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CASE REPORT

Nosocomial ventriculitis due to *Roseomonas gilardii* complicating subarachnoid haemorrhage

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Summary *Roseomonas gilardii* is a pink-pigmented, non-fermentative, Gram-negative coccobacillus that has been recognized as a rare cause of human infections. We report the first case of ventriculitis caused by *R. gilardii* in a 54-year-old man with a subarachnoid haemorrhage secondary to a vertebral artery aneurysm; discuss previous reports of this organism as a nosocomial and community-acquired pathogen, laboratory diagnosis, and patient management.

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Introduction

Roseomonas is a genus of pink-pigmented, non-fermentative, oxidative, Gram-negative coccobacilli that have been shown in recent years to be uncommon, yet potentially of clinical importance as opportunistic pathogens that can cause disseminated infections, particularly in debilitated hosts. Most clinically significant infections due to *Roseomonas* spp. have involved bacteremias in persons with central venous catheters and underlying malignancies or other chronic diseases. Due to the relative infrequency with which *Roseomonas* spp. are encountered, many hospital laboratories have minimal experience in their microbiological identification and most clinicians have not had opportunity to manage patients who develop infections with these organisms. We report the isolation of

R. gilardii from cerebrospinal fluid (CSF) in an adult with subarachnoid haemorrhage complicated by ventriculitis, summarize previous cases from the medical literature, discuss methods for laboratory characterization of these organisms and the alternatives for antimicrobial chemotherapy.

Case report

A 54-year-old male with a prior history of hypertension and coronary artery disease presented to a local community hospital with a one-day history of headache and vomiting that rapidly progressed to unconsciousness. Computerized axial tomography (CT) revealed a prominent subarachnoid haemorrhage. He was immediately transferred to the University of Alabama Hospital for neurosurgical management. Upon arrival, a ventriculostomy tube was inserted and angiography revealed an aneurysm arising from the right vertebral artery immediately below the confluence of the vertebral arteries.

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Surgical clipping was performed on hospital day two with intraoperative aneurysm rupture. On hospital day 20, a pink mucoid Gram-negative coccobacillus grew from a surveillance culture of CSF obtained from the ventriculostomy. On hospital days 24 and 25, the same micro-organism was again isolated from separate ventriculostomy fluid specimens. The ventriculostomy tube was replaced on hospital days 24, 30 and 34. Multiple blood cultures collected during this period were negative. During the period of hospital days 20 through 26, there was a CSF neutrophilic pleocytosis (WBC count $11-42 \times 10^3/\text{mm}^3$, neutrophils 28-76%) with an elevated CSF protein (64-95 mg/dl). The patient was treated with intravenous amikacin and the CSF cultures became sterile after 7 days. He died on hospital day 70 from complications of the aneurysm. Laboratory testing confirmed the organism to be *Roseomonas* spp.

Microbiological studies

A pink-pigmented Gram-negative coccobacillus was detected on trypticase soy agar with 5% sheep blood on three separate occasions after ventriculostomy fluid was incubated aerobically for 24-48 h. These bacteria were identified as *Roseomonas* spp. by the RapidID NF Plus[®] System (Remel Laboratories Lenexa, KS) with 99.99% probability. The API 20 NE (bioMérieux, Hazelwood, MO) failed to give an identification. This organism was confirmed to be *R. gilardii* by the Alabama State Public Health Bacteriology Laboratory by performance of additional biochemical tests.

A review of microbiology laboratory records at the University of Alabama at Birmingham Medical Center over a 10-year period from 1993 through 2003 revealed eight unique isolations of *R. gilardii* in addition to the present case. The species identification in each case was confirmed by the Alabama State Public Health Bacteriology Laboratory. The organism from this case report and four others recovered from blood cultures that had been stored frozen at minus 70 °C were available for further study. These four additional isolates were similar to one another biochemically and to the isolate from CSF and all were identified to genus level by the RapidID NF system.

Antimicrobial susceptibility testing was performed on all five isolates by the agar diffusion gradient (Etest) method (AB BIODISK, Solna, Sweden) using National Committee for Clinical Laboratory Standards (NCCLS) interpretive criteria for non-fermentative Gram-negative bacteria.¹ All

organisms tested were susceptible to amikacin, gentamicin, tobramycin, ciprofloxacin, gatifloxacin, imipenem, meropenem and chloramphenicol. There was uniform resistance to cefotaxime, ceftazidime, piperacillin, piperacillin/tazobactam and trimethoprim/sulfamethoxazole.

Discussion

In 1984, Gilardi and Faur² described morphological, growth, and biochemical characteristics of 21 strains of Gram-negative, pink-pigmented bacteria isolated from clinical specimens and environmental sources. Seven strains shared similar properties with one another, but they did not fit any previously published descriptions and were, therefore, designated as an unnamed taxon. These organisms were detected from blood, sputum, and CSF (one isolate from a preterm neonate). Following additional reports of bacteremias caused by pink-pigmented bacteria,^{3,4} investigators at the U.S. Centers for Disease Control and Prevention evaluated 156 clinical isolates and refined the classification of the CDC 'pink coccoid' bacteria into four separate groups.⁵ Since these isolates had identical cellular fatty acid compositions and differed only with respect to a few phenotypic and biochemical tests, they were assumed to represent different species or biotypes within a single genus. They classified two strains isolated from CSF in group I, one of which was the original CSF isolate from Gilardi and Faur's earlier study, and two additional CSF isolates were classified in Group III.² To our knowledge, these are the only previous reports of *Roseomonas* spp. isolations from CSF and no clinical information was provided regarding the patients from whom they were derived.

Rihs⁶ determined cultured and biochemical profiles, antimicrobial susceptibilities, and DNA-relatedness of 42 isolates of pink-pigmented bacteria, including some strains previously described.²⁻⁴ They proposed a new genus, *Roseomonas* that was divided into three species, *R. gilardii*, *R. cervicalis*, and *R. fauriae* with *R. gilardii* as the type species. The remaining isolates were classified as unnamed genomospecies 4, 5 and 6. More recently, Han⁸ determined the sequences of 16S rDNA of all six *Roseomonas* genomospecies and proposed further taxonomic refinements of the genus to include a new species, *R. mucosa*, and designation of two subspecies of *R. gilardii* based on these findings. It is not known how many organisms previously classified as *R. gilardii* would be reclassified according to Han's taxonomy

proposal, which has not yet been formalized, because complete biochemical analyses have not always been provided in the original reports, and because there appears to be considerable overlap in the biochemical profiles for the various species designations they propose.

The English language medical literature indexed in the U.S. National Library of Medicine contains 22 published articles describing almost 300 isolates of *Roseomonas* spp. derived from clinical specimens. These reports are summarized in Table 1. Including the present report, there are only six documented cases of persons with infections due to *Roseomonas* spp. who died and it is not clear in some of them whether the organism was of significance in causing death, owing to the coexistence of other terminal diseases. All eight individuals from our hospital with *Roseomonas* infections had comorbid conditions including vertebral artery aneurysm, Crohn's disease, or various malignancies, consistent with what has been observed by the other cases summarized in Table 1. Four of our eight *Roseomonas* isolates were from community acquired wound infections. The other four isolates were derived from patients with nosocomial bloodstream infections. This is consistent with other reports that have discovered a mixture of community and nosocomially acquired infections.⁷

Ventriculostomy fluid from the present case was culture-positive for *R. gilardii* on three separate occasions accompanied by a CSF neutrophilic pleocytosis and increased protein. Evidence that the infection was not merely associated with a contaminated ventriculostomy tube was demonstrated by subsequent isolation of the organism from CSF obtained after the ventriculostomy tube had been replaced. Although the patient died several weeks later, his infection was adequately treated as evidenced by negative follow-up cultures and the infection probably did not contribute directly to his fatal outcome. The infection in our patient with ventriculitis was associated with an indwelling ventriculostomy tube, which is comparable in many respects to the various types of central venous catheters that have been present in many cases of line-associated *Roseomonas* bacteraemia.

R. gilardii has been isolated from environmental sources such as water, but no natural reservoir has been identified.¹⁰ Lewis et al.⁹ speculated that some species may be normal skin or gastrointestinal flora of humans. Occurrence as blood culture contaminants and in various gastrointestinal infections supports this suggestion. Among isolates reported thus far, *R. gilardii* appears to be both the most common as well as the most inherently pathogenic species.⁹

Roseomonas spp. should be suspected in clinical specimens by observation of their characteristic pink, mucoid, colonies on trypticase soy agar with 5% sheep blood or chocolate agar incubated at 35 °C under aerobic conditions for 2-3 days. The colonies are catalase-positive, weakly oxidase-positive or sometimes oxidase-negative and the organisms appear in Gram-stained smears as plump coccobacilli in pairs and short chains. They grow best on Sabouraud agar and will usually grow on MacConkey agar. Enzymatic activities and ability to utilize various carbohydrate substrates vary among the species and individual strains within the genus. Some useful characteristics that differentiate *Roseomonas* spp. from another pink oxidase-positive Gram-negative bacillus, *Methylobacterium* spp., are the facts that the latter bacteria oxidize methanol, will not grow on MacConkey agar, will not grow at 42 °C, will absorb UV light, develop dry coral or pink colonies rather than mucoid ones, and appear as large vacuolated, pleomorphic Gram-negative bacilli that may resist decolorization.⁶ Several other biochemical reactions of individual *Roseomonas* spp. have been described in the numerous case reports and summary series listed in Table 1.

The ability of clinical laboratories to accurately identify *Roseomonas* spp. was assessed in an educational challenge specimen distributed by the College of American Pathologists bacteriology survey in 2000. It consisted of a simulated blood culture containing *R. gilardii* ATCC 49956. Overall, only 41.4% of 3008 respondents were able to correctly classify this organism correctly to the genus level, indicating general unfamiliarity, despite 20 years of case reports, summary studies, and descriptive information about the genus included in clinical microbiology textbooks.

The commercial biochemical system used in our laboratory, the RapidID NF Plus[®] system was accurate in identifying *Roseomonas* to the genus level in all five isolates available for testing. Another commercial identification system used for non-fermentative bacteria, the API 20 NE[®], does not contain *Roseomonas* spp. in its database and when we tested our CSF isolate the biotype did not match any organism. Vasallo¹⁵ noted that the API 20 database incorrectly identified *R. gilardii* as *Pseudomonas mesophilica*, now classified under the genus *Methylobacterium*.⁵ Given the minor biochemical differences and considerable overlap that apparently occurs among the various *Roseomonas* spp., unavailability of commercial systems that include all of the necessary substrates, frequent need for prolonged incubation, and likelihood of weak or borderline reactions, definitive identification to

Table 1 Summary of previous reports of clinically significant infections due to *Roseomonas* species

No. cases	Infection site(s)	Underlying conditions	Treatment/outcome/comments	References
7	Sputum, blood, CSF	Renal failure, diabetes, neutropenia	This was the first description of infections due to bacteria eventually known as <i>Roseomonas</i> spp. CSF isolate subsequently identified as <i>R. gilardii</i>	[2,5,6]
1	Blood of 9-month old infant with epiglottitis	None stated	Patient was discharged after a 5-day antimicrobial treatment. Organism was subsequently identified as belonging to CDC Group I	[4,5]
3	Blood	Breast cancer, Crohn's disease, leukaemia	All cultures were obtained through Hickman catheters and all three patients recovered after antimicrobial therapy	[17]
2	Blood	Leukaemia, intraabdominal abscess	Patient 1 had uneventful course following antimicrobial treatment. Patient 2 died 1 day prior to detection of bacteraemia. Organisms were detected in automated blood culture instrument after 4 and 5 days of incubation	[3]
156	Blood, CSF, respiratory tract, other sterile fluids, abscesses, aspirates, and wounds	Renal failure, diabetes mellitus, leukaemia, trauma	This study provided data to distinguish these organisms by fatty acid and biochemical analyses	[5]
1	Blood	Renal failure	Patient died one day after presentation. Organism grew in automated blood culture instrument after 48 h and was identified as CDC Group II	[18]
42	Blood, wounds, cervix, sputum, bone, breast, water and other sites	ND	This was the first designation of genus <i>Roseomonas</i> with six genomospecies	[6]
1	Bone	Steroid-dependent lung disease	This patient with vertebral osteomyelitis completed 6 weeks treatment with ofloxacin but subsequently died of respiratory failure	[10]

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Table 1 (continued)

No. cases	Infection site(s)	Underlying conditions	Treatment/outcome/comments	References
35	Blood, urogenital tract, body fluids, respiratory tract, eye, wounds	Diabetes, degenerative arthritis, leukaemia	This study described clinical manifestations of <i>Roseomonas</i> infections and noted that 40% of isolates appeared to be transient colonizers of mucosal surfaces or contaminants of sterile sites	[7]
8	Blood (7) and skin (1)	Ovarian cancer, AIDS, multiple myeloma, lymphoma, breast cancer	All seven patients with bacteraemia had central venous catheters. Seven of eight patients recovered. The 8th patient with <i>Roseomonas</i> bacteraemia had terminal AIDS and was not treated. All eight isolates represented unique features when examined by random amplified polymorphic DNA analysis	[9]
1	Blood, catheter-related bacteraemia	Leukaemia	Multiple positive blood cultures for <i>R. gilardii</i> over several weeks required treatment with several different antimicrobials. This report emphasizes the potential clinical importance of relapsing bloodstream infection due to <i>R. gilardii</i> in an immunocompromised host	[11]
1	Peritoneal fluid	Renal failure on peritoneal dialysis	Patient was successfully treated with intraperitoneal netilmicin. Household water was speculated as a source of infection but isolation of the organism from environmental sources was not successful	[19]
1	Blood	Intestinal pseudo-obstruction and catheter-related bacteraemia	Blood cultures became negative only after removal of Hickman catheter despite antimicrobial treatment	[12]

Table 1 (continued)

No. cases	Infection site(s)	Underlying conditions	Treatment/outcome/comments	References
1	Blood	Leukaemia	Three separate episodes of bacteraemia due to <i>R. gilardii</i> were documented in a patient with a Hickman catheter that ultimately necessitated removal of the device. This study also noted inability to API database to correctly identify genus <i>Roseomonas</i>	[15]
1	Blood	Breast cancer	Uneventful recovery occurred following antimicrobial treatment. This study confirmed the inability to identify <i>R. gilardii</i> using MicroScan or API 20E commercial systems	[20]
1	Peritoneal fluid	Renal failure on peritoneal dialysis	Infection was successfully treated with uneventful recovery. <i>R. fauriae</i> was proven to be a cause of peritonitis	[16]
1	Corneal ulcer	Chronic ocular disease treated with topical steroids	Patient recovered after topical treatment with ciprofloxacin leaving a large corneal scar. This report stressed importance of considering <i>Roseomonas</i> spp. as opportunistic pathogens in the setting of steroid use	[21]
1	Blood	Leukaemia	Patient had terminal leukaemia and died 2 weeks after organism was first detected despite antimicrobial treatment. Multiple isolations from bloodstream through Hickman catheter were documented. Organism identity as <i>R. gilardii</i> was confirmed using long-chain fatty acid analysis	[22]
1	Blood	Cellulitis	Patient recovered with antimicrobial therapy. Source of infection was believed to be skin with cellulites but the organism could not be recovered from blister fluid	[23]

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Table 1 (continued)

No. cases	Infection site(s)	Underlying conditions	Treatment/outcome/comments	References
1	Blood	Leukaemia	Infection resolved with antimicrobial treatment	[14]
1	Periaortic fluid	Cardiomyopathy	Infection resolved with antimicrobial treatment. <i>Roseomonas</i> spp. grew in culture of periaortic fluid after 8 days of incubation	[24]
36	Blood	ND	This study provided refinement of the taxonomy of the genus <i>Roseomonas</i> with proposal for a new species, <i>R. mucosa</i> and designation of subspecies for <i>R. gilardi</i>	[8]

ND, not described.

species level requires analysis of nucleic acid content. Thus, classification beyond the genus level should be limited to reference or research laboratories in most circumstances.

This in vitro antimicrobial susceptibilities for our five isolates were generally similar to those previously reported, but there is variation among individual species and from one report to another.^{3,9,11-15} The slow growth of many strains makes it difficult to determine susceptibilities using commercial broth microdilution systems and incubation of susceptibility tests for at least 48 h may be required.⁷ The agar gradient diffusion (Etest) method has also been employed for determining in vitro susceptibilities.^{8,14,16} Since there are no published methodological guidelines or interpretive breakpoints for minimal inhibitory concentrations (MICs) specific for *Roseomonas* spp., there are no recommendations for clinical laboratories to perform in vitro susceptibilities for individual patient management. If susceptibility testing is performed, it is best to limit reports to the MIC value and not provide an interpretation. Empiric management of infections can be guided by published reports describing antimicrobials with low MICs for *Roseomonas* spp. and which have been shown effective in eradicating the infections. Clinicians should consider aminoglycosides, carbapenems, tetracyclines, and possibly fluoroquinolones as the best treatment alternatives. In addition, careful consideration should be given for removal or change of any type of vascular catheter that may be present. However, catheter removal alone may not be sufficient.¹²

In view of the relatively small numbers of carefully described cases, much is yet to be learned about the taxonomy, optimum means for detection and identification, pathogenesis, clinical significance, and management of infections caused by *Roseomonas* spp.

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