Rothia dentocariosa Bacteremia in Children: Report of Two Cases and Review of the Literature

Chin-Ying Yang,1 Po-Ren Hsueh,2 Chun-Yi Lu,3 Hsiu-Yuan Tsai,4 Ping-Ing Lee,3 Pei-Lan Shao,2 Chung-Yi Wang,3 Tsung-Zu Wu,4 Shih-Wei Chen,1 Li-Min Huang1*

Rothia dentocariosa, a pleomorphic, fastidious, Gram-positive rod, is a normal inhabitant of the oropharynx. It is a well-known causative agent of dental plaques and periodontal disease. Generally regarded as of low virulence to humans, R. dentocariosa has been increasingly recognized as a pathogen in adults and often associated with infective endocarditis. It should not necessarily be regarded as a contaminant when the isolate comes from areas other than the oropharynx, especially from the blood. We report two cases of R. dentocariosa bacteremia, including an 8-month-old boy with repaired transposition of the great arteries, and a healthy 20-month-old girl with herpangina. [J Formos Med Assoc 2007;106(3 Suppl): S33–S38]

Key Words: bacteremia, Rothia dentocariosa

Rothia dentocariosa is a filamentous, facultatively anaerobic nonmotile, nonspore-forming, Gram-positive rod, which usually resides in the oral cavity. Originally isolated from humans in 1949 by Onishi1 in carious dentine, it was known as Actinomycyes dentocarousus. It was later reclassified in the genus Norcardia because of its aerobic growth requirement. In 1967, Georg and Brown created the new genus Rothia because of its unique cell wall composition.2 R. dentocariosa has rarely been isolated from clinical specimens and has generally been regarded as a low virulence organism. Bacteremia caused by R. dentocariosa has rarely been described in children. Here, we report Rothia bacteremia in two children and review the literature.

Case Reports

Case 1

An 8-month-old boy, who underwent an arterial switch procedure for d-transposition of the great arteries at 5 days of age, had frequent airway infections after the cardiac surgery. Ten days prior to this admission, he became febrile with cough and rhinorrhea. Symptomatic treatments and a 5-day course of amoxicillin were given. Unfortunately, his condition deteriorated. Severe cough, hoarseness, and tachypnea were noted when he presented to the emergency department. His body temperature was 36.7°C, pulse rate was 144 beats/minute, and respiratory rate was 64 breaths/minute. His throat was infected. He was edentulous.
No gingivitis was noted. Breathing sounds were coarse with diffuse wheezing and rhonchi. There were notable sub- and intercostal retractions. His heartbeats were regular with a grade III/VI systolic murmur along the left sternal border. The liver edge was 2 cm below the right costal margin and the spleen edge was 2 cm below the left costal margin. These measurements were similar when compared to the findings at his previous examination 2 weeks before. The extremities were normal without cyanosis. No nail bed hemorrhage or abnormal skin lesions were detected.

Laboratory studies showed the following values: white blood cell (WBC) count of 8990/mm$^3$ with 56.2% segmented neutrophils, 31.5% lymphocytes, and 8.2% monocytes. His hemoglobin level was 9.6 g/dL and C-reactive protein was 1.99 mg/dL (normal, <0.8 mg/dL). Serum electrolyte levels and liver function tests were within normal limits. His chest X-ray showed cardiomegaly and emphysematous changes in both lungs with a flattened diaphragm. Increased infiltration of the lower right lung field was noted. He was admitted under the impression of acute bronchiolitis. Supportive treatments with intravenous fluids, inhalation of cool, humidified oxygen, and chest hygiene care were given. On the 3rd day of hospitalization, the blood culture obtained at the emergency room grew two Gram-positive bacteria. Intravenous cephalothin (100 mg/kg/day) was given. These two bacteria were identified as Streptococcus sanguis and Rothia dentocariosa using API 32 STREP and API CORYNE (BioMerieux Vitek, Inc., Hazelwood, MO, USA), respectively. The colonies of the R. dentocariosa isolate were raised with rough concentric and irregular edges after incubation for 72 hours (Figure 1). The Gram stain smear from the culture showed pleomorphic branching rods to cocci (Figure 2). Sequence analysis of nearly complete 16S rRNA gene (1487 bp) for the R. dentocariosa isolate was also conducted using two primers (8FPL and 1492). A blastn search was performed to compare the sequence of our isolate with those in the GenBank and Ribosomal Project database. Our isolate was compatible with the identification of R. dentocariosa (accession number, AF543284). We changed the cephalothin to penicillin G (250,000 unit/kg/day) and gentamicin (7.5 mg/kg/day). Antimicrobial susceptibility of R. dentocariosa was determined by the E-test (PDM, Solna, Sweden) on Mueller-Hinton agar (BBL Microsystems, Cockeysville, MD, USA). The minimal inhibitory concentration (MIC) ranges (μg/mL) were as follows: penicillin 0.125, cephalothin 0.25, cefotaxime 0.38, gentamicin 2, amikacin 2, vancomycin 2, clindamycin 1, erythromycin 0.023, and chloramphenicol 1.5. The precordial echocardiogram showed mild stenosis of the neoorta and mild regurgitation of neoaortic and pulmonary arteries. There was no vegetation. Blood cultures obtained on
the 3rd day of hospitalization before the use of cephalothin was negative. Parenteral antibiotics were used for 5 days. The patient was discharged on the 12th day of hospitalization after improvement of his respiratory condition. No complications developed during follow-up.

Case 2
A 20-month-old girl with no underlying disease presented to our emergency department because of fever and a seizure attack. At home, she had a sudden loss of consciousness, upward gazing, and tonic posturing of the extremities. This lasted for 5 minutes and she regained consciousness soon after. On physical examination, she appeared lethargic. Her body temperature was 38.8°C, heart rate was 120 beats/minute, and respiration rate was 34 breaths/minute. Her pupils were isocoric with prompt light reflex. There were multiple vesicles over the soft palate and buccal mucosa. There was no gingivitis or dental caries. Chest, cardiac, abdominal, integumentary, and neurologic examinations were unremarkable. Her WBC count was 10,430/mm3 with 65.3% segmented neutrophils, 26.7% lymphocytes, and 5.9% monocytes. Her serum electrolyte levels, blood glucose, and liver function tests were all within normal limits. The result of her lumbar puncture showed clear cerebrospinal fluid (CSF) with glucose concentration of 63 mg/dL, total protein concentration of 15 mg/dL, and no nucleated cells. She was admitted under the impression of herpangina and possible febrile convulsion. She received intravenous fluids and antipyretics. No antibiotics were given. Her clinical condition improved quickly and she was discharged 2 days later. The blood culture obtained at the emergency room grew R. dentocariosa. Bacterial culture of her CSF was negative. Her follow-up electroencephalography was normal. The seizure episode at the emergency department was interpreted as febrile convulsion. No further blood culture was obtained due to her good clinical condition on follow-up visits. No complication was detected. Initial isolate was lost for further antimicrobial susceptibility testing.

Discussion
R. dentocariosa has been most frequently isolated from oropharyngeal secretions, sputum, and carious teeth. Although it has also been isolated from blood, heart valves, ascitic fluid, CSF, urine, bone, pubic aspirate, eyes, and pleural and joint effusions, the clinical significance of many of these isolates remains unclear. Kong et al., in a review of specimens over 8 years from two reference laboratories in France, showed a total of 103 specimens, of which 69 were isolated from the respiratory tract and were most likely contaminants. Only 19 cases had positive blood cultures and most of them were transient bacteremia.

However, in 1969, Roth and Flanagan5 experimentally induced abscess formation in mice, via local injections, thus demonstrating a pathogenic potential for R. dentocariosa. To date, 20 cases of infectious endocarditis6–20 and 12 patients with extracardiac infection21–30 caused by R. dentocariosa have been reported in the English literature. Most of them were immunocompromised adults or those with pre-existing cardiac disease (mitral valve prolapse, bicuspid aortic valve, rheumatic mitral valvular disease, prosthetic valve) and poor oral hygiene. Only five patients younger than 18 years of age have been reported (Table). In 1975, Scharfen27 presented a 17-year-old girl with an infected pilonidal cyst, which required surgical drainage. Recently, a 4-year-old, immunocompetent Japanese girl was reported to have severe acute tonsillitis with a pseudomembrane.30 Neither of the two had evidence of blood stream infection. The other three patients had infective endocarditis; two of them were complicated with mycotic aneurysms.9,12,20

We present two children with bacteremia caused by this rare pathogen, R. dentocariosa. In case 1, the isolated organisms, R. dentocariosa and S. sanguis, are commonly found as normal flora in the oropharynx. In case 2, the mucosal damage caused by herpangina might have provided the portal of entry for the bacteria. Although we did not perform throat bacterial culture in either case, the bacteria probably invaded the blood through...
the injured oral mucosa. Both cases had benign clinical courses and complete recovery despite the fact that case 1 had a pre-existing complex congenital heart disease. The second blood culture in case 1 without using antimicrobial agent was already negative. No antimicrobial agent was given in case 2. The clinical courses of the two cases were compatible with self-limited transient bacteremia by low virulent pathogen.

Microbiologically, R. dentocariosa is a slow-growing (3-7 days) organism with an optimum growth temperature of 37°C. Its growth is best under aerobic conditions, but it is able to survive microaerophilically. On 5% horse blood agar, white-grey small (1 mm) smooth colonies with entire edges are seen after 24 hours of incubation. The colonies are raised with rough convex protuberances. Negative reactions include oxidase, urease, indole, and lactose. The major glucose fermentation products of R. dentocariosa are lactic and acetic acids, in contrast to succinate and propionic acid in Actinomyces and Propionibacterium. The growth rates, lack of partial acid fastness, absence of aerial mycelium, and fermentation of sugars are helpful for distinguishing Rothia from other Gram-positive rods. The API CORYNE test strips are useful for identification and typically yield codes 7050125 or 7052125. Additional chemotaxonomic analyses (e.g. continuous flow analysis chromatography) may help differentiate Rothia from other Gram-positive rods. The application of 16S rRNA gene sequencing also provides good identification results. Although there are no National Committee for Clinical Laboratory Standard protocols for susceptibility testing of Rothia, most isolates from clinical cases are susceptible to penicillin, amoxicillin, and cephalosporins. The growth rates, lack of partial acid fastness, absence of aerial mycelium, and fermentation of sugars are helpful for distinguishing Rothia from other Gram-positive rods. The API CORYNE test strips are useful for identification and typically yield codes 7050125 or 7052125. Additional chemotaxonomic analyses (e.g. continuous flow analysis chromatography) may help differentiate Rothia from other Gram-positive rods. The application of 16S rRNA gene sequencing also provides good identification results. Although there are no National Committee for Clinical Laboratory Standard protocols for susceptibility testing of Rothia, most isolates from clinical cases are susceptible to penicillin, amoxicillin, and cephalosporins.
the literature are susceptible to penicillins, cephalosporins, erythromycin, vancomycin, aminoglycosides, tetracycline, chloramphenicol, and trimethoprim/sulfamethoxazole. Reported penicillin MICs are low, ranging from \(<0.016\) mg/L to \(0.12\) mg/L.\(^{10,11,15,17,19,24}\) Also, favorable outcome with penicillin therapy suggest \textit{in vivo} susceptibility. However, vancomycin treatment failure has also been reported.\(^7,13\)

In this report, we observed that \textit{R. dentocariosa} bacteremia could develop in immunocompetent children when oral mucosa is injured. The clinical course is usually benign as transient bacteremia. But, since there were growing numbers of case reports of serious systemic infections caused by \textit{R. dentocariosa},\(^4,6–29\) it should not necessarily be regarded as a contaminant when the isolate comes from areas other than the oropharynx. Penicillin, the drug of choice, should be used once the blood culture is positive. The duration of antimicrobial agent use depends on the following culture results. In immunocompromised patients and those with heart disease and poor dental hygiene, prompt identification and antimicrobial susceptibility testing are important to achieve good clinical response.

References