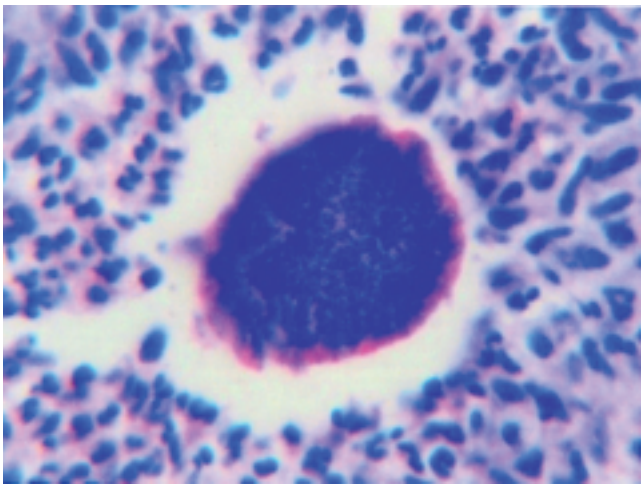


Figure 1. Skin biopsy shows an inflammatory infiltrate circumferential to an arteriole with red cell extravasation as indicated by the white arrow. The black arrow identifies botryomycosis with Splendore-Hoeppli phenomenon (diameter 60 μm) (original magnification ×10; H&E stain).



Botryomycosis is a histologic finding of a basophilic bacterial cluster and a surrounding reaction known as Splendore-Hoeppeli (S-H) phenomenon. The S-H phenomenon is an eosinophilic matrix with club-like projections around the aggregate that can also be seen in fungal and parasitic infections, providing etymology for the term "botryomycosis" sounding similar to "mycetoma." Botryomycosis is an uncommon finding that has only been reported anecdotally. Its exact pathogenic mechanism is unclear, although it is usually associated with chronic, suppurative bacterial infections.

Figure 2. Skin biopsy shows mid-dermal mixed polynuclear and histiocytic inflammatory reaction against a single microbial aggregate 60 μm in diameter with a thin eosinophilic coating consistent with botryomycosis with Splendore-Hoeppeli phenomenon (original magnification ×100, oil immersion; H&E stain).

Cases of botryomycosis have been described in both immune-competent and immunocompromised hosts (e.g., cystic fibrosis and lupus)[1,2]. Suggested predisposing factors include alcoholism, diabetes, trauma, liver disease, chronic corticosteroid use, malnutrition, and acquired immunodeficiency syndrome[3-6].

Clinically, botryomycosis has been associated with both cutaneous and visceral infections. Cutaneous findings are more commonly seen with manifestations including abscesses, nodules, ulcers, and fistulas with visible purulent matter[7]. Occasionally, botryomycosis has been associated with dermatoses such as follicular mucinosis[8].

Several bacteria have been implicated in botryomycosis, with *Staphylococcus aureus* being the most common organism[3]. Although commonly associated with acne vulgaris, *P. acnes* has not been reported in cutaneous botryomycosis. It has, however, been reported in cases of cerebral, hepatic, and gastrointestinal botryomycosis[9-11].

Since botryomycosis is usually seen with chronic infections, we hypothesized that our patient's hyperkeratotic plaques represented a clinical manifestation of botryomycosis via a chronic infectious process, and her current presentation of purpuric lesions resulted from an acute on chronic infection. The immunosuppressed state from her liver transplant, PBC, and diabetes potentially predisposed her to infection. We also speculated that her history of bilateral lower extremity cellulitis could have represented a similar acute flare of a chronic process. Because treatment of her chronic infection would potentially reduce her risk for future acute infections, we started a prolonged course of doxycycline, an antibiotic that covers *P. acnes* without interfering with cyclosporine levels.

After 5 months of doxycycline treatment, she had a reduction in the diameter of the hyperkeratotic lesions. She is still taking doxycycline with the ultimate hope of complete resolution of the lesions.

To our knowledge this is the first reported case of botryomycosis in a patient with infection-related small-vessel vasculitis. The finding of botryomycosis histologically can be helpful in supporting an infection-related diagnosis and may have important therapeutic implications.

REFERENCES

1. Katznelsen D, Vawter GF, Foley GE, Shwachman H. Botryomycosis, a complication cystic fibrosis. Report of 7 cases. J Pediatr 1964;65:525-39.
2. Follows GA, Mathew J, Lucas S, Black M, Goodship T. Cutaneous botryomycosis in a patient with lupus nephritis. Nephrol Dial Transplant 1988;13:3200-1.
3. Mehregan DA, Su WPD, Anhalt JP. Cutaneous botryomycosis. J Am Acad Dermatol 1991;24:393-6.
4. Hacker P. Botryomycosis. Int J Dermatol 1983;22:455-8.
5. Bonifaz A, Carrasco E. Botryomycosis. Int J Dermatol 1996;35:381-8.
6. Winslow DJ. Botryomycosis. Am J Pathol 1959;35:153-76.
7. Elder DE, Elenitsas R, Johnson BL Jr, Murphy GF, editors. Lever's histopathology of the skin. 9th ed. Baltimore: Lippincott Williams & Wilkins; 2004:583-5.
8. Harman RR, English MP, Halford M, Saihan EM, Greenham LW. Botryomycosis: a complication of extensive follicular mucinosis. Br J Dermatol 1980;102:215-22.
9. Schlossberg D, Keeney GE, Lifton LJ, Azizhkan RG. Anaerobic botryomycosis. J Clin Microbiol 1980;11:184-5.
10. Schwartz DA, Finkelstein SD. Propionibacterium acnes cerebral botryomycosis. Am J Clin Pathol 1986;86:682-5.
11. Wada R, Kawamura C, Inoue S, Watanabe K, Kaimori M, Yagihashi S. Granulomatous colitis associated with botryomycosis of propionibacterium acnes. Arch Pathol Lab Med 2001;125:1491-3.