Rothia dentocariosa Infection in a Critically III Patient with Multiple Myeloma- First Case Report from India

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ABSTRACT

Microbiology Section

Rothia dentocariosa is a Gram positive organism, known to cause infection very rarely in immunocompromised patients. We report isolation of *Rothia dentocariosa* in blood and Cerebrospinal Fluid (CSF) of an elderly patient with multiple myeloma. The present case highlights pathogenic role of an uncommon Gram positive organism. To the best of our knowledge *Rothia dentocariosa* is being reported for the first time from India, in an immunocompromised patient with haematological malignancy.

Keywords: Bacteraemia, Cerebrospinal fluid, Malignancy

CASE REPORT

A 57-year-old male patient diagnosed with multiple myeloma presented to emergency with complaints of altered sensorium and progressive weakness of both upper and lower limbs for three days. The patient was on regular chemotherapeutic drugs including steroids, vincristine, adriamycin and melphalan. The investigation of patient revealed haemoglobin of 8.6 gm/dL, Total Leucocyte Count (TLC) of 12.24x10³ UL, blood urea 32 mg/dL, serum creatinine 0.8 mg/dL, total bilirubin 0.2 mg/dL, alanine aminotransferase 38 U/L and aspartate aminotransferase 44 U/L. Neuroimaging of the brain showed multiple ill defined hyper dense lesions in left cortical and subcortical areas.

Due to high grade fever and focal neurological deficits, blood and CSF were sent for microbiological examination. The patient was empirically started on parenteral amikacin (1 gm/day) and ceftriaxone (1 gm/day)

Blood and CSF specimens were processed using standard microbiological procedures. Gram stained smear of the CSF showed few pus cells with Gram positive cocci, bacilli and filaments. Based on Gram stain report the patient was started on metronidazole (500 mg TDS) and vancomycin (1 gm/day). CSF was inoculated on blood agar and MacConkey agar. After 48 hours of incubation at 37°C, blood agar showed 0.5 mm, dry, white opaque colonies [Table/Fig-1], and MacConkey agar showed tiny, dry, pale colonies. *Nocardia* spp. was suspected on basis of Gram stain of CSF which revealed Gram positive bacilli with filaments and growth on blood agar showing dry, opaque white colonies. Modified Ziehl-Neelsen staining was done on the smears from growth on the culture plate and the CSF which did not reveal any evidence of *Nocardia*. The blood sample, which was incubated in BactT/Alert 3D (Bio Me'rieux, Durham, North Carolina/



[**Table/Fig-1]:** a) Dry, wrinkled, white colonies of *Rothia dentocariosa* on plate of blood agar; b) Magnified image of dry, wrinkled white colonies on blood agar.

USA), showed a positive signal after 72 hours of incubation. Gram stain from the broth showed Gram positive filaments. The broth was subcultured on blood agar and MacConkey agar. Growth similar to that from CSF was obtained on blood and MacConkey agar after 48 hours of aerobic incubation at 37°C. The growth on blood agar from CSF as well as blood culture was subjected to Gram staining which showed Gram positive bacilli with few filaments. A set of biochemical reactions were put to differentiate the Gram positive organisms having similar Gram stain picture [Table/Fig-2]. Gram positive rod and coccus forms can occur in *Arthrobacter* spp., *Brevibacterium* spp., *Cellulomonas* spp., *Dermabacter* spp., *Oerskovia* spp. and *Rothia dentocariosa*. Presence of fermentative metabolism, organism being non motile, white pigmented colonies, lactose non fermenter, nitrate reducer and no decarboxylation of lysine and ornithine favoured the identification of causative agent as *Rothia* spp. [1-3].

Rothia mucilaginosa and Rothia aeria are Gram positive cocci but Rothia dentocariosa shows Gram positive bacilli with rudimentary branching. Rothia mucilaginosa produces smooth mucoid colonies whereas Rothia dentocariosa produces white, dry, wrinkled colonies [Table/Fig-1] [2]; which further support the identification of isolate as Rothia dentocariosa.

Biochemical test	Result					
Catalase	Positive					
Oxidase	Negative					
Hanging drop	Non motile					
Nitrate reduction	Positive					
Triple sugar iron agar	A/A*					
Urease	Negative					
Sugar fermentation						
Maltose	Fermented					
Trehalose	Fermented					
Glucose	Fermented					
Fructose	Fermented					
Sucrose	Fermented					
Salicin	Fermented					
Inositol	Not fermented					
Lactose	Not fermented					
Amino acid decarboxylation						
Lysine	Not decarboxylated					
Ornithine	Not decarboxylated					
[Table/Fig-2]: Biochemical test results done for identification of the isolate.						

Antibiotic susceptibility testing was done by Kirby-Bauer disc diffusion method on blood agar. We assessed the organism drug susceptibility as per 2014 Clinical and Laboratory Standards Institute (CLSI) guidelines for *Staphylococcus* (M 100-S 24) as no CLSI guideline is given for *Rothia dentocariosa* [4]. The isolate was found to be sensitive to tetracycline, ciprofloxacin, gentamicin, linezolid and vancomycin. It was resistant to erythromycin, clindamycin, cefoxitin and penicillin. The patient was on vancomycin and metronidazole, following our antibiotic sensitivity testing vancomycin was continued for one or more day. Condition of the patient deteriorated and he succumbed to the illness by the eighth day of hospitilsation.

DISCUSSION

Rothia dentocariosa, a member of family Micrococcaceae, is a Gram positive organism found in the human oral cavity [5,6]. *Rothia dentocariosa* is a pleomorphic Gram positive bacterium that is seen as coccoid, rods and filamentous forms with possible branching [6,7]. They are non motile and non acid fast [7].

Roth in 1957 isolated the organism from dental plaque and caries; it was then called variously as *Actinomyces dentocariosa*, *Nocardia dentocariosa* or *Nocardia salivae*. In 1967, detailed identification was done by Brown and genus *Rothia* was created [7]. In 1975, the first human infection (periappendiceal abscess) caused by *Rothia dentocariosa* was described [8]. On sheep blood agar after 24 hours of incubation at 37°C, colonies are non haemolytic, small, dry, white and adherent to media. On prolonged incubation the surface becomes rough with colonies showing a spoked wheel appearance, no aerial mycelia are seen [7].

Rothia can be differentiated from *Nocardia* as there is lack of acid fastness, absence of aerial mycelia and they ferment carbohydrates-features which are not seen in *Nocardia*. Actinomycetes grow anaerobically but *Rothia* spp. grows best aerobically which is used as the differentiating feature [5].

In a review article by Von Graevenitz A, fermentation of sugars such as fructose, glucose, maltose and sucrose by *Rothia* spp. was found to be 100% positive and that of ribose, salicin and trehalose was found to be more than 90% positive. Fermentation of arabinose, cellobiose, glycogen, inositol, mannose, starch and xylose was 100% negative; whereas lactose, mannitol, raffinose, rhamnose were 90% negative [3].

Rothia is known to cause infections such as bacteraemia, endocarditis, meningitis, peritonitis, bone and joint infection, pneumonia, skin and soft tissue infection, endophthalmitis and prosthetic device infection [9].

Rothia is known to cause infections especially in immunecompromised patients. Common source of bacteraemia among cancer patients are gut translocation, mucositis and catheter related infection. Risk factors for invasive disease are neutropenia and haematological malignancy, diabetes mellitus, chronic alcoholism, chronic liver disease and infection with HIV [9]. Our patient had multiple myeloma and was on steroids.

[Table/Fig-3,4] briefly outline the reports of *Rothia dentocariosa* isolated from various specimens among cancer patients and from blood across various parts of world respectively.

Reference	Underlying medical condition	Number of isolates	Complication	Specimen	Year and place of isolation	Treatment given and response to treatment
Schiff MJ et al., [11]	AML	1	Pneumonia	BAL; transthoracic aspirate	1987; New York	Clindamycin; recovered
Pers C et al., [10]	CLL	1	Septicaemia	Blood	1987; Denmark	Penicillin; expired
Wallet F et al., [12]	Lung cancer	2	Pneumonia	BAL	1997; France	Amoxicillin clavulanic acid, Trimethoprim sulphamethoxazole; recovered
Kong R et al., [6]	Hepatic carcinoma	1	Endocarditis	Heart valves	1998; France	Netilmycin, metronidazole and amoxicillin, recovered
Salamon SA and Prag J [5]	 Rectal cancer Tooth abscess Previous myocardial infarction, diverticulitis 	3	Septicaemia	Blood	2002; Denmark	1. no antibiotics- expired 2. and 3. penicillin G-recovered

[Table/Fig-3]: Rothia dentocariosa isolated from different specimens of cancer patients across various parts of the world. *AML- Acute Myeloid Leukaemia, BAL- Broncho Alveolar Lavage, CLL – Chronic Lymphocytic Leukaemia.

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Reference	Underlying medical condition	Number of isolates	Complication	Specimen	Year and place of isolation	Treatment given and response to treatment
Isaacson JH and Grenko RT [13]	Bicuspid aortic valve	1	Endocarditis, brain abscess	Blood	1988; Vermont	Penicillin, gentamycin; recovered
Binder D et al., [14]	1 mitral regurgitation, aortic insufficiency 2. prosthetic aortic valve 3. aortic composite graft All 3 patients had periodontal disease	3	1 Endocarditis and multiple brain abscess 2. Endocarditis 3. Endocarditis	Valve and blood	1997; Switzerland	 Penicillin, netilmicin, vancomycin; expired Rifampicin, ciprofloxacin; recovered Rifampicin, ceftriaxone; recovered
Ricaurte JC et al., [8]	Root canal done	1	Endocarditis and multiple intracranial haemorrhage	Blood	2001; New York	Vancomycin, gentamicin and penicillin G; recovered
Boudewijns M et al., [7]	treated for congenital bicuspid valve	1	Endocarditis, subarachnoid haemorrhage and intracranial aneurysm	Blood	2003; Belgium	Penicillin and amikacin; recovered
Sadhu A et al., [15]	Mitral valve prolapse with MR, dental extractions	1	Multiple cerebellar haemorrhages	Blood	2005; Arizona, USA	Penicillin G and gentamycin, recovered
Present study	Multiple myeloma	1	Brain abscess	Blood, cerebrospinal fluid	2015; India	Vancomycin, expired

[Table/Fig-4]: Rothia dentocariosa isolated from blood having central nervous system complications

Rothia dentocariosa has been isolated from both haematological and solid malignancy patients. Salamon SA et al., and Pers C et al., have reported isolation of *Rothia* from blood among cancer patients [5,10]. The antibiotic regimen for this organism has not been described. Treatment given to these oncology patients was clindamycin, penicillin, amoxicillin-clavulanic acid and trimethoprimsulfamethoxazole [5,6,10-12]. In our patient, vancomycin was given as the strain was resistant to penicillin.

Isaacson JH et al., and Binder D et al., had shown brain abscess as a complication due to *Rothia dentocariosa* [13,14]. Ricaurte JC et al., reported a patient having endocarditis and multiple intracranial haemorrhages due to *Rothia dentocariosa* following a root canal treatment. The patient responded to treatment with vancomycin [8]. In 2003, Boudewijns M et al., reported a case of endocarditis, subarachnoid haemorrhage and intracranial aneurysm caused by *Rothia dentocariosa* and the patient recovered with penicillin and amikacin treatment [7]. Sadhu A et al., had discussed multiple cerebellar haemorrhages as a complication and the patient responded to penicillin and gentamicin treatment [15].

CONCLUSION

To the best of literature search, isolates of *Rothia dentocariosa* have not been reported among patients with haematological malignancy from India. *Rothia dentocariosa* is a low virulence organism, but is an emerging pathogen among immunocompromised patients. It is difficult to identify this organism and it can easily be mistaken for a contaminant. It is routinely not included in the database of automated systems. Hence, this organism is under-reported. Suspicion of this organism is important while treating immunocompromised patients with bacteraemia.

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