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CASE REPORT

Ralstonia Mannitolilytica: An increasingly recognized healthcare-associated pathogen

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Abstract
Ralstonia species are more frequently being recognised as causative agents of serious healthcare-associated infection especially among immunocompromised individuals. *Ralstonia* species are environmental, non-fermenting, aerobic, Gram-negative bacilli typically found in water and soil. *Ralstonia mannitolilytica, Ralstonia pickettii* and *Ralstonia insidiosa* have been responsible for human infections such as bacteraemia and bone infection. Central nervous system infection and infection in immune competent individuals are uncommon. We report a case of ventriculoperitoneal shunt infection and meningitis caused by *R. mannitolilytica* in an immune competent 11-month-old female.

Introduction

Ralstonia species have been identified as an emerging, healthcare-associated opportunistic pathogen especially among immunocompromised patients.[1] They are a group of Gram-negative aerobic, non-fermenting organisms which are ubiquitous in water and soil.[2] Clinically relevant species include *R. mannitolilytica*, *R. pickettii* and *R. insidiosa*. The epidemiology of infections caused by *Ralstonia* spp. has not been fully elucidated and much of the literature is in the form of case reports and case series.[1,2] We describe a case of ventriculoperitoneal (VP) shunt infection and meningitis caused by *R. mannitolilytica* in an immune competent child.

Case report

An 11-month-old, HIV-unexposed female infant with two VP shunts *in situ* was admitted with generalised seizures, a decreased level of consciousness and VP shunt infection and meningitis.

The patient was born at 33 weeks gestation and her birth weight was 1920 grams. The neonatal period was complicated by jejunal atresia requiring resection and end-to-end anastomosis on the second day of life, and *Escherichia coli* urinary tract infection with bacteraemia on day 11 of life. During this episode, cerebrospinal fluid (CSF) analysis was normal. She was treated with meropenem for 14 days, had a good clinical response, and was discharged.

At 6 weeks of life, she presented with an enlarged head and a tense, bulging anterior fontanelle. A brain computerised tomography (CT) scan demonstrated ventriculomegaly with multiloculated hydrocephalus. Cerebrospinal fluid cell count was unsuccessful due to excessive debris, but biochemistry analysis revealed a low glucose (0.6mmol/L), and a very high protein (17.17g/L), with *E. coli* isolated on culture. An external ventricular drain (EVD) was inserted initially, with a left and a right VP shunt inserted thereafter to adequately drain the multiloculated hydrocephalus. Intravenous ceftriaxone (susceptible) was administered for 28 days, and once clinically well (although she did have marked neurodevelopment impairment) the patient was discharged with regular follow-up.

Table 1. Cerebrospinal fluid (CSF) results during the Ralstonia mannitolilytica infection episode

Day of admission	DAY 1	DAY 1	DAY 6	DAY 7	DAY 22
Site of CSF collection	CSF from right VP shunt	CSF from left VP shunt	CSF from right EVD	CSF from left EVD	CSF from new right VP shunt
CSF Glucose (mmol/L)	2.0	3.3	0.6	0.6	1.5
CSF Protein (g/L)	4.33	0.21	2.44	0.75	0.21
CSF Polymorphs (cells/μL)	2	0	0	11	0
CSF Lymphocytes (cells/μL)	91	1	10	48	0
CSF Erythrocytes (cells/μL)	15	140	8	29	14
CSF Gram stain	negative	negative	negative	negative	negative
CSF Culture	*R. mannitol-ilytica*	No growth	No growth	No growth	No growth

At 11 months of age, during a routine neurosurgical clinic visit, the child was noted to have a fluctuating swollen mass on the anterior abdominal wall near the right VP shunt. Incision and drainage (I&D) of a localised abscess along the distal shunt track was performed and intravenous ceftriaxone was administered for 5 days with good clinical response. During this episode CSF analysis was normal and

the child was discharged. One week later, the child was readmitted with seizures, a decreased level of consciousness, dehiscence of the I&D wound and extrusion of the affected right VP shunt. The child was commenced on meropenem and vancomycin empirically and a brain CT scan showed a multiloculated hydrocephalus. Both the right and left VP shunts were removed as part of the source control measures for a shunt infection with meningitis, and a right and left EVD was inserted. During surgery, and prior to removal of the shunts, CSF was collected from both shunts and sent for CSF analysis and culture (Table 1). *Ralstonia mannitolilytica* was isolated from the right VP shunt only and the antibiotic susceptibility results is summarised in Table 2. Repeat CSF cultures collected during this episode were negative (Table 1). The child clinically improved to her baseline during the admission and was treated with meropenem for 22 days. After the right and left EVDs were removed, two new VP shunts were inserted, and the child was discharged with outpatient clinic follow-up.

Table 2. Antibiotic susceptibility results of the *Ralstonia mannitolilytica*

Antibiotic	**Susceptibility**
Trimethoprim-sulfamethoxazole	Sensitive
Ceftazidime	Intermediate
Cefepime	Sensitive
Piperacillin-tazobactam	Intermediate
Imipenem	Sensitive
Meropenem	Sensitive
Ciprofloxacin	Sensitive
Gentamicin	Resistant
Amikacin	Resistant

Discussion

Though rare, *R. mannitolilytica* is an important cause of opportunistic infection in hospitalised patients globally.[3,4]. It has been associated with a wide variety of infections in diverse settings including hospital outbreaks. The only other report of *R. mannitolilytica* in South Africa described an outbreak of *R. mannitolilytica* bacteraemia among 16 adult dialysis patients at a tertiary hospital in Pretoria. The source of infection was a contaminated water system supplying the dialysis unit.[2] Although, to our knowledge this is the first report describing invasive *R. mannitolilytica* infection in an immune competent child in South Africa, this is the second report of infection in a young child in Africa. Owusu *et al* in Ghana first reported concomitant *R. mannitolilytica* bacteraemia in a 2-year-old child with severe *Plasmodium falciparum* malaria.[6] Infections in children outside the neonatal period remain rare. Besides the Ghanaian case, a report from Peru described a 5-year-old child with leukaemia and *R. mannitolilytica* bloodstream infection and is the only other reported childhood case outside the neonatal period.[7]

R. mannitolilytica has been associated with hospital outbreaks in neonates, immunocompromised patients, patients with chronic conditions and prolonged hospital stay.[6,7] Water contamination is a major source of infection in outbreaks, including outbreaks in dialysis units.[2] Shankar *et al* reported another outbreak among dialysed adult patients in India.[4] Outbreaks of *R. mannitolilytica* bacteraemia among adult cancer patients were reported from India and China .[1,8] Risk factors for *R. mannitolilytica* infection include indwelling catheters, central venous lines, and chemo-ports.[5,6] Besides bacteraemia, *R. mannitolilytica* has been responsible for a variety of organ specific infections including endocarditis, osteomyelitis, respiratory infection in patients with cystic fibrosis and chronic obstructive pulmonary disease, meningitis, abdominal infection and urinary tract infection.[1-10] *R. mannitolilytica* infections may affect all age groups but mainly occurs in neonates and the elderly. Those with underlying immunosuppressive conditions are at particular risk, and infection with *R. mannitolilytica* has been reported globally.[1-11]

Drug susceptibility of *R. mannitolilytica* clinical isolates is variable, with most isolates being inherently multidrug resistant.[1-11] The isolate from our patient was not susceptible to the aminoglycosides, ceftazadime and piperacillin-tazobactam, but was susceptible to cefepime, meropenem, imipenem,

trimethoprim-sulfamethoxazole and ciprofloxacin. Aminoglycoside resistance is a consistent finding in many published reports, while susceptibility to beta-lactam antibiotics such as cephalosporins and carbapenems is variable.[3-8] In the outbreak in the haemodialysis unit in Pretoria all isolates had identical susceptibility results, being resistant to amoxicillin/clavulanic acid, ceftazidime, ertapenem, meropenem, tobramycin, aztreonam and colistin, while remaining susceptible to piperacillin tazobactam, ciprofloxacin, levofloxacin, co-trimoxazole, ceftriaxone, cefuroxime, cefepime and imipenem.[2]

Reported mechanisms of resistance of *Ralstonia* species to beta-lactam antibiotics have been ascribed to the presence of extended spectrum and inducible beta-lactamases such as *bla*-$_{\text{OXA-60}}$, *bla*-$_{\text{OXA-22}}$, *bla*-$_{\text{OXA-443}}$ and *bla*-$_{\text{OXA-444}}$.[5,11] Widespread resistance to aminoglycosides is due to the presence of an aminoglycoside acetyl-transferase.[12] Virulence factors permitting biofilm production have also been demonstrated in some isolates.[1]

Antimicrobial treatment for *R. mannitolilytica* is usually individualised, based on the specific susceptibility results of the cultured isolate and the site of infection.[1-11] Many isolates are multidrug resistant even when first reported in a particular geographical location.[3-6] This suggest that *R. mannitolilytica* is an inherently multidrug resistant organism (MDR) which is a concern as the organism continues to circulate in hospital settings.[8] Preventing transmission and infection through appropriate infection prevention practices is an important intervention in healthcare settings, particularly through the avoidance of contamination of hospital water systems and therapeutic products such as intravenous fluids. Timely removal of medical devices is also critical as the organism has potential to form biofilms .[2-8]

Conclusion

R. mannitolilytica is an emerging global healthcare-associated opportunistic infection. Our case is the first published report of clinical infection caused by *R. mannitolilytica* in an immune competent child in South Africa. As many clinical isolates are multi-drug resistant, optimising antibiotic therapy is dependent on susceptibility results. Optimal infection prevention practices, particularly in immunosuppressed individuals should be augmented to lower the risk of infection.

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