Rhodococcus Ventriculoperitoneal Shunt Infection with Meningitis and Peritonitis in an Immunocompetent Child

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KEY WORDS: children, meningitis, peritonitis, *Rhodococcus*, ventriculoperitoneal shunt

IMAJ 2021; 23: 745–747

Rhodococcus spp. (mostly *Rhodococcus equi*) are intracellular aerobic, gram-positive, and weakly acid-fast coccobacilli, identified as a pathogen in various animals (e.g., foals, cattle, goats) and commonly found in the soil of farms [1]. Infection is acquired via inhalation from soil, inoculation into wounds or mucous membranes, or ingestion in immunocompromised patients. Immunocompetent patients, although rarely infected, are more likely to present with a localized disease [2]. *Rhodococcus* can infect macrophages and survive inside lysosomes. The resulting defective intracellular processing leads to necrotizing granulomatous reaction dominated by macrophages. The necrotizing granulomas may subsequently coalesce to form abscesses [1,2].

The manifestations of the disease caused by *R. equi* are diverse, although pulmonary infection is present in approximately 80% of cases [1]. The radiologic findings have described ill-defined and irregular consolidation areas of cavitation in the lungs, similar to *Mycobacterium tuberculosis* [2]. Approximately 10–15% of infections occur in immunocompetent hosts, with the remainder being diagnosed in patients with human immunodeficiency virus infections and other immunocompromised patients [1]. Patients may present with infection at a single site or at multiple sites and relapses are common.

We describe the case of an immunocompetent child with meningitis, peritonitis, and ventriculoperitoneal (VP) shunt infection due to *Rhodococcus* spp.

PATIENT DESCRIPTION

A 3-year-old girl of Jewish ethnicity presented with periumbilical pain and low-grade fever of 38°C for the last 24 hours, without headache, vomiting, or neurological symptoms.

She was born preterm at 30 + 2 weeks gestational age and was diagnosed after birth with bilateral intraventricular hemorrhage grade 3 and posthemorrhagic hydrocephalus. A right VP shunt was inserted at the age of 3 months. During the next 2.75 years she developed normally and was in a good medical condition, without additional hospitalizations. At the age of 2 years and 10 months, she started vomiting, without any findings in the neurological examination. A VP shunt tap revealed normal cerebrospinal fluid (CSF) parameters, and the CSF culture returned without growth. A magnetic resonance imaging examination was unremarkable. A week later, right torticollis and somnolence alternating with irritability were noted. A head CT showed ventricular asymmetry with left ventricle enlargement, suggesting shunt malfunction. The CSF culture was negative and she underwent a new left VP shunt insertion.

During hospitalization, abdominal tenderness was noted, with erythema and crust formation around the abdominal surgical incision site of the VP shunt. The laboratory tests were unremarkable except for elevated C-reactive protein (CRP) (12 mg/dl, normal values 0.2–5.0). An abdominal ultrasound revealed a small collection area in the middle upper abdomen and suboptimal visualization of the abdominal end of the VP shunt, with a small amount of free intra-abdominal fluid. Treatment with piperacillin/tazobactam (90 mg/kg qid) was started. The abdominal fluid and blood cultures returned negative. A left shunt tap showed one WBC/mm3, glucose 46 mg/dl, and protein 35 mg/dl. The gram stain of the CSF was positive for gram-positive bacilli and vancomycin (20 mg/kg tid) was added to therapy. The patient continued to have low-grade fever, abdominal pain, and headache. An abdominal CT showed the VP-shunt traversing several pelvic collections and terminating at the lower abdomen. Dilated small bowel was seen with collapsed distal ileum indicating small bowel obstruction. Piperacillin/tazobactam was discontinued and treatment was modified to meropenem (40 mg/kg tid) and vancomycin (20 mg/kg tid). The CSF culture (reported after 72 hours of incubation) grew *Rhodococcus* spp. (identified by MALDI-TOF MS using VITEK MS system, Biomérieux, France). Subsequent taps from the left and right shunts were still positive for *Rhodococcus* spp. for a 7-days period. On day 7 of hospitalization, the patient started vomiting and became lethargic and decrease of Glasgow Coma Scale score

from 15 to 10 was noted. The head CT was unchanged. The patient underwent emergency right and left shunt removal, and an external ventricular drainage insertion was performed followed by an abdominal laparoscopy which revealed peritonitis with free serous fluid in the peritoneal cavity, omental dehiscence, and intestinal swelling. The aerobic and anaerobic cultures from the peritoneal fluid were negative. The CSF culture obtained during surgery was positive for *Rhodococcus* spp. Intravenous rifampin (20 mg/kg once daily) was added. All post-surgery cultures from CSF, blood, and abdominal fluid returned negative and vancomycin was discontinued.

After 2 weeks of negative CSF cultures, a new VP shunt was inserted without further complications. The girl completed a 4-week course of antibiotic treatment with meropenem and rifampin and was discharged home with no symptoms or neurologic sequelae. Long-term follow-up during the next 3 years revealed no CSF or abdominal findings suggestive of infection and no neurologic sequelae.

COMMENT

We presented here a report of an immunocompetent child with meningitis, peritonitis, and VP shunt infection due to *Rhodococcus* spp.

In a review from 2001 [3] describing 19 immunocompetent patients with *R. equi* infection (6 children aged 9 months to 9 years), a wide range of infections were reported, varying from localized ones secondary to trauma to fatal systemic infection. Systemic infections included 8 cases of pulmonary infection and one of fever without origin. Endophtalmitis, traumatic meningitis, lymphadenitis, septic arthritis, and mandibular osteitis represented the spectrum of localized infections described in the study. The patients with osteitis experienced a relapse after being on combination oral therapy for 8 months. Two (11%) patients, aged 76 and 83 years and diagnosed with bilateral pneumonia, died during therapy.

Table 1 shows a summary of our PubMed search for the reported cases (including the present case) of *Rhodococcus* infection diagnosed in immunocompetent children during the period 1968–2019 including our report. Of the eight patients aged 2 months to 9 years, three had central nervous system pathologies following perinatal intraventricular hemorrhages, with development of hydrocephalus and placement of VP shunts. Purulent meningitis was diagnosed in four cases and endophtalmitis, septic arthritis, peritonitis, cervical lymphadenitis, and lymphangitis in one patient each. None of the patients had pulmonary involvement or peritonitis.

Our patient developed meningitis and subsequent peritonitis following *Rhodococcus* shunt infection after shunt malfunction and new shunt insertion. Following deterioration in the general condition after 7 days of therapy, the VP shunts were removed and replaced by an external VP shunt. An emergency laparoscopy for drainage of the infected peritoneal fluid collections was performed and rifampin was added to treatment, with rapid CSF sterilization and improvement in the clinical condition. Recommended antibiotics with good efficacy against *Rhodococcus* include ciprofloxacin, macrolides, carbapenems, vancomycin, and rifampicin. Combined use of multiple antibiotics may lead to synergistic effects [2,3]. Approximately 40% of the isolates are resistant to penicillins, cephalosporins, trimethoprim-sulfamethoxazole, clindamycin, and ampicillin-sulbactam [2]. The duration and intensity of treatment should be determined by the immunological status of the host and the nature of the pathologic lesion. In immunocompromised

Table 1. Reported cases of immunocompetent pediatric patients with *Rhodococcus* infection (1968–2019)

Reference	Year of publication	Age at diagnosis	Underlying condition/disease	Clinical and laboratory presentation	Isolate source
Boughton et al. [3]	1980	5.5 months	Intraventricular hemorrhage and congenital hydrocephalus, VP* shunt	Fever, lethargy, stiff neck, meningitis	CSF
Kedlaya et al. [4]	1988	9 years	Corneal laceration with tip of umbrella	Endophthalmitis	Eye wound
Kedlaya et al. [4]	1994	4 years	Nail puncture wound at construction site	Septic arthritis of knee	Articular fluid
Kedlaya et al. [4]	1994	3 years	Exposure to dogs	Cervical adenopathy	Lymph node
Kedlaya et al. [4]	1994	9 years	NA**	Lymphangitis	NA*
Kedlaya et al. [4]	1997	6 years	Eye perforation, contamination with horse feces and soil	Fever, meningeal signs, meningitis	CSF
Strunk et al. [5]	2007	2 months	Prematurity, intraventricular hemorrhage grade 3, Hydrocephalus, VP shunt	Apnea, seizures, meningitis	CSF
Present case	2019	3 years	Intraventricular hemorrhage grade 3, hydrocephalus, VP shunt	Low grade fever, abdominal tenderness, lethargy, meningitis, peritonitis	CSF

CSF = cerebrospinal fluid, IVH = intraventricular hemorrhage, NA = not available, VP = ventriculoperitoneal

patients, prolonged therapy courses with two antibiotics have generally been recommended. However, in immunocompetent patients, selected local infections without systemic involvement (e.g., lymphadenitis, lymphangitis) may be treated with either short courses of parenteral antibiotics or a 4-8-week course of oral antibiotics [3].

CONCLUSIONS

We presented a case of a *Rhodococcus* VP shunt infection complicated by peritonitis and meningitis, treated by shunt removal and prolonged antibiotic therapy, with a favorable clinical long-term outcome. Although mainly diagnosed in immunocompromised children, *Rhodococcus* should be taken into consideration in the management of serious bacterial infections in immunocompetent patients as well, particularly those with VP shunt infections.

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Capsule

Immunology arms for autoantibody responses

Systemic lupus erythematosus (SLE) is a condition characterized by the activation of autoreactive B and T cells and the production of antibodies against nucleic acids and associated binding proteins. Germinal centers (GCs), areas within lymphoid organs where mature B cells expand and differentiate with T cell help, are thought to play an important role in this process. **Chiang** et al. found that when the costimulatory molecules CD80 and CD86 were specifically deleted from B cells, GC formation was inhibited in a B cell-driven mouse model of SLE. The disappearance of autoimmune GCs resulted in a loss of RNA-associated autoantibodies but not the anti-DNA and connective tissue autoantibody repertoire. Thus, separate extrafollicular and GC-derived pathways may control discrete arms of the autoantibody response in this disease.

J Immunol 2021; 10.4049/jimmunol.2100548
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Capsule

Unravelling the collateral damage of antibiotics on gut bacteria

Antibiotics are used to fight pathogens but also target commensal bacteria, disturbing the composition of gut microbiota and causing dysbiosis and disease. Despite this well-known collateral damage, the activity spectrum of different antibiotic classes on gut bacteria remains poorly characterized. **Maier** et al. characterized another 144 antibiotics from a previous screen of more than 1000 drugs on 38 representative human gut microbiome species. Antibiotic classes exhibited distinct inhibition spectra, including generation dependence for quinolones and phylogeny independence for β-lactams. Macrolides and tetracyclines, both prototypic bacteriostatic protein synthesis inhibitors, inhibited nearly all commensals tested but also killed several species. Killed bacteria were more readily eliminated from in vitro communities than those inhibited. This species-specific killing activity challenges the long-standing distinction between bactericidal and bacteriostatic antibiotic classes and provides a possible explanation for the strong effect of macrolides on animal and human gut microbiomes. To mitigate this collateral damage of macrolides and tetracyclines, we screened for drugs that specifically antagonized the antibiotic activity against abundant *Bacteroides* species but not against relevant pathogens. Such antidotes selectively protected *Bacteroides* species from erythromycin treatment in human-stool-derived communities and gnotobiotic mice. These findings illluminate the activity spectra of antibiotics in commensal bacteria and suggest strategies to circumvent their adverse effects on the gut microbiota.

Nature 2021; 599: 120
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