

***Cupriavidus pauculus* (*Ralstonia paucula*) concomitant meningitis and septicemia in a neonate: First case report from India**

***S Duggal, R Gur, R Nayar, SR Rongpharpi, D Jain, RK Gupta**

Abstract

Ralstonia paucula (formerly classified as CDC (Centre for Disease Control) group IVc-2, *Wautersia paucula*; recently renamed as *Cupriavidus pauculus*) is an environmental Gram-negative bacillus isolated from water sources and can cause serious human infections. Patients recover bacteriologically indicating low virulence. A total of 32 cases have been reported world-wide, but no isolation has ever been reported from cerebrospinal fluid or in India. The first case of *R. paucula* meningitis and septicemia is being reported here along with the brief summary of cases reported world-wide.

Key words: *Cupriavidus pauculus*, meningitis, neonate, septicemia

Introduction

Cupriavidus pauculus of family *Burkholderiaceae* is an environmental Gram-negative bacillus, which can rarely cause opportunistic infections especially in high risk patients. Isolation from a clinical specimen is generally treated with high index of suspicion and usually regarded

*Corresponding author (email: <shaliniduggal2005@rediffmail.com>)

Department of Microbiology (SD, RG, RN, SRR),
and Department of Paediatrics (DJ, RKG),
Dr. Baba Saheb Ambedkar Hospital, New Delhi, India

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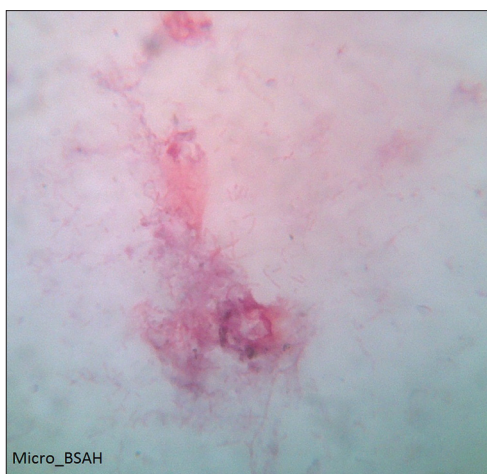


Figure 1: Gram-negative bacilli with necrotic cells in centrifuged cerebrospinal fluid deposit

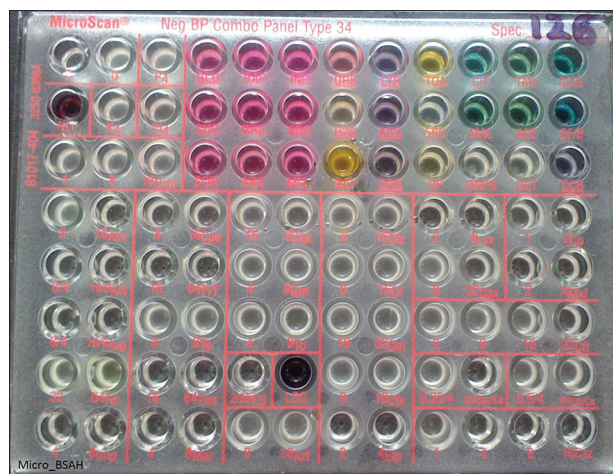


Figure 2: Gram-negative panel (Dade Behring) showing biochemical reactions and antimicrobial susceptibility of the test isolate

as contamination unless proven otherwise. It has been incriminated in pseudo-outbreaks,^[1,2] but may be considered a pathogen if isolated from a sterile body fluid and correlates with clinical condition. We report hereby, the first case of *Ralstonia paucula* from cerebrospinal fluid (CSF) and blood of a neonate in India.

Case Report

A 6-day old neonate presented to our institution in July 2012 with complaints of fever, poor feeding, lethargy and abnormal cry. He was delivered full term vaginally by a trained birth attendant at a small neighbourhood clinic. The parents informed that his cry was delayed at birth and suctioning was done. The baby could not accept mother's feed; therefore, enteral feeds were started with diluted cow's milk using an unsterile cotton swab. On day three, he developed fever for which he was treated with oral cefaclor. The baby's condition continued to deteriorate and on 6th day of life, he was brought to paediatric emergency of our hospital.

On examination, baby had facial grimace, occasional tonic posturing and shrilled cry. Mild icterus and subtle seizures were noted. He weighed 3.15 kg; heart rate and respiratory rate were increased, temperature was 100°F. Systemic examination revealed distended abdomen, but no organomegaly. There was a large cephalhematoma, anterior fontanelle was normal and no sutural diastasis was seen. Tone was slightly increased, neonatal reflexes including sucking and rooting were sluggish, but deep tender reflexes were normal. In light of the above findings a provisional diagnosis of 'late onset neonatal sepsis with meningitis' was made and treatment was initiated with parenteral cefotaxime and amikacin in anti-meningitic doses.

Investigations revealed mild thrombocytopenia, hyperbilirubinemia and raised C-reactive protein;

haemoglobin, leukocyte count and blood sugar were normal. CSF cell count was 270/mm³ with 90% lymphocytes and 10% polymorphs, protein was 195 mg% and sugar 13 mg%. Gram stain of centrifuged CSF deposit showed pus cells with faint staining Gram-negative bacilli, mostly extracellular [Figure 1]. CSF culture showed pure growth of Gram-negative organisms (>10⁵ CFU/ml) after overnight incubation at 37°C on blood agar, chocolate agar and MacConkey agar. The colonies were non haemolytic, non-lactose fermenter, non-pigmented 1-2 mm size and easily emulsifiable. The bacilli were actively motile; catalase and oxidase positive, therefore presumptively identified as *Pseudomonas spp.* Conventional biochemical reactions showed positive results for urease hydrolysis, citrate production and nitrate reduction while indole test was negative, hydrogen sulphide was not produced and sugars (glucose, lactose, sucrose) were not fermented. Gram-negative panel was also set up (N34 panel, Dade Behring Microscan Autoscan-4, Siemens, 2007) for identification and antimicrobial susceptibility testing. The isolate was identified as *R. paucula* (listed in its software) with 99.99% probability. The paediatric Bactec blood culture also signalled positive and on subculture, similar growth was obtained with identical biotype and antibiograms [Figure 2]. The panels were read manually also and compared with biochemical reactions mentioned in the literature.^[3] Molecular analysis of the isolate could not be done. The isolates were susceptible to ceftazidime, levofloxacin, co-trimoxazole, amoxicillin/clavulanic acid, piperacillin/tazobactam, ticarcillin/clavulanic acid, imipenem and meropenem; intermediate susceptible to ciprofloxacin; resistant to amikacin, gentamicin, tobramycin, ceftriaxone, cefotaxime, aztreonam and tetracycline (determined by Minimum inhibitory concentration in µg/ml). Final diagnosis of '*R. paucula* septicemia with *Ralstonia paucula* meningitis' was made. Antibiotic therapy was changed to injection ceftazidime (150 mg/kg/day in two divided doses) and

steroids were not given. Defervescence was observed after 4 days and repeat blood culture was sterile. The baby started accepting mother's feed, his cry improved; he depicted age-appropriate activities and was discharged in stable condition after 3 weeks.

Epidemiological investigations were done to rule out transmission. Mother's blood, urine and breast milk

cultures were sterile; they were done to rule out vertical transmission as she had given history of fever and urinary tract infection in second trimester. She also revealed that for enteral feeding, diluted cow's milk was used. It was boiled and stored in plastic bottle at room temperature till further use. Therefore, cow's milk, water used for dilution and a sample of cotton swab were also cultured. All these samples showed growth of different types of bacteria, but none was

Table 1: Chart review of CDC group IV c-2/*Ralstonia paucula*/*Cupriavidus pauculus* infections identified world-wide (chronological order)

Authors	Site	Cases	Age/Sex	Source	Risk factors	Treatment*	Country
Hansen ^[6] 1985	Peritoneal fluid	Single	53 years/M	Hospital, ?Peritoneal catheter	Glomerulonephritis	TO, CZ, SXT	NA
Dan ^[7] 1986	Blood	Single	37 years/M	Community, ?Source	Plasma cell leukemia	CTX, AK	Israel
Crowe ^[8] 1987	Blood	Single	55 years/M	Hospital, ?Source	DM, multiple surgical interventions	FOX, GM	Boston USA
Zapardiel ^[9] 1991	Peritoneal fluid	Single	58 years/M	Hospital, ?Peritoneal catheter	CAPD	TO, CIP, CTX, SXT	Spain
Arduino ^[10] 1993	Blood	Single	77 years/M	Hospital, ?I/v catheter	NHL	Catheter removal	Brazil
Ramos ^[11] 1993	Blood	Single	10 years/F	?Community, ?Hickman catheter	ALL	CRO	Spain
Musso ^[12] 1994	Pus (Tenosynovitis)	Single	73 years/F	Community. ?Cat bite ?Tap water	None identified	Doxycycline	France
Anderson ^[13] 1996	Blood	Single	30 years/M	Hospital. ?water ? CVC	AIDS	ZOX	Chicago, USA
Moissenet ^[14] 1996	Blood	Five	1 months, 3 months, 11 years, 11 years, 14 years	Hospital, ?Source	Immunocompromised	3: CAZ+AK, 1: IPM+AK, 1: none	France
Arance ^[15] 1997	Blood	Single	20 years/M	Hospital, I/v catheter	HSCT	IPM, CIP	Spain
Martino ^[16] 1998	Blood	Three	NA	Hospital, ?CVC	HSCT	CTX, CIP, IPM	Spain
Salar ^[17] 1998	Blood	Single	71 years/F	Hospital, ?Source	ALL, prolonged hospitalization	CAZ, AK	Spain
Noyola ^[18] 1999	Blood	Single	6 months/F	Community, ?Source	Delivered pre-term	CTX	Houston, USA
Thayu ^[19] 1999	Blood	Single	NA	NA	AML	NA	New Haven, USA
Vay ^[20] 2007	Blood	Single	NA	NA	CRF, repeated hemodialysis	NA	Argentina
Kim ^[21] 2007	Corneal scrapping	Single	26 years/F	Community, Lens solution	Corneal ulcer	CAZ	Korea
Azcona-Gutierrez ^[22] 2008	Tracheal aspirates	Four	NA	Hospital, ?Ventilator	Mechanical ventilation	NA	Spain

Contd...

Table 1: Contd...

Authors	Site	Cases	Age/Sex	Source	Risk factors	Treatment*	Country
Tasbakan ^[23] 2010	BAL fluid	Single	47 years/F	Hospital, ?Ventilator	Breast carcinoma	IPM	Turkey
Stovall ^[24] 2010	Blood	Four	4 months/ 3 years/ neonate/16 m	Hospital, ?ECMO	Cardio-respiratory failure	MER, FEP, CIP	Arkansas, USA
Aydin ^[25] 2012	Blood	Single	Neonate	Community ?Source	None identified	CAZ	Turkey
Present case, 2012	CSF, blood	Single	6 days/M	Community ?Source	None identified	CAZ	India

*Treatment relevant to the isolate, all patients recovered. NA: Detail not available, TO: Tobramycin, CZ: Cefazolin, SXT: Trimethoprim/sulphamethoxazole, CIP: Ciprofloxacin, FEP: Cefepime, MER: Meropenem, IPM: Imipenem, CTX: Cefotaxime, FOX: Cefoxitin, GM: Gentamicin, CRO: Ceftriaxone, CAZ: Ceftazidime, AK: Amikacin, ZOX: Ceftizoxime, DM: Diabetes mellitus, CAPD: Chronic ambulatory peritoneal dialysis, NHL: Non Hodgkin's lymphoma, ALL: Acute lymphoblastic leukemia, CVC: Central venous catheter, AIDS: Aquired immunodeficiency syndrome, HSCT: Hematopoietic stem cell transplant, AML: Acute monoblastic leukemia, CRF: Chronic renal failure, I/v: Intravenous, BAL: Broncho-alveolar lavage, ECMO: Extracorporeal membrane oxygenation, CDC: Centre for Disease Control

identified as *Ralstonia paucula*. Though the exact source of this infection could not be identified, it was thought to have possibly resulted from environmental contamination during feeding. The importance of hand and environmental hygiene was explained to the parents.

Discussion

Ralstonia paucula belongs to genus '*Ralstonia*', named in honour of an American bacteriologist; E. Ralston and species '*paucula*' to indicate that these strains only rarely cause human infections. It was initially known as CDC group IV c-2 organism,^[4] later genus *Wautersia* was introduced to include species of *Ralstonia*, which were carbohydrate non fermenters, colistin (10 µg) susceptible and motile by peritrichous flagella. However, after 16S rRNA gene sequencing, it has finally been placed in the genus *Cupriavidus*, species *pauculus*.

These are environmental bacteria which may be found in soil, water or on plants. It has been implicated in pseudo-outbreaks of skin and superficial site infections^[1] and bacteremia.^[2] Nosocomial transmission is ruled out in this case as patient was admitted with features of septicemia and meningitis. Contamination in laboratory is also not possible since both CSF and blood samples were received in sterile containers; gram stain of CSF was suggestive of bacterial infection, CSF count of this organism was high^[5] and *Ralstonia* was not isolated from any other samples. This infection appears to have either been community acquired; through oral route, as indicated by the feeding history or acquired during suctioning at birth as *Ralstonia* has been frequently isolated from indwelling devices.

Cephalhematoma was present, which could have formed during prolonged delivery. In this case, concomitantly positive CSF and blood cultures have supported its role as a pathogen. Patient was successfully treated with ceftazidime, the only

third generation cephalosporin to which it was sensitive. Though, validated methods of antimicrobial susceptibility test and treatment guidelines are lacking for *Cupriavidus*, results were inferred on the basis of lowest MIC values showing no growth. Few reports have cited dual antibiotic therapy for this organism, in other cases cure has been achieved by a third generation cephalosporin or carbapenem [Table 1].

Case reports on this organism are limited, including cases of bacteremia, peritonitis, pneumonia, tenosynovitis [Table 1]. This organism has never been implicated as a causative agent of meningitis before. Also, this is the first case reporting its isolation from India. This case highlights the fact that these organisms can cause community acquired infections, which can be completely cured if identified and treated appropriately. Therefore, initial effort should be to prevent spread of these organisms, but if infection occurs, it should be promptly identified, treated and tracked to prevent further spread.

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