A Marble under the Skin
(See page 1579 for the Photo Quiz)

Figure 1. Lesion on the left knee

Diagnosis: Cutaneous botryomycosis.

The first description of botryomycosis dates to 1817, in which Bollinger described a case in a horse as a complication of castration. Multiple abscesses with granulomas and granulomatous inflammation were found in pus and tissue of the animal. The term “botryomycosis” was subsequently coined in 1884 by Rivolta, because the appearance of granules resembled that of bunches of grapes (“botrys” in Greek), and because he thought that the disease was due to a fungal infection (“mycosis”). The first human cases were reported in 1903 by Lig nières and Spitz. It was not until 1919 that Magrou noted that the granules were actually clusters of closely adherent bacteria and that the infection was not caused by fungi. He initially described a case due to Staphylococcus aureus, but subsequent cases were found to involve other pathogenic bacteria, as well [1]. In 1959, Winslow [2] published the largest and most comprehensive review of botryomycosis up to that time and proposed a classification system that differentiated botryomycosis into a visceral form and the more common cutaneous forms on the basis of 48 cases in humans reported in the literature.

Botryomycosis is a chronic localized bacterial infection that is usually polymicrobial and is sometimes associated with a foreign body, penetrating injury, or local trauma (as in our case) [1, 3]. S. aureus, Pseudomonas aeruginosa, and other organisms are frequently recovered by aerobic and anaerobic culture; S. aureus and P. aeruginosa are the pathogens that are isolated most often [3, 4]. Patients usually present with chronic, nonhealing skin lesions with granules (figure 1), possible sinus tracts, nodules, fistulae, ulcers, or abscesses. Infection can spread locally to involve muscle, bone, and organs, such as the heart, lung, liver, brain, kidney, prostate gland, eye, mouth, and pericardium [1, 3, 5, 6]. Botryomycosis has been reported sporadically worldwide, with a male-to-female ratio of 3:2 [6], and affects patients of all ages [7]. Cases have been reported in patients with chronic granulomatous disease, immunoglobulin deficiencies, AIDS, diabetes mellitus, cystic fibrosis, alcoholism, steroid treatment, liver disorders, postoperative complications, and trauma [2, 4].

The histologic hallmarks of the disease are the grains or granules that form from aggregates of bacteria and are usually confined to skin and soft tissue but occasionally involve viscera. They represent bacterial microcolonies and are 0.2–2.0 mm in diameter, soft, and yellow or white. Macroscopically, the granules of botryomycosis are indistinguishable from the so-called sulfur granules of actinomycosis or mycetoma. Hematoxylin-eosin staining does not differentiate among actinomycosis, mycetoma, and botryomycosis, because the host response is similar in each of these infections, and identification of the pathogens requires specific stains and culture. Individual bacteria and granules are enmeshed by Splendore-Hoeppli material [6]. The Splendore-Hoeppli phenomenon describes the radiating eosinophilic deposits, rich in immunoglobulins, host-derived materials, and possibly parasitic antigens, that form around fungi, helminths, or bacterial colonies in tissue. It was originally described in 1908 by Splendore in sporotrichosis and was later observed by Hoeppli in histologic sections of schistosomiasis [8]. The mechanisms that lead to the formation of granules and the defects in the host response that lead to the inability to eradicate the bacteria are not fully understood.

Histopathologic slides of a biopsy sample obtained from our patient showed acute and chronic inflammation with benign reactive epidermal hyperplasia, focal collections of polymorphonuclear cells, and aggregates of bacteria within areas of acute inflammation (figure 2). These aggregates were surrounded by amorphous eosinophilic material consistent with proteinaceous
Splendore-Hoeppli material (figure 2). Gram stain of tissue samples showed gram-negative bacilli and gram-positive cocci (figure 3). Bacteriologic culture grew moderate β-hemolytic streptococci (non-serogroup A), few P. aeruginosa, and mixed anaerobic flora (including Bacteroides fragilis but not Actinomyces species).

When amenable, optimal therapy includes surgical resection with appropriate prolonged antibiotic therapy based on culture results. Medical management alone often does not result in cure or eradication. Cutaneous forms of botryomycosis tend to respond better to treatment than do visceral forms. Our patient underwent surgical excision of the lesion and was treated with antimicrobial therapy. She was treated initially with 3 weeks of intravenous piperacillin-tazobactam and then with oral ampicillin-sulbactam and ciprofloxacin for an additional 4 weeks. She refused skin grafting, but 10 weeks after excision (3 weeks after discontinuation of antibiotic therapy), she was seen at a follow-up visit and had a well-granulating wound (figure 4). Several months later, further follow-up by telephone indicated continued resolution without complication.

Acknowledgments

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