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CASE REPORT
Neonatal

Rhizobium radiobacter infection in a preterm infant and review of the literature

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ABSTRACT

Rhizobium radiobacter (*R. radiobacter*) is a soil-borne opportunistic pathogen that can cause infections in both adults and children, as well as infections associated with invasive procedures and catheters. In neonates, both term and preterm, it can cause bacteremia and systemic infections. This study presents a case of *R. radiobacter* infection in a preterm neonate, which was effectively managed with antibiotic therapy for early neonatal sepsis. Furthermore, we conducted a literature review on the clinical manifestations and management strategies of *R. radiobacter* infections during the neonatal period, in accordance with current medical literature.

Keywords: Agrobacterium tumefaciens; newborn; pediatric; *Rhizobium radiobacter*.

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Preterm bir bebekte *Rhizobium radiobacter* enfeksiyonu ve literatürün gözden geçirilmesi

ÖZET

Rhizobium radiobacter (*R. radiobacter*) toprak kaynaklı fırsatçı bir patojendir. Erişkinlerde ve çocuklarda immün yetmezlik, girişimsel işlemler ve kateterle ilişkili enfeksiyonlara; term ve preterm yenidoğanda bakteriyemi ve sistemik enfeksiyonlara yol açar. Burada preterm bir bebekte antibiyoterapi ile kolayca kontrol altına alınan, erken neonatal sepsis etkeni olarak karşılaştığımız *R. radiobacter* olgusunu ve yenidoğan döneminde bu *R. radiobacter* enfeksiyonlarının klinik görünümü ve yönetimi ile ilgili bir literatür incelemesini sunuyoruz.

Anahtar Kelimeler: Agrobacterium tumefaciens; pediatrik; Rhizobium radiobacter; yenidoğan.

INTRODUCTION

Rhizobium is a soil-borne, aerobic, non-spore, non-fermentative, motile, gram-negative bacillus with tumorigenic effects on plants and an opportunistic pathogen in humans (1–3). Infections caused by *Rhizobium radiobacter*, which are rarely seen in humans, include peritonitis, urinary tract infection, endophthalmitis, pulmonary abscess, and bacteremia in immunocompromised patients (4). It causes catheter-related infections by forming a slime layer and mucoid colony with its extracellular polysaccharide structure (4, 5). Immunocompromised children or those undergoing invasive procedures and catheterization are susceptible to *R. radiobacter* infections. Out of the eight neonatal cases reported, five were preterm births. In two term cases, no identifiable risk factors were found. Our case is the fourth early neonatal sepsis case in the literature. We present a review of the clinical presentation and management of *Rhizobium* infections in the newborn.

CASE REPORT

A 30-year-old primigravid mother delivered a boy, 32 weeks and 3 days old, by caesarean section for preterm labor and anhydramnios. The baby weighed 1980 grams. There was no need for resuscitation. The APGAR score was 8 at 1 minute and 9 at 5 minutes. The patient was transferred to the neonatal intensive care unit due to prematurity and respiratory distress.

It was discovered that the mother resided in a rural area and was employed as a gardener. She experienced a urinary tract infection during her pregnancy and suffered from premature rupture of membranes 18 hours prior to delivery. There was no presence of foul-smelling vaginal discharge, and the amniotic fluid was clear.

The infant presented with tachypnea, intercostal retraction, nasal flaring, and low oxygen saturation. Nasal intermittent ventilation was used for treatment. Central venous catheterization was not necessary. A blood culture was obtained from a peripheral vein using complete aseptic technique and inoculated into an aerobic pediatric blood culture bottle (BD Bactec™ plus aerobic pediatric). C-reactive protein was negative, and the complete blood count was normal. Empirical treatment with penicillin G and gentamicin, appropriate for gestational week and postnatal age, was initiated due to prematurity and premature rupture of membranes. Additionally, minimal enteral nutrition was started using breast milk.

On postnatal day 2, the baby exhibited hypoactivity and lethargy, accompanied by gastric distension and vomiting. No fever was present. The first blood culture detected the growth of gram-negative bacilli at the 48th hour postnatal. The repeated C-reactive protein test was negative, and the complete blood count revealed a leukocyte count of 9200/mm^3, lymphocyte count of 1400/mm^3, PMNL count of 7300/mm^3, and platelet count of 243000/mm^3. A lumbar puncture was performed. On direct examination, the cerebrospinal fluid (CSF) was clear, and no cells or microorganisms were observed. Biochemical analysis was normal, and a CSF culture was taken. Treatment with penicillin G and gentamicin was discontinued at postnatal 48th hour, and empirical treatment with cefotaxime and amikacin was started.

The initial blood culture agent was subcultured on brain heart infusion broth, MacConkey agar, and 5% sheep blood agar. Following overnight incubation, a non-lactose fermenting, translucent colony measuring 1–2 mm was grown on MacConkey agar. Similar non-hemolytic colony morphology was observed on blood agar. The isolate was identified as *Rhizobium radiobacter* with 99% probability by VITEK-2 using a gram-negative card (Biomerieux™, France). As the EUCAST v10 and CLSI M100 guidelines do not provide limit values for this bacterium, the VITEK-2 device, AST N-326 antibiogram card did not provide MIC (minimum inhibition concentration) values. To gain an idea about the agents used in treatment in the literature, the antibiogram card was visually read, revealing low MIC values for cefotaxime and amikacin (MIC value obtained by liquid microdilution for cefotaxime and imipenem was ≤2 µg/ml, and for amikacin was ≤8 µg/ml). The disc diffusion method was used to perform an antibiogram, which showed zone diameter formation in the cefotaxime, cefepime, amikacin, and imipenem antibiotics.

Following 48 hours of cefotaxime and amikacin treatments, the infant's respiratory distress completely resolved, eliminating the need for mechanical ventilation or supplemental oxygen. The patient exhibited good activity levels and tolerated breastfeeding

well. No bacterial growth was detected in the pediatric aerobic blood culture after 72 hours of antibiotic therapy, even after 7 days of incubation. Similarly, no growth was observed in the cerebrospinal fluid culture after 72 hours of incubation.

After the blood culture showed no bacterial growth, the antibiotic treatment was extended for an additional ten days. This included cefotaxime, administered at a dose of 50 mg/kg every 12 hours for the first fourteen days, followed by dosing every 8 hours. Amikacin was administered at a dose of 18 mg/kg every 36 hours for the initial seven days, and then adjusted to 15 mg/kg every 24 hours.

Transcranial and abdominal ultrasonography findings were normal. A blood culture conducted one week after completing the antibiotic regimen showed no microbial growth. The patient was discharged at 20 days of age. Follow-up examinations were conducted when the patient was 91 days old and 45 weeks postmenstrual age. Growth and developmental parameters were recorded as normal.

DISCUSSION

English language literature was searched on PubMed National Library of Medicine using the terms '*Rhizobium radiobacter*', '*Agrobacterium tumefaciens*', pediatric, and 'neonate'. References were reviewed to identify additional cases. Neonatal cases were defined as premature cases who did not complete the 44th postmenstrual week and term cases under 30 days postnatally.

Rhizobium, formerly known as *Agrobacterium*, is a microorganism commonly found in soil and plants worldwide. It has tumorigenic effects in plants and can cause opportunistic infections in humans (1). There are five known species of *Rhizobium* (*Rhizobium radiobacter*, *Rhizobium rhizogenes, Rhizobium rubi, Rhizobium undicola, Rhizobium vitis*), with *R. radiobacter* having low virulence and being the only one known to be pathogenic in humans (2). The microorganism is an aerobic, gram-negative bacillus that is motile due to its peritrichous flagella. It is non-spore-forming and non-fermentative (3). Its extracellular polysaccharide structure allows it to form mucoid colonies in carbohydrate-rich medium and the slime layer (4, 5).

This pathogen is rarely detected in clinical samples. The method by which it infects humans is not known. Hospital-acquired infections account for 92.2% of known *Rhizobium* infections. There are also cases linked to soil contact (6, 7). Lai et al. (2) suggest conducting surveillance studies to determine the reservoir and source of infection or contamination, as well as potential modes of infection transmission in the hospital environment. Detection of *Rhizobium* growth in a blood culture is considered contamination (8). The study by Pereira et al. (9) focused on contamination of a saline provider in the microbiology laboratory. Rogues et al. (10) identified contamination due to blood being collected from fifteen newborn babies in non-sterile citrated tubes before blood culture collection. A study reported that the source of contamination was calcium gluconate used in total parenteral nutrition units (11).

Infections caused by *R. radiobacter* are highly correlated with the presence of foreign plastic materials. The polysaccharide structure and slime layer of the bacteria facilitate this process. The first reported case of human infection was endocarditis in a patient with a prosthetic heart valve (12). This bacterium can cause a range of clinical conditions, including catheter-related bacteremia, peritonitis in patients undergoing continuous ambulatory peritoneal dialysis (13), urinary tract infections (14), and rarely endophthalmitis, endocarditis (12–15), and pulmonary abscess (16). The main risk factors for both adult and pediatric patients are immunosuppression and the presence of foreign plastic material. *Rhizobium radiobacter* was detected in the lung aspirate of patients with cystic fibrosis (17). Cases of acute and chronic endophthalmitis caused by *R. radiobacter* have been reported in adults who underwent intravitreal injection and cataract surgery (18–20).

There are forty-seven cases of pediatric patients in the literature. Among the 26 cases reported from China in 2014, 21 were under the age of two. The majority of cases were related to the presence of a catheter and poor catheter care (21). Two pediatric cases had peritonitis not accompanied by systemic infection, which developed while peritoneal dialysis was being performed due to end-stage renal failure (22). Other cases of pediatric patients are associated with central venous catheter-related bacteremia. Nine patients had acute lymphoblastic leukemia (23), four had solid tumors, two had severe combined immunodeficiency (24), one had HIV infection (25), one had viral infection-associated hemophagocytic syndrome, one had chronic severe thrombocytopenia, one had aplastic anemia, and one had short bowel syndrome. All patients had an underlying chronic disease. As *R. radiobacter* exhibits irregular patterns of antibiotic sensitivity and resistance to many antibiotics, the choice of antibiotics used in each case may vary (25).

The patient was admitted due to decreased fetal movements and uterine contractions. A pregnant woman was found to have *R. radiobacter* growth in her peripheral blood culture, despite having no fever, bleeding, or rupture of membranes. The same bacteria was detected in the blood culture taken from the umbilical vein of a male fetus who was stillborn vaginally at the 30th week of gestation. However, it was emphasized that the cause of intrauterine death in this case was not due to *R. radiobacter* infection. It was suggested that syphilis or asphyxia due to the nuchal cord could be the cause of death (26).

There are eight reported cases of neonatal *R. radiobacter* infection (Table 1).

The first reported case of neonatal *R. radiobacter* infection was by Farina et al. (27). On the 13th day after birth, the baby developed a fever. The baby was born vaginally and discharged without any issues on the 4th day. The infant exhibited an increase in acute phase reactants and weight loss. Although urine and cerebrospinal fluid cultures showed no growth, *R. radiobacter* was detected in the peripheral blood culture. The infant's abdominal and transfontanel ultrasonography and chest radiography were normal. The clinical and microbiological

Table 1. Newborn cases with *R. radiobacter* infection

Reference and publication year	Postnatal age (day)	Risk factors	Treatment
Our case	1	Preterm, PPROM, maternal soil contact	Cefotaxime and amikacin
27–1996	13	Term, no known risk factors	Ampicillin
28–2011	1	Term, home birth, consumption of herbal tea	Cefepim and gentamicin
29–2013	115	Preterm, CVC	Meropenem and amikacin
1–2015	4	Term, no known risk factors	Imipenem and gentamicin
30–2020	2	Preterm, PPROM, IAI	Imipenem and gentamicin
31–2020	21	Preterm, PICC, jejunal atresia	Meropenem and colistin
32–2022	1	Preterm, maternal heart failure	Meropenem and amikacin
33–2022	?	Preterm, no known risk factors	Cephalosporin

PPROM: Preterm premature rupture of membranes; CVC: Central venous catheter; IAI: Intraamniotic infection; PICC: Peripherally inserted central venous catheter.

response of the baby treated with ampicillin for 9 days can be explained by the transient nature of *R. radiobacter* bacteremia and its low virulence (27).

R. radiobacter was cultured from the blood of a term baby whose mother used evening primrose oil during pregnancy and gave birth in water at home due to recurrent apnea on the first postnatal day. The complete blood count and cerebrospinal fluid evaluations were normal. Empirical ampicillin treatment was discontinued, and the baby received cefepime and gentamicin for 14 days. Clinical and laboratory findings improved rapidly, and no growth was detected in control blood cultures. The examination performed at the age of three months was normal. According to a report, *R. radiobacter* infection may occur in a newborn even without a central venous catheter, and in the absence of known immunodeficiency (28).

Kahn et al. (29) reported the growth of *R. radiobacter* in a blood culture taken on the 115th postnatal day from a newborn with a central venous catheter. The infant was born as a twin at the 25th week of gestation and presented with fever and abdominal distension. The patient clinically improved with meropenem treatment, and subsequent blood culture controls were sterile. The patient died on the 143rd postnatal day for reasons unrelated to infection.

R. radiobacter growth in blood culture was reported in a baby who presented with fever, tachypnea, inability to feed, and lethargy on the 4th postnatal day, with increased C-reactive protein and leukocytosis. This baby, whose prenatal history was unremarkable and who spent the first three postnatal days without any problems, was treated with imipenem and gentamicin, and there was no growth in the control blood culture. His examination at seven months of age was normal. It has been reported that *R. radiobacter* infection may occur in term newborn babies without any risk factors (1).

In a preterm baby born spontaneously vaginally to a mother with a history of PPROM and foul-smelling vaginal discharge, *R. radiobacter* was isolated from the blood culture taken due to symptoms of fever, lethargy, poor feeding, and respiratory distress that started on the second postnatal day. It was hypothesized that corticosteroids might have been a risk factor for *R. radiobacter* infection in this baby, who received corticosteroids due to preterm birth (30).

A term neonatal case of central venous catheter-associated bloodstream infection (CLABSI) was confirmed in a preterm infant who underwent surgery for jejunal atresia on the 2nd day after birth and was monitored with a peripherally located central venous catheter. On the 21st day after birth, the infant exhibited lethargy and apnea, and *R. radiobacter* was detected in both peripheral venous and catheter blood cultures. This is the first confirmed case of CLABSI in a neonate (31).

A neonate born preterm via vaginal delivery to a mother with suspected congestive heart failure and peripartum cardiomyopathy developed respiratory distress and hemodynamic instability, requiring the use of vasoactive drugs. Opacities were detected on chest radiography, and *R. radiobacter* was grown in blood culture. The mother's blood culture result was not reported in the first neonatal case resulting in death in the literature (32).

Patel et al. (33) reported *R. radiobacter* sepsis in a preterm newborn with no known risk factors.

This is the ninth neonatal case reported in the literature. Early neonatal sepsis was diagnosed based on the premature rupture of membranes, the mother's history of contact with soil, the onset of symptoms immediately after birth, and the growth of *R. radiobacter* in the blood culture taken within the first hours after birth. Intraamniotic infection was not considered as the mother did not exhibit any symptoms such as foul-smelling vaginal discharge, fever, uterine tenderness, and laboratory parameters were not indicative of an infection. Additionally, our patient has no history of catheters. Blood culture was taken with complete asepsis. No blood was taken into a citrated tube, and total parenteral nutrition was not required. Clinical findings were detected in our patient that could not be explained solely

by preterm birth. Our case represents the first reported growth of *R. radiobacter* in our microbiology laboratory. Therefore, it was not considered a contamination in our case. The clinical presentation of mild sepsis in our patient, their rapid recovery, and the absence of persistent growth in control blood cultures may be attributed to the low virulence of the causative agent, as reported in the literature. As with other neonatal cases reported, primary immunodeficiency was not considered in our patient. The antibiogram revealed that the agent, previously reported to have a variable antibiotic sensitivity profile, was sensitive to cefotaxime and amikacin. Treatment resulted in a good clinical and microbiological response.

R. radiobacter is an opportunistic pathogen with low virulence and a variable antibiotic susceptibility pattern. It may cause early and late neonatal sepsis in newborns without being a risk factor. It usually causes mild sepsis. A history of contact with soil, as in our case, can be considered a risk factor. The inflammatory trigger caused by this infection may be the cause of premature rupture of membranes and preterm birth. This is the first reported case of neonatal infection with this rare microorganism in our country.

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