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Claire Duployez, Marie-Eve Edun-Renard, Eric Kipnis, Rodrigue Dessein,
Rémi Le Guern

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1 **TITLE:** Bacteremia due to *Kosakonia cowanii* in a preterm neonate.

2

3 **AUTHORS:** Claire Duployez^{1,2}, Marie-Eve Edun-Renard³, Eric Kipnis^{2,4}, Rodrigue

4 Dessein^{1,2}, Rémi Le Guern^{1,2}

5

6 **AUTHORS AFFILIATIONS:**

7 ¹ Laboratoire de Bactériologie, CHU Lille, F-59000 Lille, France.

8 ² Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019 - UMR 9017 - CIIL
9 - Center for Infection and Immunity of Lille, F-59000 Lille, France.

10 ³ Unité des Soins Intensifs, Service de Néonatalogie, CHU Lille, F-59000 Lille, France.

11 ⁴ Pôle d'Anesthésie-Réanimation, CHU Lille, F-59000 Lille, France.

12

13 **CORRESPONDING AUTHOR:** Dr Claire DUPLOYEZ

14 claire.duployez@chru-lille.fr

15 Laboratoire de Bactériologie-Institut de Microbiologie

16 Centre de Biologie Pathologie

17 F-59037-Lille Cedex, France

18 Telephone number: +33-320.445.480

19 Fax number: +33-320.444.895

20

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22 **ABSTRACT**

23 **Objective:** Low-weight birth infants admitted to neonatal intensive care units are at
24 high risk of hospital-acquired infections by opportunistic pathogens. The gut microbiota of
25 preterm neonates lacks commensal bacteria providing a barrier against pathogens. We report a
26 case of bacteremia due to *Kosakonia cowanii* in a preterm neonate.

27 **Case report:** Caesarian-section delivered a female baby of 680g at 28 weeks of
28 gestation due to intrauterine growth retardation and fetal rhythm abnormalities. On day 27,
29 two blood cultures grew Gram-negative bacilli in a context of functional ileus. No reliable
30 identification could be obtained using MALDI-TOF mass spectrometry, biochemical
31 reactions with the VITEK 2 GN ID card, or 16S rDNA sequencing. *Kosakonia cowanii* was
32 finally identified by *gyrB* sequencing. The source of infection may have been either the
33 central venous catheter or translocation from the gut microbiota. Evolution was favorable
34 after 14 days of cefepime (combined with amikacin for five days) and central venous catheter
35 removal.

36 **Conclusion:** *Kosakonia cowanii* is a member of the *Enterobacteriaceae* family that
37 was recently reclassified from the *Enterobacter* genus. Human infections due to *K. cowanii*
38 are scarce and have mainly been associated with traumatic inoculation from plants or transient
39 gut colonization. *K. cowanii* may be an underestimated opportunistic pathogen in susceptible
40 populations such as preterm neonates.

41 **KEY-WORDS:** Bacteriological Techniques; *Kosakonia cowanii*; Prematurity

42

43

44 **Introduction**

45 Healthcare-associated infections frequently occur in neonatal intensive care units, with
46 a peak incidence reported between the 10th and 22nd day of life¹. Incidence of late-onset sepsis
47 is inversely correlated to birth weight: 36.3% of neonates with a gestational age under 28
48 weeks had at least one episode of sepsis compared to 29.6% for moderately preterm, 17.5%
49 for late preterm, and 16.5% for full term infants¹. Risk factors include the immature innate
50 immune system of preterm neonates, prolonged hospitalization, use of invasive medical
51 procedures, and failure of early enteral feeding with breast milk^{1,2}. Moreover, the gut
52 microbiota of preterm neonates lacks commensal bacteria providing resistance against
53 pathogens³. Thus, the risk of infection due to translocation from the intestinal tract may
54 increase. Indeed, Stewart et al. found that the the causative agent of late-onset sepsis in
55 preterm neonates was within the dominant genus of the gut microbiome⁴. *Enterobacter*
56 species are the most abundant bacteria present in preterm neonates' gut, especially after
57 antimicrobial therapy⁵. *Kosakonia cowanii* is a member of the *Enterobacteriaceae* family that
58 was recently reclassified from the *Enterobacter* genus⁶. *K. cowanii* is frequently encountered
59 as a plant pathogen but rarely described in human infections. We present a case of bacteremia
60 due to *K. cowanii* in a preterm neonate.

61

62 **Case report**

63 Caesarian-section delivered a female baby of 680g at 28 weeks of gestation due to intrauterine
64 growth retardation and fetal rhythm abnormalities. A central venous catheter was inserted,
65 and enteral nutrition with pasteurized breast milk was initiated on day 1 of life. On day 10, the
66 neonate presented bacterial sepsis due to *Staphylococcus epidermidis* : he had fever at 38°C,
67 frequent apneas with bradycardia and desaturation. Continuous Positive Airway Pressure

68 (CPAP) and transfusion of one unit of packed red blood cells were required. The evolution
69 was favorable after ten days of antimicrobial therapy with vancomycin.

70 On day 27, the baby presented abdominal distension with residual feeds attributed to a
71 functional ileus, since she had no rectal bleeding nor vomiting. Hemodynamic and respiratory
72 functions deteriorated again, requiring endotracheal intubation from day 28 to day 31,
73 transfusion of five units of packed red blood cells and daily platelet transfusion from day 27
74 to day 34. Enteral feeding was temporarily stopped.

75 Blood cultures from day 27 yielded Gram-negative bacilli after 16 hours of incubation. No
76 reliable identification was assessed by MALDI-TOF spectrometry mass (Bruker Daltonics,
77 Wissembourg, France); the best score was 1.54 for *K. cowanii*. Biochemical reactions using
78 VITEK 2 GN ID card (BioMérieux, Marcy l'Etoile, France) identified the strain as *Pantoea*
79 spp., with a probability of 97%. However, the strain fermented sorbitol and did not use
80 malonate; those two characteristics distinguish *K. cowanii* from *Pantoea agglomerans*.

81 Sequencing of 16S rDNA was performed using universal primers 91E
82 (TCAAAGKAATTGACGGGGGC-3) and 13BS (CCCGGGAACGTATTCAC) on the 3500
83 Dx Genetic Analyzer (Life Technologies, Cergy-Pontoise, France)⁷. Definitive identification
84 could not be obtained from the 16S partial sequence, because 99% identity out of 431 base
85 pairs was found for *K. cowanii*, *Salmonella enterica*, and *Atlantibacter hermannii*. Thus, *gyrB*
86 sequencing was performed using the primers UP1
87 (GAAGTCATCATGACCGTTCTGCAYGCNGGNGGNAARTTYGA) and 181r
88 (CAGGAAACAGCTATGACCARRTGNGTNCCNCC) for amplification, followed by UP1-
89 seq (GAAGTCATCATGACCGTTCTGCA) and 181r-seq (CAGGAAACAGCTATGACC)
90 for sequencing⁸. *gyrB* sequencing identified the isolate as *K. cowanii*, showing 99% identity
91 out of 521 base pairs with *K. cowanii* type strain JCM 10956 (Genbank accession number

92 JX425012.1). A phylogenetic tree based on *gyrB* sequences (Figure 1) was constructed in
93 MEGA X⁹, using the minimum evolution method.

94 *In vitro* antimicrobial susceptibility was determined by Mueller-Hinton agar disc diffusion
95 using the critical zone diameters recommended by the CASFM –EUCAST (version 2020) and
96 using an automated method (VITEK 2, BioMérieux, Marcy l’Etoile, France). Interestingly,
97 this strain did not produce an AmpC β -lactamase as expected from a former *Enterobacter*
98 species, but a penicillinase. The strain was resistant to amoxicillin (MIC \geq 32 mg/L),
99 ticarcillin (MIC \geq 128 mg/L), and piperacillin (MIC = 64 mg/L); all the other beta-lactams
100 were active, including amoxicillin-clavulanate (MIC \leq 2 mg/L) and cephalosporins (MIC \leq 1
101 mg/L for cefotaxime, ceftriaxone, and cefepime).

102 After 14 days of cefepime, initiated on day 27 (combined with amikacin for five days) and
103 central venous catheter removal, evolution was favorable. Antimicrobial therapy and
104 laboratory values are represented as a timeline in Figure 2. Blood cultures remained sterile
105 after catheter change; *K. cowanii* also grew from the central venous catheter (10^3 CFU / mL),
106 indicating it could be the infection source. The neonate was discharged from the hospital after
107 three months of life, weighing 2615g for 48 cms.

108

109 **Discussion**

110 Until 2013, the *Kosakonia* genus was part of the genus *Enterobacter*. Many species
111 from the *Kosakonia* genus (*K. radicincitans*, *K. sacchari*, *K. oryzae*, *K. cowanii*, *K. arachidis*)
112 have been isolated from plants, and only a few human infections have been described¹⁰.
113 *K. cowanii* was first described from a patient sample but is mostly isolated from
114 environmental samples, including soil and trees. *K. cowanii* may promote plant growth and be
115 identified as an endophyte in trees with symptoms of blight⁶. Human infections due to
116 *K. cowanii* are scarce. They have been associated with traumatic inoculation from plants. In a

117 case, rhabdomyolysis due to bacteremia was observed after rose thorn prick¹¹. More recently,
118 Berinson *et al.* reported a case of acute cholecystitis in an immunocompromised patient
119 without penetrating trauma¹², suggesting the origin of the infection may be food
120 contamination. The authors suggested that transient colonization of the gut by *K. cowanii* may
121 have caused acute cholecystitis in an immunocompromised patient.

122 Low-weight birth infants admitted in neonatal intensive care units are at high risk of
123 hospital-acquired infections by opportunistic pathogens². No case of *K. cowanii* opportunistic
124 infections in low-weight birth infants had been reported in the literature yet. Our case report
125 highlights that *K. cowanii* may be a relevant cause of infections in the population of preterm
126 neonates. Preterm neonates are vulnerable to infections caused by opportunistic foodborne
127 pathogens since their local natural barrier is immature, and secretory immunoglobulins A are
128 lacking during the first days of life. *K. cowanii* was previously isolated from powdered infant
129 milk formula¹³. However, food contamination may not be the origin of infection in our case
130 since the neonate was fed with pasteurized breast milk. In our patient, the source of infection
131 may have been bacterial translocation from the gut microbiota. Indeed, previous studies
132 showed that the pathogen identified in blood culture for late-onset sepsis in preterm infants
133 was usually abundant in the gut microbiome⁴. Additional risk factors of bacterial sepsis in
134 this population include a central venous catheter, parenteral nutrition, and steroids¹⁴. Another
135 hypothesis for the infection source may have been the central venous catheter, as suggested by
136 the positive bacteriological culture of the catheter.

137 Other environmental species, mostly former members of the *Enterobacter* group, were
138 described as pathogens for neonates. The typical example is *Cronobacter sakazakii*, which
139 has been isolated from environmental sources, milk, and infant formula, causing severe
140 infections, especially bacteremia in preterm neonates^{6,15}. Powdered infant formula has been
141 reported as the most commonly identified transmission vehicle of this bacterium¹⁵.

142 Berinson et al. suggested that *K. cowanii* might be an underestimated pathogen in
143 children¹². Indeed, in a retrospective study about pediatric infections due to
144 *Pantoea agglomerans*, seven patients out of 53 (13%) had a history of penetrating trauma
145 with a stick, plant thorn, or glass shard¹⁶. As shown in our case report, *K. cowanii* may be
146 falsely identified as *P. agglomerans* using biochemical reactions. It may be one of the reasons
147 for the few human infections described in the literature. The development of new
148 bacteriological techniques such as MALDI-TOF mass spectrometry and molecular biology
149 may improve our ability to identify this bacterium. *K. cowanii* is probably an underestimated
150 opportunistic pathogen in susceptible populations such as preterm neonates.

151

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153

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172 *Pluralibacter gergoviae* comb. nov. and *Pluralibacter pyrinus* comb. nov., respectively, *E.*
173 *cowanii*, *E. radicincitans*, *E. oryzae* and *E. arachidis* into *Kosakonia* gen. nov. as *Kosakonia*
174 *cowanii* comb. nov., *Kosakonia radicincitans* comb. nov., *Kosakonia oryzae* comb. nov. and
175 *Kosakonia arachidis* comb. nov., respectively, and *E. turicensis*, *E. helveticus* and *E. pulveris*
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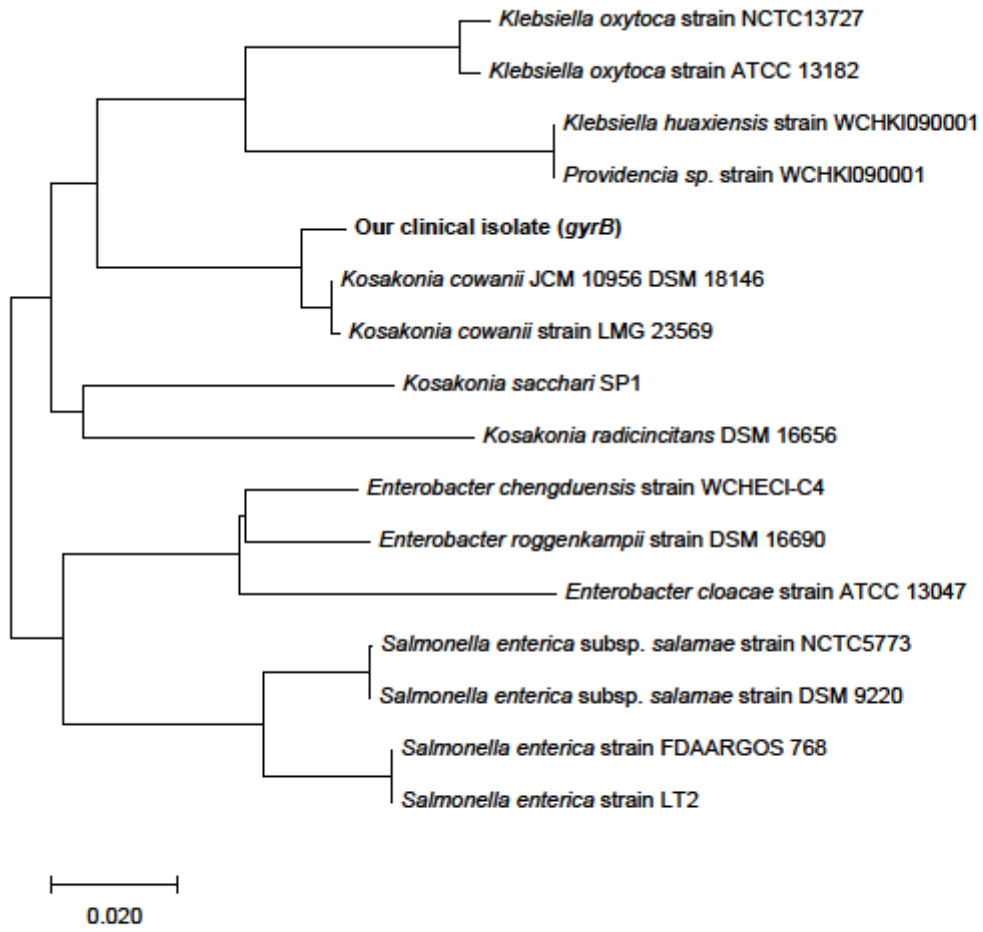
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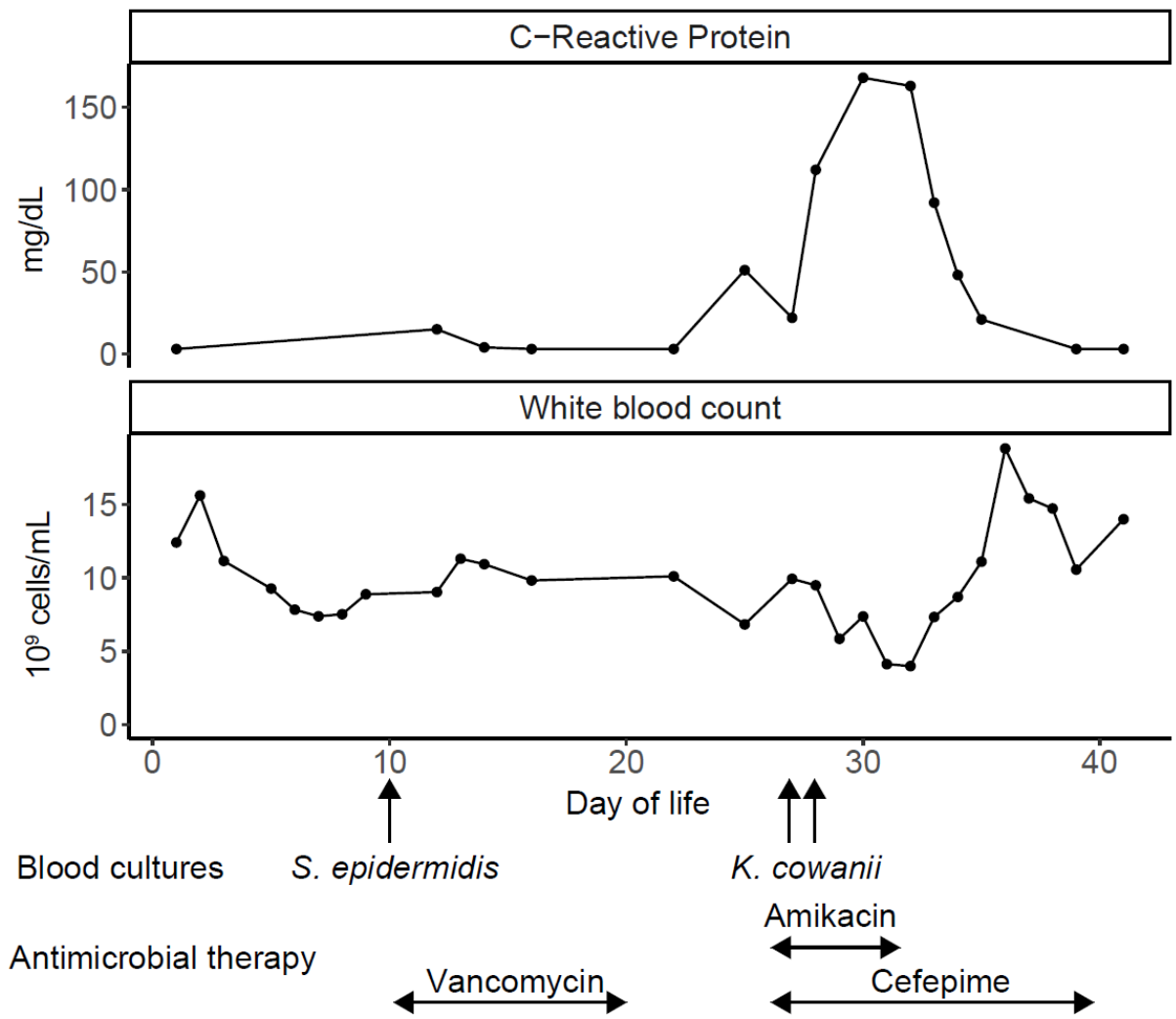
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204 **Figure 1.** Phylogenetic tree based on *gyrB* sequences.



205
206

207 **Figure 2.** Timeline visualization of laboratory data and antimicrobial therapy.



208