Title: Bacteremia caused by Comamonas kerstersii in a patient with diverticulosis.
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Journal: Journal of clinical microbiology
Year: 2014 Mar
Volume: 52
Issue: 3
Pages: 1009-12
DOI: 10.1128/JCM.02942-13

Title: *Comamonas kerstersii* bacteremia in a patient with diverticulosis

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Keywords: *Comamonas kerstersii*, bacteremia, intra-abdominal infection, *Delftia acidovorans*, MALDI-TOF.

Abstract: 40 words

Text: 1232 words

ABSTRACT

We report for the first time a case of bacteremia caused by *Comamonas kerstersii* in a 65-year-old patient with sign of diverticulosis. In addition, we review the isolation of *Comamonas* sp. and related organisms in our hospital over 25 years.

CASE REPORT

Comamonas kerstersii is a non-fermenting β-Proteobacteria described in 2003 that has long been considered as non-pathogenic (19). This organism has been recently associated with intra-abdominal infection consecutive to perforation of the digestive tract (1). Herein, we describe a case of polymicrobial bacteremia due to *Comamonas kerstersii* and *Bacteroides fragilis* in a 65-year-old diabetic man that was admitted to the emergency department of the hospital due to sudden onset of fever and chills. The patient reported episodes of vomiting and diarrhea and mentioned that he drank water from a small river. Stool cultures did not disclose *Salmonella*, *Shigella, Aeromonas* or *Campylobacter* species. The detection of *Clostridium difficile* toxin A and B and glutamate dehydrogenase antigen was also negative. Blood cultures (two pairs of bottles) were drown from a peripheral vein and the patient was discharged under treatment with oral ciprofloxacin for a gastroenteritis of unknown origin. The Blood cultures were processed into a BACTEC FX automated blood culture system (Becton Dickinson, Sparks, MD). A first aerobic blood culture bottle became positive and the Gram staining revealed the presence of long filamentous Gram-negative bacilli (Figure 1). The bacterial identification by MALDI-TOF (Bruker Daltonics GmbH, Leipzig, Germany) analysis was performed the same day using a protocol that we recently developed based on the analyses of a bacterial pellet preparation from the blood bottles (5, 16, 17). The strain was identified as *Comamonas* kerstersii, a Gram-negative non-fermentative bacterium, and prompted the hospitalization of the patient. The patient was afebrile at that time, but palpation of the left lower abdominal quadrant was painful. An abdominal CT scan revealed diverticulosis without evidence of diverticulitis. Consecutively, the anaerobic blood bottles from the same pair became positive for

47 *Bacteroides fragilis*. We monitored the following MIC (µg.ml) for the *Comamonas kerstersii* strain:
48 ceftazidime, 0.75; meropenem, 0.004; minocycline, 0.38; levofloxacin, 4; co-trimoxazole, >32;
49 ciprofloxacin, 32. For the *Bacteroides fragilis* strain, the MIC were: amoxicillin-clavulanate, 1.5;
50 piperacillin-tazobac, 6; imipenem, 0.12; meropenem, 0.025; metronidazole, 0.25; clindamycin, 16;
51 ciprofloxacin, 32. A treatment of imipenem-cilastatine was given for 10 days and the patient recovered.
52 The final diagnosis was a mixed bacteremia with *Comamonas kerstersii* and *Bacteroides fragilis* in the
53 setting of a diverticulosis.

54

55 Comamonads are Gram negative, non-fermentative bacteria, oxydase- and catalase-positive, largely
56 motile due to the presence of polar flagella. The *Comamonas* genus originally contained *Comamonas*
57 *terrigena, Comamonas testosteroni* (previously *Pseudomonas testosteroni*) and *Comamonas acidovorans*
58 (previously *Pseudomonas acidovorans*) (6). It now contains seventeen species while *Comamonas*
59 *acidovorans* has been separated from the *Comamonas* genus on the basis of 16S rRNA and is now known
60 as *Delftia acidovorans* **(20)**. Although ubiquitously distributed in the environment (soil and water),
61 *Comamonas* and *Delftia* sp. are rarely associated with infections in humans. However, several
62 publications have incriminated *Comamonas testosteroni* and *Delftia acidovorans* in particular in human
63 diseases, including severe invasive infections such as bacteremia and meningitis (2-4, 7, 10, 11, 20).

64 *Comamonas kerstersii*, described in 2003 (19), has recently been reported as an agent of intra-abdominal
65 infection by Almuzara and colleagues (1). The present case is the first report of *Comamonas kerstersii*
66 bacteremia. We initially performed the identification of the strain at the species level directly from the
67 positive blood bottle using MALDI-TOF, with a spectral score of 2.176 (5, 16, 17). Subsequently, it was
68 recovered both from the blood agar plate (with a spectral score of 2.26), on which the growth was
69 maximal and from the "chocolate" agar plate that is supplemented with NAD (factor V) and hemin (factor
70 X). We also proceeded to the amplification and sequencing of the 16S rRNA ribosomal gene in order to
71 confirm the MALDI-TOF identification of this strain (8). The analysis of the sequences using the BLAST

V2.0 software (http://www.ncbi.nlm.nih.gov/BLAST/) showed 100% of identity with the sequences corresponding to the 16S RNA ribosomal gene of *Comamonas kerstersii* strain LMG 5323 (19). From both the blood bottle and the agar plates, the strain appeared as an extremely long Gram-negative filamentous bacillus which is a very unusual phenotype for bacteria of this genus (Figure 1). The *Comamonas* and *Delftia* strains previously isolated in our hospital are Gram-negative short bacilli or rods (Figure 1), which is the morphology described for these organisms (19, 20).

Translocation from the digestive tract seems to be a predominant cause of infections by *Delftia* and *Comamonas* species. Recently, Hagiya and colleagues reported a *Delftia acidovorans* bacteremia in a 46-year-old woman caused by translocation of the bacteria consecutive to pesticide poisoning (10). A bacteremia caused by *Comamonas testosteroni* was previously reported, in a 22-year-old man with perforated appendix (9). In the four cases reported by Almuzara and colleagues, the *Comamonas kerstersii* strains were isolated from intra-abdominal collections (1). We previously identified another *Comamonas kerstersii* strain in an intra-peritoneal collection of an 11-year-old child with a perforated appendix (table 1 and figure 1). Herein, the digestive origin of the *Comamonas kerstersii* strain is supported by the fact that: i) the patient reported abdominal pain, vomiting and diarrhea, ii) the CT scan revealed evidence of diverticulosis, and iii) the enteric bacteria *Bacteroides fragilis* was isolated from the blood culture in this setting. The infection could originate from the water that the patient drank in the countryside.

Comamonads have been rarely associated with infection in humans despite their ubiquitous distribution in the environment possibly due to the difficulty to accurately distinguish *Comamonas* species from *Pseudomonas* species in the pre-MALDI-TOF area (1). Alternatively, *Comamonads* could have been under-recognized due to their common occurrence in the setting of a polymicrobial infection. In our 1027-bed tertiary care university hospital, thirty-three *Comamonas* sp. strains and thirty-eight *Delftia acidovorans* strains where isolated from 1997 to 2013. They were primarily isolated from respiratory samples (33%), urogenital samples (23%) and digestive samples (21%); bacteremia represented 5% (three

patients) of all cases (Table 1). All 3 cases were poly-microbial bacteremia. The first bacteremia case was due to *Comamonas testosteroni* in association with *Streptococcus parasanguis* and *Ralstonia pickettii* in a 33-year old man. A second case involved *Delftia acidovorans* in association with *Streptococcus agalactiae* in blood cultures from a 61-year-old man. The last case is the present *Comamonas kerstersii* and *Bacteroides fragilis* co-infection.

Like *Delftia acidovorans*, *Comamonas testosteroni* is the *Comamonas* species predominantly associated with bacteremia (table 1) **(7, 9, 10, 20)**. Translocation from the digestive tract and catheters are the predominant source of infection (9, 10, 13-15). Children or patients with compromised immune systems (AIDS or patients treated with chemotherapies) appear to be particularly at risk to develop *Comamonas* sp. or *Delftia acidovorans* bacteremia (12, 13). Interestingly, Khan and colleagues reported a fatal outcome in an 4-year old immuno-competent child presenting a *Delftia acidovorans* bacteremia (12). The patient presented herein did not display any sign of immunodeficiency suggesting that such bacteremia may also occur in the absence of immunosuppression. The likely high inoculum in the water that was drunk and the diabetic status of the patient are two significant co-factors that may explain the occurrence of a bacteremia in the setting of a gastro-intestinal infection. Similarly, a *Comamonas* species bacteremia has been associated with exposure to possibly contaminated water of a fish tank (18).

This report reveals that *Comamonas kerstersii* and other non-fermenting related bacteria may be involved in severe diseases independently of perforation of the digestive tract. Moreover, this report highlights the usefulness of MALDI-TOF in redefining the epidemiology and clinical syndromes due to some non-fermentative Gram negative bacteria that were difficult to identify in the pre-MALDI-TOF area.

ACKNOWLEDGEMENTS

We are grateful to all the technicians of the Diagnostic Microbiology Laboratory of the Lausanne Hospital for their technical contribution. In particular, we thank Maria Senra-Ortiz and Christian Durussel.

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Figure legend:

Figure 1: Gram staining of *Comamonas kerstersii, Comamonas testosteroni* and *Delftia acidovorans* strains isolated in clinical samples from Lausanne University Hospital. (A) The *Comamonas kerstersii* strain of the present case report directly from the blood-cultures bottle or B after culture on blood agar medium. The strain displays long filaments when compared to the other strains that appears as Gram-negative short bacilli or rods. C) A *Comamonas kerstersii* strain identified in an intra-peritoneal collection of an 11-year-old child with a perforated appendix. D) *Comamonas testosteroni* involved in a bacteremia in a 33-year- old man. E) *Delftia acidovorans* identified in blood cultures from a 61-year-old man.

Table 1: *Comamonas* sp. and *Delfia acidovorans* isolated from clinical samples in the Lausanne University Hospital from 1997 to 2013.

	Respiratory and ENT[a]	Urogenital[b]	Intra-abdominal[c]	Skin	Blood culture	Surgical wound	Others[d]	Total patient (samples)	% of patient
Deltia acidovorans	19 (20)	12 (13)	-	5	1 (13)	-	1 (4)	38 (55)	54.3
Comamonas testosteroni	2 (4)	3	8	1 (4)	1	4 (5)	1	20 (26)	28.57
Comamonas kerstersii	-	-	1	-	1	-	-	2	2.86
Comamonas aquatica	-	1 (4)	-	-	-	-	-	1 (4)	1.43
Comamonas specis[(e)]	2	- (2)	6 (8)	1	-	-	- (1)	9 (14)	12.86
Number of patients (number of samples)	23 (26)	16 (22)	15 (17)	7 (10)	3 (15)	4 (5)	2 (6)	70 (101)	100
Percentage of patients (percentage of samples)	32.86 (25.74)	22.86 (21,78)	21.43 (16,83)	10 (9.9)	4.29 (14.85)	5.71 (4.95)	2.85 (5.94)	100	

[a]Ear nose and thoat

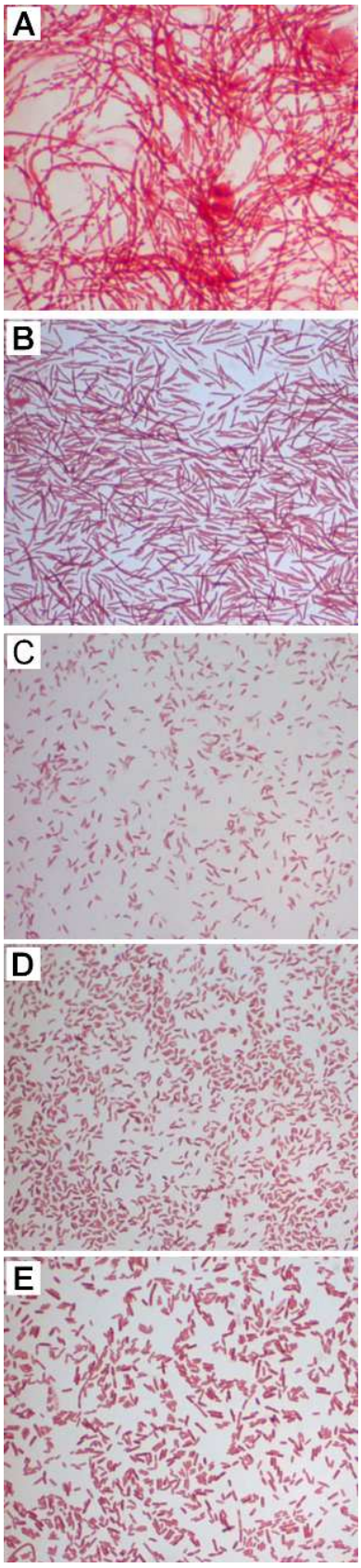
[b]Urine, vaginal swab and placenta

[c]ascitic fluid, peritoneal fluid, penrose liquid, kehr drain

[d]stools (1), bone fragment (1), orifice smear (1)

[e]no identification at the species level

Number represent patients, brackets represent the number of samples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