Septic Arthritis and Osteomyelitis Caused by an Organism of the Genus *Rhodococcus*

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We describe a previously healthy, immunologically normal young girl who presented painless swelling of fingers, a toe, and one knee. Roentgenograms were consistent with osteomyelitis of the phalanges and knee effusion. Rice bodies (corpora oryzoidea) were identified in viscous fluid obtained from the knee during arthroscopy. Culture of this fluid grew an organism initially believed to be a member of the genus *Nocardia* but which was later presumptively identified as a member of the genus *Rhodococcus*. The patient was successfully treated with a combination of erythromycin and amoxicillin for a total of 6 months. Previously reported cases of this unusual infection and the microbiological features of the organism are reviewed. The significance of rice bodies found in joint fluid and the therapy of this infection are discussed.

The rhodochrous group consists of a collection of microorganisms which are taxonomically related to the genera *Nocardia* and *Mycobacterium*. Goodfellow and Alderson in 1977 proposed that this group of organisms be assigned to the genus *Rhodococcus* (6). Infections with these microorganisms are extremely rare. Only nine cases are recorded in the literature (2, 12, 15–17); none were associated with septic arthritis or osteomyelitis, and only three occurred in children (4, 16, 17). A young girl who presented painless enlargement of several joints and had an organism belonging to the genus *Rhodococcus* isolated from synovial fluid from a knee is described.

**Case report.** A 29-month-old white female was in good health until July 1976 when she developed painless swelling of the index finger of the left hand and third toe of the left foot, with no limitation of motion, erythema, or warmth. There was no history of trauma, rash, recent illness, immunization, or exposure to tuberculosis. The family had a healthy pet cat. In November 1976, similar swelling of the left thumb occurred, and she was referred to the University of Kentucky Medical Center. Positive physical findings included fusiform swelling of the index finger and thumb of the left hand and the left third toe; the right knee was swollen, but not tender. There was no erythema or limitation of any joint motion.

The leukocyte count was 10,100 per mm³ with a normal differential; the hematocrit was 36.4%. The erythrocyte sedimentation rate was 30 mm/h (Westergren). The VDRL was nonreactive, and fungal serologies (to *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Aspergillus* sp., and *Coccidioides immitis*) were negative. A Nitro Blue Tetrazolium test was normal, and positive skin tests to candida and streptokinase-streptodornase antigens were elicited. Quantitative determinations for immunoglobulins G, A, and M were 1,170, 80, and 184 mg/100 ml, respectively (all in the normal range at this institution for the patient's age). Skin tests to histoplasmin, tuberculin, cat scratch antigen, and nontuberculous mycobacterial antigens (including scotochromogens, photochromogens, and nonchromogens) were nonreactive. A roentgenogram of the proximal phalanx of the left index finger demonstrated mild broadening with periosteal reaction and moderate osteoporosis with surrounding soft tissue swelling. An X-ray of the right knee revealed effusion and soft tissue swelling, but no bony abnormality.

Arthrocentesis of the right knee on 16 November 1976 yielded 2 ml of serous fluid which was sent for aerobic and anaerobic bacterial culture, fungal culture and smears, and cultures for mycobacteria; all cultures were sterile initially. Seven days later, the child was admitted for arthroscopy and synovial biopsy of the knee and bone biopsy of the index finger. Abundant viscous fluid containing rice bodies (corpora oryzoidea) (Fig. 1) was obtained from the knee. The fluid had a leukocyte count of 11,750 per mm³ with 97% mononuclear and 3% polymorphonuclear cells, an erythrocyte count of 250 per mm³,

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of the right wrist were noted. A roentgenogram of the wrist was normal. The isoniazid was discontinued, and treatment was begun with erythromycin and amoxicillin, both in a dose of 50 mg/kg per day. The patient was treated with this combination for 6 months. Roentgenograms taken in February, 1977, revealed no significant change. By mid-May of 1977, however, her thumb and index finger on the left hand were less swollen, her right wrist had a full range of motion, and her right knee had no effusion. In January 1979, she had some residual swelling of her left index finger and thumb, left third toe, and right wrist and knee, but had a full range of motion in all joints and no erythema, warmth, or tenderness. Repeat roentgenograms showed remodeling of bone in the digits previously involved.

**Properties of the isolated microorganism.** The organism isolated from the patient was well characterized. On Bennett agar, it formed tiny filamentous colonies and larger, round colonies with smooth margins at day 3; at days 7 and 14, there were more smooth than filamentous colonies. No aerial hyphae were identified. At day 5, cultures grown on glycerol agar revealed small coccobacilli, none of which were acid-fast.

Hydrolysates of whole cells were subjected to chromatographic analysis by the methods of Gordon et al. (9). The organism contained the meso form of diaminopimelic acid, arabinose, galactose, and the lipid LCN-A. These properties are characteristic of not only some species of Nocardia, but also of strains of the *Rhodococcus* genus.

The organism can be assigned to the rhodochrous group based on its colonial morphology, lack of acid-fastness, and chromatographic characteristics (R. E. Gordon, personal communication). The genus *Rhodococcus* has now been recognized (18); the organism likely belongs to this genus. The physiological properties of the organism (Table 2) do not permit species assignment. Gordon believes it is most like the strains of the species *rhodochrous* that she tentatively earlier assigned (9, 10) to the genus *Mycobacterium*. It differs, however, in four of its properties (non-acid production from d-sorbitol, nonutilization of citrate and malate, and resistance to rifampin) from a typical strain of *Mycobacterium rhodochrous* (9) and does not exactly match any of the recognized species of *Rhodococcus* (6).

**Discussion.** The rhodochrous group of microorganisms consists of gram-positive, aerobic, sometimes slightly acid-fast coccobacilli. *M. rhodochrous* was originally named and described
Acid production Glucose, glycerol, maltose, mannitol, mannose, trehalose, xylose

Oxidation Glucose

Hydrolysis Starch, esculin

Utilization Lactate, succinate

Oxidation Glucose

Decomposition Adenine, casein, hypoxanthine, tyrosine, urea, xanthine

Reduction Nitrate to nitrite

Deamination Phenylalanine

Growth

Medium Sabouraud dextrose broth

Temp (°C) 10, 28, 35

Survival At 50°C for 8 h

Resistance To rifampin, salicylate

TABLE 2. Physiological characteristics of a genus Rhodococcus isolate

<table>
<thead>
<tr>
<th>Determination</th>
<th>Physiological property</th>
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<tbody>
<tr>
<td>Acid production</td>
<td>Positive</td>
</tr>
<tr>
<td>Glucose, glycerol, maltose, mannitol, mannose, trehalose, xylose</td>
<td>Adonitol, arabinose, cellobirose, dulcitol, erythritol, galactose, inositol, lactose, melezitose, melibiose, α-methyl-d-glucoside, raffinose, rhamnose, α-erythritol, d-sorbitol</td>
</tr>
<tr>
<td>Hydrolysis</td>
<td>Starch, esculin</td>
</tr>
<tr>
<td>Utilization</td>
<td>Lactate, succinate</td>
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<tr>
<td>Oxidation</td>
<td>Glucose</td>
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<tr>
<td>Decomposition</td>
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<tr>
<td>Reduction</td>
<td>Nitrate to nitrite</td>
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<tr>
<td>Deamination</td>
<td>Phenylalanine</td>
</tr>
<tr>
<td>Growth Medium Temp (°C)</td>
<td>Sabouraud dextrose broth</td>
</tr>
<tr>
<td>10, 28, 35</td>
<td>MacConkey, methyl violet, and pyrnone agars 40, 45, 52</td>
</tr>
<tr>
<td>Survival</td>
<td>At 50°C for 8 h</td>
</tr>
<tr>
<td>Resistance</td>
<td>To rifampin, salicylate</td>
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</table>

by Overbeck in 1891 and extensively studied by Gordon (8, 10, 11). Morphological, biochemical, genetic, and immunological studies have demonstrated that this is a heterogeneous group of microorganisms whose characteristics overlap the genera Nocardia and Mycobacterium (12). A number of names have been proposed for a new genus into which these organisms could be grouped, including Gordona (19), Jensenia (7), and Rhodococcus (6). The latter is now the accepted genus for the rhodochrous group (18), although there is not universal agreement with its description.

These organisms form orange or red colonies at 28 and 37°C when grown on Sabouraud dextrose agar (12); growth usually appears in 3 to 4 days. The organism from our patient did not appear in culture the day 17. Microscopy generally reveals pleomorphic actinomycetes, forming branching filaments at some stage in their growth. True mycelia and spores are not formed. The organisms may be partially acid-fast (6); however, this property may be lost soon after isolation (2).

Species of Rhodococcus may have similar colonial morphology as those of Mycobacterium. Gordon and Mihm (10) demonstrated that cultures of mycobacteria and the rhodochrous group, with very few exceptions, produce dense colonies with smooth margins, dense colonies with a halo of filaments or filamentous colonies; no aerial hyphae are observed. Rhodochrous organisms may be differentiated from the rapidly growing mycobacteria by their only slight acid-fastness, ability to utilize succrose as a sole carbon source, inability to use trimethylene diamine as a simultaneous nitrogen and carbon source, and absence of arylsulfatase activity at 2 weeks (19). In addition, although the lipid LCN-A is often found in hydrolysates of whole cells of Rhodococcus, it has not been demonstrated in cultures of the mycobacteria (R. E. Gordon, personal communication).

Chromatography is not as helpful in distinguishing members of the genus Rhodococcus from those of Nocardia, since both may contain meso-diaminopimelic acid, arabinose, galactose, and LCN-A. Colonial morphology, however, is more useful. In contrast to the rhodococci, cultures of nocardia usually form filamentous colonies without smooth margins and, with only some exceptions, aerial hyphae are seen (10, 14). Members of Rhodococcus may also be distinguished from the clinically common Nocardia species by their ability to form acid from mannose, usual ability to reduce nitrate, and ability to utilize sucrose as a sole carbon source (19).

It would thus appear that, based on colonial morphology, lack of acid-fastness, and chromatographic data, the organism isolated from our patient belongs to the Rhodococcus genus. Unfortunately, its physiological properties do not permit species assignment, and thus it must be considered an atypical strain.

Rhodochrous group organisms have been recovered from a variety of sources, including plants, animals, and soil (8, 11). They are usually nonvirulent saprophytes (19), but have been isolated from humans. Alture-Weber et al. (2) report two cases of pneumonia with sepsis in which an organism of the rhodochrous group was recovered from both blood and lung tissue at autopsy. Skin lesions caused by rhodochrous group organisms were reported in a rider whose horse had similar lesions (15). Haburchak et al. (12) reported three cases in debilitated persons. Rhodochrous organisms apparently caused pericarditis in a 2-year-old child (16) and meningoencephalitis (17) in a second child. Most recently, Boughton and Atkin (4) report a ventric-
ular peritoneal shunt infection caused by a member of the rhodochrous complex in a 5-month-old infant.

The relationship of the infection seen in our patient to these previously reported infections is uncertain, since the relationship of the organism isolated from this patient to those cultured from other patients is not defined. Our patient appeared to have a previously unreported focus of infection, that of septic arthritis of the knee and probable osteomyelitis of the phalanges. The mode of entry was unclear, but hematogenous dissemination from unrecognized skin trauma seems most likely.

The rhodochrous group has been isolated primarily from patients who are immunocompromised or debilitated (2, 12). Studies have demonstrated the ability of these organisms to cause disease in animals receiving massive doses of steroids (12). Although Rhodococcus may become pathogenic under such circumstances, it may cause disease in apparently normal hosts. Although extensive investigations were not performed in our patient, she appeared to be immunologically normal.

Rice bodies were found in the knee joint. These were small, opaque, round or oval, soft and elastic gelatinous particles and consisted of amorphous fibrinoid material surrounded by hyperplastic synovium. Albrecht et al. (1), in a biochemical and electron microscopic study of rice bodies from rheumatoid arthritis patients, discovered they were composed of fibrin, fibrin-like mucoproteins, and small amounts of lipid. Rice bodies have been reported in joints after trauma with hemorrhage and in chronic synovitis, such as occurs in tuberculous infections (1, 13). They represent an end product of synovial inflammation, proliferation, and subsequent degeneration.

The proper treatment of infections caused by Rhodococcus spp. is unknown. The child with meningocencephalitis reported by Simon (17) improved after treatment with tetracycline and streptomycin. The rhodochrous isolates from two other patients (2) were susceptible to penicillin, tetracycline, erythromycin, neomycin, streptomycin, kanamycin, and novobiocin. Two of three patients reported by Haburchak et al. (12) showed improvement after treatment with agents having little in vitro activity against the rhodochrous organisms; the third patient had no evidence of disease at autopsy. Minocycline appeared to be the most consistently active drug in vitro against these organisms. The patient with ventricular peritoneal shunt infection reported by Boughton and Atkin (4) responded to ampicillin, methicillin, and intraventricular cephalothin initially and then continued to improve on penicillin and intraventricular gentamicin. Believing initially that our patient had a nocardial infection, we treated her with erythromycin and amoxicillin. Bach et al. (3) and Finland et al. (5) have demonstrated that ampicillin and erythromycin act synergistically against most strains of Nocardia asteroides; the efficacy of this combination in treatment of infections caused by Rhodococcus spp. has not been established. There are few data in the literature from which recommendations can be formulated as to duration of therapy of Rhodococcus spp. infections; 6 months appeared to be adequate in our patient.

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LITERATURE CITED