Primary Pulmonary Botryomycosis: Case Report and Review

Susan J. Bersoff-Matcha, Charles C. Roper, Helen Liapis, and J. Russell Little

Botryomycosis is an uncommon bacterial disease characterized by the microscopic formation of eosinophilic granules that resemble those of infection by Actinomyces species. The diagnosis of botryomycosis can be made when microscopic inspection and culture of the granules reveal gram-positive cocci or gram-negative bacilli. Botryomycosis is caused by common bacterial pathogens including Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa, yet the host and microbial factors that contribute to the pathobiology remain unknown. Pulmonary botryomycosis can resemble actinomycosis, tuberculosis, or invasive carcinoma by causing a mass lesion with constitutional symptoms. Radiographically, it invades bone and disrupts tissue planes. Successful treatment often requires a combination of both surgical debridement and long-term antimicrobial therapy. We report a case of primary pulmonary botryomycosis and review the literature on this unusual infectious process.

A 67-year-old man was admitted to Barnes-Jewish Hospital (St. Louis) in late October 1996 for an open lung biopsy of a left pleural lung mass. The patient was first brought to medical attention in early August 1996 when he began experiencing progressive left posterior chest wall and back pain and a 20-lb weight loss. He denied cough, night sweats, or fevers. A chest roentgenogram revealed a 6-cm mass in the superior segment of the left lower lobe.

The patient was a retired road construction worker who recalled extensive exposure to inhaled cement dust for many years. He had no known exposure to tuberculosis but admitted to a history of cigarette smoking (110 packs per year) and multiple lower respiratory infections in recent years. Other medical history included hypothyroidism treated with levothyroxine sodium and asthma that was controlled with β-agonist and steroid inhalers. The patient’s surgical history was significant for hemigastrectomy and partial transverse colectomy for peptic ulcer disease 4 years before the present illness. His only known drug allergy was to a quinolone antibiotic, which had caused shortness of breath.

A CT scan obtained in September 1996 revealed a left posterior intrathoracic mass with bony invasion into the thoracic spine and the left posterior sixth and seventh ribs. The patient underwent CT-guided needle biopsy of the mass, and patholog-
The platelet count was 667,000/l. Liver and renal function. The patient's absolute CD4+ count was normal, and oil red O staining showed that the neutrophil oxidative burst activity was normal, and the patient agreed to additional diagnostic tests. A sweat chloride level of 290/9c48$$mr07 02-05-98 22:00:47 cida UC: CID 1998;26 (March) Primary Pulmonary Botryomycosis

Discussion
Since its initial description in humans in 1913 [11], the disease known as botryomycosis has been difficult to distinguish from actinomycosis. Pathologically, actinomycosis, like botryomycosis, can display the Splendore-Hoeppli phenomenon [12]. The two diseases are satisfactorily distinguished,
however, when Brown and Brenn gram staining (for gram-positive bacteria) and Grocott-Gomori methenamine–silver nitrate staining fail to identify the branching organisms of actinomycosis. Routine gram staining of the granules of botryomycosis may show the responsible organism. For our patient, Brown-Hopps gram staining (for gram-negative bacteria) revealed gram-negative rods consistent with growth in culture of *P. aeruginosa*.

Flynn and Felson [13] and Neuhauser [14] reported that radiographic evidence of contiguous involvement of lung tissue, pleura, and bone is so strongly suggestive of actinomycosis that it should prompt the clinician to include this disease in the differential diagnosis. All three of these radiographic findings were demonstrated in our case. Furthermore, our patient’s clinical course resembled that of pulmonary actinomycosis: an indolent systemic syndrome dominated by several months of chest pain and weight loss.

Infection with *Actinomyces* species usually requires disruption of a mucosal barrier. This disruption may be created iatrogenically, as in a surgical procedure [15], or by a foreign body such as an intrauterine device [16]. Pulmonary actinomycosis, however, is usually attributed to aspiration. The factors that induce the formation of the granules of botryomycosis have not been identified, but both bacterial and host factors have been implicated. Some of the earliest reports of botryomycosis
more, they found that most of the afflicted animals had foreign bodies associated with their lesions. Our patient had no evident foreign material in or around his lung mass, but perhaps his years in road construction led to inhalation of significant amounts of particulate matter that could act as a nidus for granule formation.

Although there is no direct evidence to suggest that the immune status of the host plays a role in actinomycosis, immune deficiency does seem to predispose patients to botryomycosis. A review of the literature by Brunken et al. [10] noted that many patients had immunologic abnormalities. Paz et al. [20] described one patient whose first manifestation of chronic granulomatous disease was pulmonary botryomycosis; they recommended that any patient for whom visceral botryomycosis is diagnosed should be evaluated for the presence of chronic granulomatous disease. Seven cases of primary pulmonary botryomycosis have been described in patients with cystic fibrosis [21], possibly implying a breakdown in local defenses. Our patient almost certainly had abnormal local immune defenses; he admitted to a long history of tobacco abuse that contributed to his chronic lung disease, and his treatment included inhaled steroids, which also serve to change the local immune environment. These factors, combined with the potential for serious malnutrition from weight loss, may have provided a suitable local environment for botryomycosis.

Some of the more recent cases of botryomycosis in immunocompromised hosts have been described in patients with HIV infection [9, 22]. As in most patients with botryomycosis, patients with HIV infection usually present with cutaneous disease. Perhaps the depletion of the CD4+ subset of T lymphocytes in some way permits this infection. Yet, botryomycosis remains rare even in this patient population. It is interesting that our patient was found to have a low CD4+ cell count and cutaneous anergy to delayed-type hypersensitivity skin testing. It is difficult to know whether this immune defect was present before his infection or was the result of chronic infection. In the study by Brunken et al. [10], most patients with botryomycosis were found to have defects in cellular immunity as evidenced by weak T cell proliferative responses to mitogen stimulation; these defects, however, resolved after excision of the lesion and treatment with antibiotics. Our patient’s CD4+ cell count rose to 451/mm3 after 4 weeks of intravenous antibiotic therapy.

Because botryomycosis is rare, we reviewed the literature for guidance on duration of therapy and expected clinical outcome. Our review of the English-language literature via MEDLINE (key words, “botryomycosis” and “pulmonary” or “visceral”), however, yielded only seven reports of cases of primary pulmonary botryomycosis. The organisms (when isolated), treatments, and outcomes in these cases are listed in table 1. As expected, nearly all patients received antibiotic therapy; five investigators treated their patients with surgery. When long-term follow-up was addressed, most patients were reported to have a clinical response to the chosen therapy.

Figure 3. Eosinophilic granules displaying the Splendore-Hoeppli phenomenon in a patient with primary pulmonary botryomycosis (original magnification, ×400; hematoxylin-eosin stain). Brown-Hopps gram staining of these granules revealed dense clusters of gram-negative rods (not shown).

suggested that, like actinomycosis, a foreign body was required to provoke granule formation. Plaut [17] described a diabetic patient who was found to have a part of a broomcorn plant as the nidus for her intraabdominal botryomycotic infection. In the cases reported by Kimmelstiel and Oden [4], a fishbone was the inciting foreign body.

Other investigators have suggested that it is the size of the inoculum [3] or the virulence of the organism [18] that determines whether bacteria will produce granules. In 1973, Shults et al. [19] reported on staphylococcal botryomycosis found in a “pathogen-free” mouse colony. Their results revealed that only certain strains of mice were susceptible to disfiguring facial lesions that were histologically identified as botryomycosis. In addition, they found that most of the staphylococci responsible for these lesions bore a specific bacteriophage. These findings suggested that it is not only the host but also factors in the bacteria that play a role in granule formation. Further-
Table 1. Summary of data on all reported cases of primary pulmonary botryomycosis.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age/sex</th>
<th>Risk factor</th>
<th>Microbiology</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>[9]</td>
<td>36 y/M</td>
<td>HIV infection/AIDS</td>
<td>Staphylococcus aureus (presumed)</td>
<td>Oral amoxicillin/clavulanate</td>
<td>Resolution, fibrosis after 6 mo</td>
</tr>
<tr>
<td>[21]</td>
<td>66 y/F</td>
<td>None</td>
<td>Microscopy showed gram-positive coccal and bacillary colonies, cultures negative</td>
<td>Surgery and intravenous antibiotics for 2 w</td>
<td>Resolution</td>
</tr>
<tr>
<td>[20]</td>
<td>19 y/F</td>
<td>Chronic granulomatous disease</td>
<td>Staining with methylene blue showed curved rods, cultures negative</td>
<td>Intravenous gentamicin and nafcillin</td>
<td>Clinical response to therapy</td>
</tr>
<tr>
<td>[24]</td>
<td>28 y/M</td>
<td>Pulmonary sequestration</td>
<td>Gram-positive bacterial masses</td>
<td>Surgery only</td>
<td>Clinical response at 6 mo</td>
</tr>
<tr>
<td>[25]</td>
<td>53 y/F</td>
<td>Diabetes mellitus</td>
<td>Gram-positive bacterial filaments, cultures yielded Bacillus species</td>
<td>Surgery only</td>
<td>Not reported</td>
</tr>
<tr>
<td>[21]*</td>
<td>9 mo to 12 y/M (3 patients), F (4 patients)</td>
<td>Cystic fibrosis</td>
<td>Pseudomonas aeruginosa, M. pyogenes var. aureus</td>
<td>Surgery for 3 patients, intravenous chloramphenicol and erythromycin for 7 patients</td>
<td>5 patients died, 2 patients still living at time of report</td>
</tr>
<tr>
<td>[6]</td>
<td>47 y/M</td>
<td>None</td>
<td>Microaerophilic nonhemolytic Streptococcus species</td>
<td>Oral tetracycline, surgery</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

NOTE. Table lists all human cases of primary pulmonary botryomycosis identified by a MEDLINE search of the English-language literature. Other cases were subsequently identified in the references of certain articles. References are listed by publication date in reverse chronological order.

* Seven cases.

Botryomycosis is an unusual bacterial infection that may mimic infection by Actinomyces species. Although infrequently diagnosed, botryomycosis should be considered in the differential diagnosis of any lesion where there is disruption of tissue planes, erosion into bone, and granule formation.

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References