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Bacteremia due to *Lachnoanaerobaculum umeaense* in a patient with acute myeloid leukemia during chemotherapy: A case report, and a review of the literature

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4 1 **Bacteremia due to *Lachnoanaerobaculum umeaense* in a patient with acute**
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6 2 **myeloid leukemia during chemotherapy: a case report, and a review of**
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8 3 **the literature.**
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11 4 **Julie Bodin¹, Maria-Pilar Gallego-Hernanz², Chloé Plouzeau Jayle³, Anthony Michaud³, Lauranne**
12
13 5 **Broutin³, Julie Cremniter^{3,4}, Christophe Burucoa^{3,4} and Maxime Pichon^{3,4, *}**
14

15 6 1 Université de Poitiers, Faculté de Médecine et Pharmacie, 86000 Poitiers, France ;

16 7 2 CHU de Poitiers, Service d'Hématologie Clinique, 86021 Poitiers, France

17 8 3 CHU de Poitiers, Département des Agents Infectieux, 86021 Poitiers, France

18 9 4 Université de Poitiers, INSERM U1070 Pharmacologie des Agents Antimicrobiens et
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20
21
22 10 Antibiorésistance, 86022 Poitiers, France.

23
24 11 * Correspondence: maxime.pichon@chu-poitiers.fr (M.P.); Tel.: +33-0549444143
25

26 12 **Abstract:** The present case reports a bacteremia due to *Lachnoanaerobaculum umeaense* (a Gram-positive,
27
28 13 filamentous, rod-shaped, anaerobic, spore-forming bacillus present in the human oral microbiota) in a
29
30 14 patient treated for acute myeloid leukemia. After failed identification by MALDI-TOF, identification was
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32 15 done by sequencing of 16s rRNA. The patient was successfully treated with Co-amoxiclav and
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34 16 ciprofloxacin for seven days. Comparison of V1-V3 regions of the bacterial 16S rDNA gene with published
35
36 17 sequences failed to classify the strain as pathogenic or non-pathogenic based on this phylogenetic
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38 18 classification alone. Although *L. umeaense* is known to be associated with bacteremia in patients with
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40 19 acute myeloid leukaemia, this clinical case argues for further studies that will lead to more efficient
41
42 20 classification of the infection by these microorganisms.

43 21 **Keywords:** *Lachnoaerobaculum umeaense*; bacteremia; 16S rRNA gene sequencing; phylogenetic analysis;
44 22 acute myeloid leukemia.
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23 **Introduction**

24 The present case describes a bacteremia caused by *Lachnoanaerobaculum umeaense* in an 85-year-old man
25 with acute myeloid leukemia undergoing chemotherapy and discusses the characteristics of this infection
26 and drug susceptibility. This case was supported by phylogenetic analyses to examine the pathogenicity
27 determination of these *Lachnoanaerobaculum* sp.

28 **Clinical relevance of genus *Lachnoanaerobaculum***

29 *Lachnoanaerobaculum* species are known to be obligate anaerobes, Gram-positive, filamentous, spore-
30 forming rod-shaped bacilli. The genus *Lachnoanaerobaculum*, which was registered as a new genus in 2012,
31 belongs to the family *Lachnospiraceae* and is composed of *Lachnoanaerobaculum umeaense*,
32 *Lachnoanaerobaculum oral*, *Lachnoanaerobaculum sabbureum*, and *Lachnoanaerobaculum gingivalis* [1]. These
33 species were first isolated from the small intestine biopsy of a young girl with celiac disease in 2007, saliva
34 from a healthy young man in 1998, dental plaque from a healthy young man, and human subgingival
35 plaque from a gingivitis lesion in 2019 [2].

36 The genus *Lachnoanaerobaculum* is present in the human mouth and intestine. With regard to the intestinal
37 microbiota, decrease in the abundance of *Lachnoanaerobaculum* may be associated with more severe
38 functional constipation [3]. According to the literature, it constitutes a small proportion of the oral
39 microbiome, with total relative abundance of less than 5% [4]. These bacteria are known to be more
40 numerous in the saliva of smokers and in the intestines of lean people [5]. In addition, anaerobic
41 bloodstream infections are increasingly recognized as an important sequela of high-dose chemotherapy
42 [6].

43 To date, there are few reports in the literature of human infections caused by these microorganisms. In
44 2021, the first case of *L. gingivalis* bacteremia was reported in a patient with acute myeloid leukemia who
45 presented with oral mucositis during high-dose chemotherapy. The bacterium, identified by 16S rRNA
46 gene analysis, showed sensitivity to a number of drug classes and intermediate sensitivity to moxifloxacin
47 [2]. The first case of bacteremia caused by *L. oral*, identified by MALDI-TOF, was described in a patient
48 with acute lymphocytic leukemia undergoing chemotherapy. The Antibiotic Susceptibility Testing (AST)
49 profile showed sensitivity to anti-microbial therapies (including beta-lactam, clindamycin, and
50 metronidazole). However, it also showed high minimum inhibitory concentration (MIC) values for
51 fluoroquinolones, suggesting possible development of resistance to fluoroquinolones [7].

52 **Description of the case**

53 An 85-year-old man with a history of acute myeloid leukemia was admitted to the emergency room of the
54 Poitiers University Hospital, complaining of gingival pain, loss of appetite and weight [8].

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4 55 Ten days before admission, the most recent available biological investigations showed drug-induced
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6 56 anemia and aplasia for which anti-infective prophylaxis with cotrimoxazole, valaciclovir and
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8 57 posaconazole was initiated.

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10 58 On arrival, he was febrile at 38.7°C and hemodynamically stable with normal vitals (respiratory rate <
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12 59 25/min, blood pressure 111/56 mmHg, GCS 15, oxygen saturation 97%, heart rate 86bpm). Clinical
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14 60 examination was normal, without palpated adenopathy except for the revelation of an intraoral infection.
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16 61 The latter of fungal appearance with a white indurated lesion and ulcerations on the left inner cheek
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18 62 revealed, after biopsy for histologic examination, that the tissue contained numerous actinomycosis grains
19
20 63 and was necrotic, without visible structures that were suspect for malignancy. At the time of admission,
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22 64 blood tests showed cytopenia: aplasia (leukocyte count: 1.2 G/l, neutrophil count: 0.02 G/l), anemia
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24 65 (hemoglobin: 7.6 g/dl) without thrombocytopenia (platelet count: 183 G/l), in a context of inflammation
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26 66 (CRP: 72 mg/l). Anaerobic blood cultures became positive after approximately 36 hours of incubation
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28 67 using the BacT/Alert 3D system (bioMerieux, Marcy-l'étoile, France).

29
30 68 Direct examination of the blood culture smear showed fine Gram-negative discolored rods (Figure 1.A.)
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32 69 (congruent with the literature, describing *Lachnoanaerobaculum* sp. as Gram-positive rods that can easily be
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34 70 discolored). Identification of the organism by MALDI-TOF MS (Vitek MS, bioMerieux), performed
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36 71 according to manufacturer's recommendations, failed (confidence below the recommended threshold)
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38 72 even after several subcultures on blood agar (Figure 1.B.).

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40 73 **Figure 1. A/Direct microscopic examination of *Lachnoanaerobaculum umeaense* after Gram staining**
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42 74 **(x1000 magnification). B/Colonies of *Lachnoanaerobaculum umeaense* isolated on blood agar.** The
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44 75 colonies from subcultures could be considered eroded edge and were not hemolytic.

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46 76 Genetic identification by sequencing of the V1-V3 region of the 16S rDNA was performed (as previously
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48 77 described in [9]) and identified *Lachnoanaerobaculum* sp. after analysis using NCBI reference sequences
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50 78 (BLASTn) and BIBI-IV [10]. Finally, a retrospective phylogenetic analysis was performed using Seaview
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52 79 V4 [11–15].

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54 80 Even before species identification, the drug susceptibility of the isolate was determined using the disk
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56 81 diffusion method according to the CA-SFM recommendations [16]. It revealed multi-sensitivity to all the
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58 82 antimicrobials tested (co-amoxiclav, piperacillin-tazobactam, imipenem, clindamycin, rifampicin,
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60 83 linezolid, and metronidazole). The MIC values obtained using the Etest (bioMerieux), thereafter were as
61
62 84 follows: amoxicillin <0.016mg/l (breakpoint 0.5 mg/l) ciprofloxacin >256mg/l (breakpoint 0.5 mg/l),
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64 85 objectifying the fluoroquinolone resistance described in the literature [7]. Based on these results, treatment
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66 86 with co-amoxiclav 3 grams and ciprofloxacin 1 gram (to cover possible non-identified pathogen) per day

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4 87 was introduced for seven days to enlarge the antimicrobial spectrum of action. Due to the patient's
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6 88 excellent clinical tolerance (apyrexia) and improved biological parameters, including a decrease in C-
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8 89 reactive protein, improved leukocyte counts and normalization of ionogram, hepatic, and coagulation
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10 90 assays, the patient was discharged from the hospital. Even though the treatment resulted in apyrexia a
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12 91 few days later, a second episode of infection occurred a week later, without microbial exploration. Indeed,
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14 92 given his poor leukemic prognosis and therapeutic escape, it was collectively decided to stop the
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16 93 treatments (including antibiotics and symptomatic therapy). He died a few weeks later in a context of
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18 94 radiologically suspected invasive pulmonary aspergillosis.

19 95 The obtained sequence of the bacterial strain (deposited on GenBank under accession number: OR186325)
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21 96 was compared to the sequences published in the literature at the time of writing (June 2023) (Figure 2.).
22
23 97 Evolutionary analyses were performed on 606 informative positions in the final data set in MEGA11 [17].
24
25 98 Sequences were represented according to the origin of the strains. Thirteen sequences isolated from
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27 99 strains of human origin and considered non-pathogenic are shown here. Other sequences from strains
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29 100 isolated of human origin and considered pathogenic (n=11) and from strains isolated of environmental
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31 101 origin (n= 11) are also represented. The trees of these partial 16S rDNA gene sequences were not sufficient
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33 102 to classify these strains according to clinical outcome or bacterial strain origin ($p > 0.05$). Finally, the
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35 103 present strain revealed significant proximity with non-pathogenic strains of human origin such as *L.*
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37 104 *umeanse* [18].

38 105 **Figure 3. Phylogenetic analysis of *Lachnoanaerobaculum* sp. sequences.** In red are represented
39
40 106 sequences from isolated strain of human origin and considered as pathogenic. In green are represented
41
42 107 sequences from isolated strain of human origin and considered as non-pathogenic. In blue are represented
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44 108 sequences from isolated strain of environmental origin. The percentage of replicate trees in which the
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46 109 associated taxa clustered together in the bootstrap test (1000 replicates) are shown next to the branches.
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48 110 The evolutionary history was inferred using the Neighbor-Joining method. All ambiguous positions were
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50 111 removed for each pair of sequences (pairwise removal option). The bootstrap consensus tree deduced
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52 112 from 1000 replicates is considered to represent the evolutionary history of the analyzed taxa. The
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54 113 percentage of replicate trees in which the associated taxa clustered in the bootstrap test is indicated next to
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56 114 the branches (only bootstrap values ≥ 70 have been shown).

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4 115 **Discussion**

5
6 116 The genus *Lachnoanaerobaculum* is a rod-shaped, obligate anaerobic, spore-forming, Gram-positive bacillus
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8 117 that is easily discolored and may appear Gram-negative. For this reason, the initial diagnosis was false,
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10 118 finding a Gram-negative bacterium on direct examination after Gram staining. In addition, the present
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12 119 bacillus has morphological characteristics and culture conditions like those described in previous reports.
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14 120 Quinolone resistance is a growing concern in many bacterial species, including *Lachnoanaerobaculum* sp.,
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16 121 as in the present case. This Gram-positive anaerobic bacterium has recently shown the ability to develop
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18 122 resistance mechanisms against quinolones, which are commonly used antibiotics for bacterial infections.
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20 123 Studies have revealed the emergence of mutations targeting topoisomerase enzymes, the primary targets
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22 124 of quinolones, thereby altering their affinity for the antibiotics. These findings underscore the importance
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24 125 of monitoring and of understanding resistance mechanisms in this bacterial species, the objective being to
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26 126 ensure the ongoing effectiveness of quinolones as therapeutic agents.

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28 127 As mentioned previously and summarized in Table 1., only two reports of bacteremia due to
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30 128 *Lachnoanaerobaculum*.sp have been described in the literature involving *L. gingivalis* and *L. oral* and they
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32 129 occurred in patients with the same condition as this patient [19,20]. Both had been diagnosed with acute
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34 130 myeloid or lymphoid leukemia and were undergoing chemotherapy. However, the patient in the present
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36 131 case was a non-smoker, whereas the patients in the previous reports were smokers. Several studies have
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38 132 suggested that smoking affects the oral microbiome, which may increase the risk of *Lachnoanaerobaculum*
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40 133 sp. entering the bloodstream from the oral cavity [5]. This indicates that factors such as smoking history
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42 134 may play a role in the susceptibility to *Lachnoanaerobaculum* infections in chemotherapy patients. Further
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44 135 research is needed to explore the potential impact of smoking and other host-related factors on the
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46 136 development of *Lachnoanaerobaculum* infections in this population and its potential association with fungal
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48 137 infection.

49 138 **Table 1. Comparison between the different strains of *Lachnoanaerobaculum* spp.**

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51 139 It should be noted that in this case, contrary to Sanger sequencing of the bacterial 16S rDNA, and due to a
52
53 140 lack of library database, MALDI-TOF did not identify the bacterium . Sanger sequencing of 16S rDNA for
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55 141 identification purposes is a valuable approach in characterizing bacterial infections in cases where other
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57 142 methods, such as MALDI-TOF mass spectrometry, have failed to provide accurate identification. Sanger
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59 143 sequencing of 16S rDNA gene offers high resolution and sensitivity, thereby enabling the detection and
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61 144 characterization of bacteria that are not identifiable through other techniques. By employing this
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63 145 approach, clinicians can obtain precise information about the infectious agent, which is essential for
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65 146 guiding appropriate treatment choices. Studies such as Janda and Abbott (2007) have demonstrated the

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4 147 utility of Sanger sequencing of 16S rDNA gene in resolving cases of complex bacterial infections that are
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6 148 non-identifiable by MALDI-TOF [20]. A previous study showed that 42.1% of anaerobic bacteria not
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8 149 identified by MALDI-TOF-MS were correctly identified by 16S rDNA gene analysis [21]. Moreover, PCR
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10 150 technique is costly and time-consuming. As a result, *Lachnoanaerobaculum* sp. infection may have been
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12 151 overlooked in clinical laboratories [2,7].

13 152 It is important to note that the genus *Lachnoanaerobaculum* is not only composed of pathogenic bacteria,
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15 153 but also has biomarker properties for neoplastic or inflammatory diseases. Indeed, with the exception of
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17 154 the publications cited above, numerous publications have reported modulation of its presence and/or
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19 155 abundance in the oropharyngeal, salivary and respiratory microbiomes; i/ in pathological situations (not
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21 156 only in white spot lesions, in Vogt-Koyanagi-Harada disease), in esophagitis, or recurrent aphthous
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23 157 stomatitis, in oral cancer, in respiratory cancers with chromosomal aberration),[21–26] but also ii/ in
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25 158 relation to habits (decrease in patients who are constipated, obese or heavy consumers of sugary drinks
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27 159 and increase in smokers)[3,5,27,28]. Finally, it is a marker of the efficacy of certain therapies (decrease with
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29 160 the use of mouthwashes or in HIV-positive patients who respond to vaccination against COVID19) or the
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31 161 prognosis of the evolution of an infectious disease (such as COVID19)[29–31].

32 162 In conclusion, *Lachnoanaerobaculum umeanense* bloodstream infection should be considered in patients with
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34 163 hematologic cancer during chemotherapy. The present case supports previous clinical information and
35
36 164 provides additional data on the characteristics of *Lachnoanaerobaculum* sp. infections, microbiologic
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38 165 diagnosis, and drug susceptibility.

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48
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50
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52
53 174 agreed to the published version of the manuscript.

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60 178 *Lachnoanaerobaculum umeaense* gen. nov., sp. nov., isolated from the human small intestine, and
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Figure 1.

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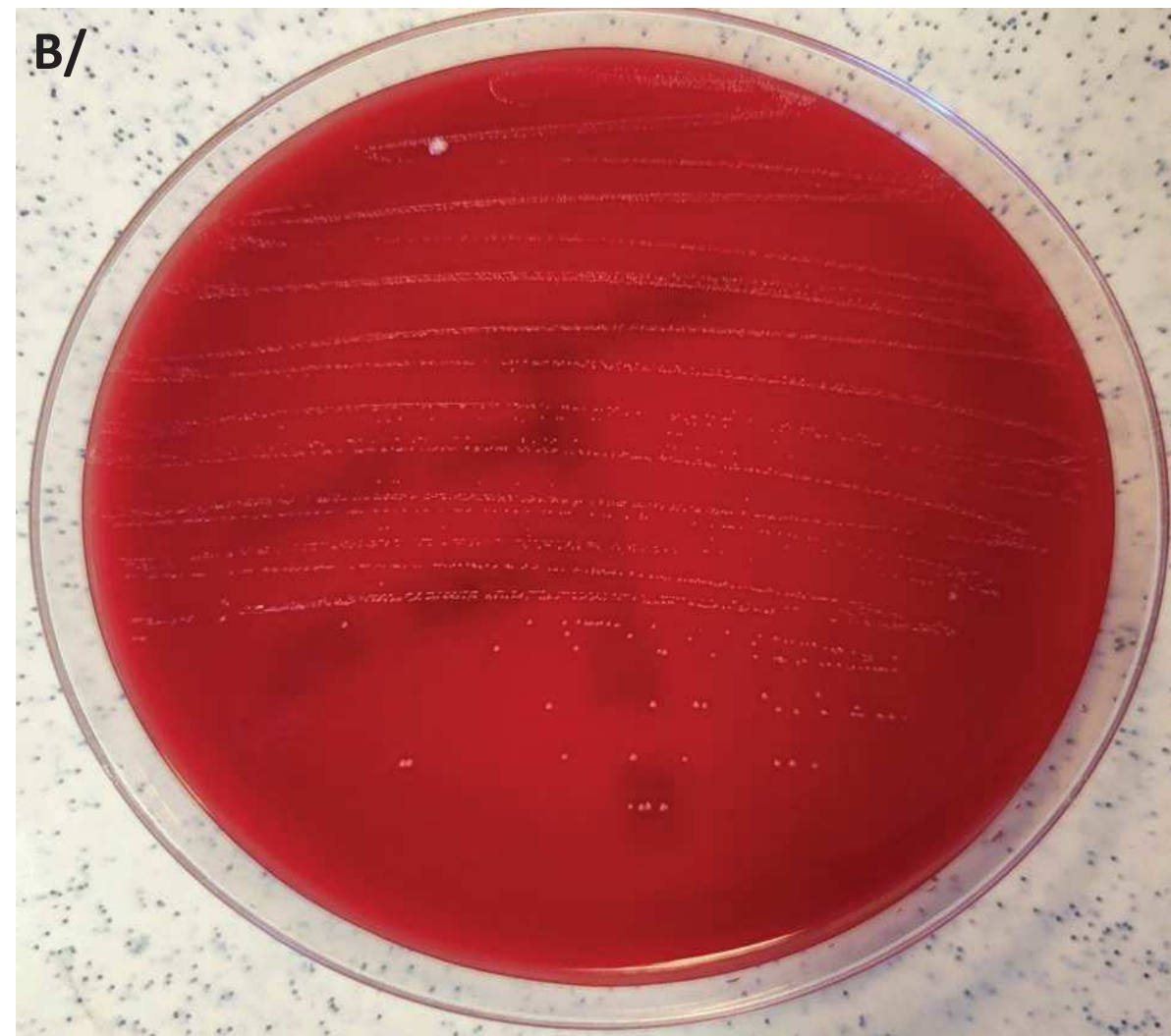
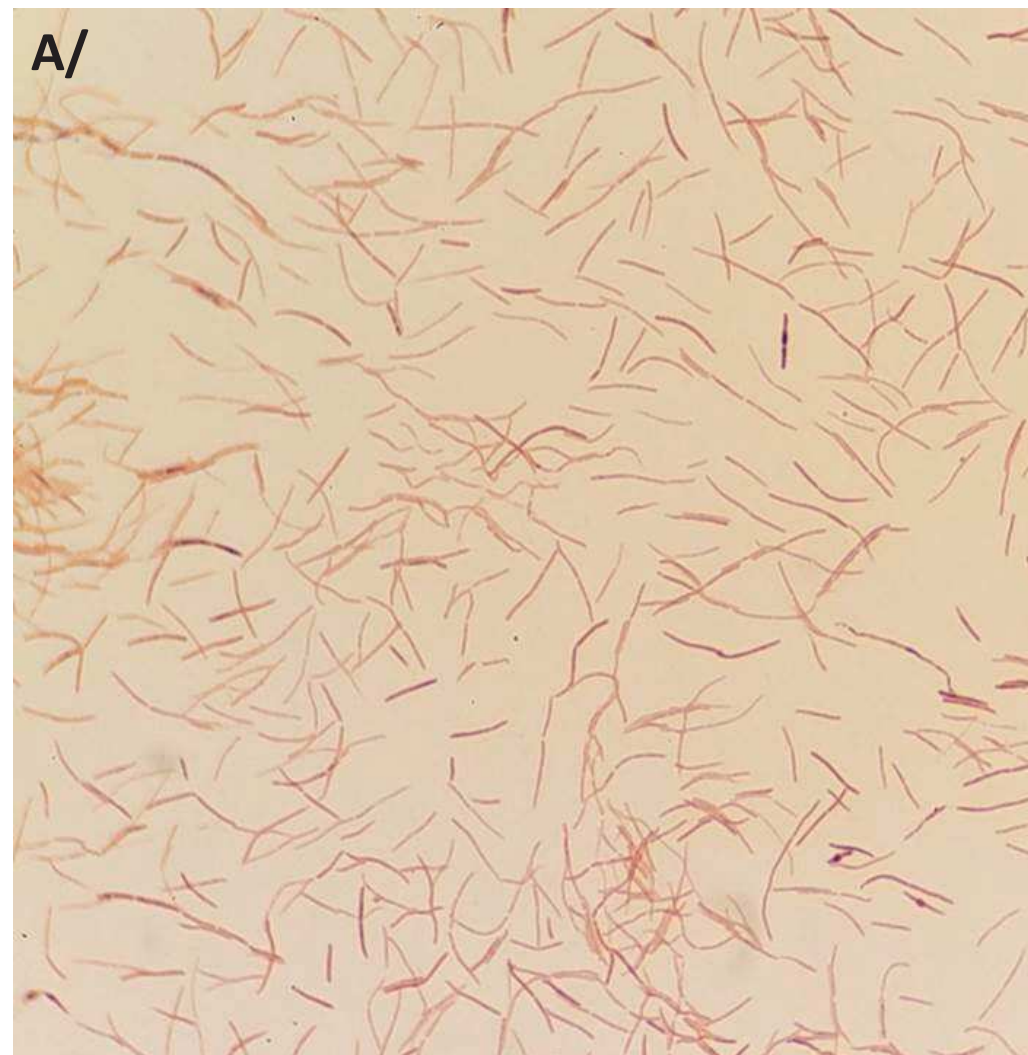
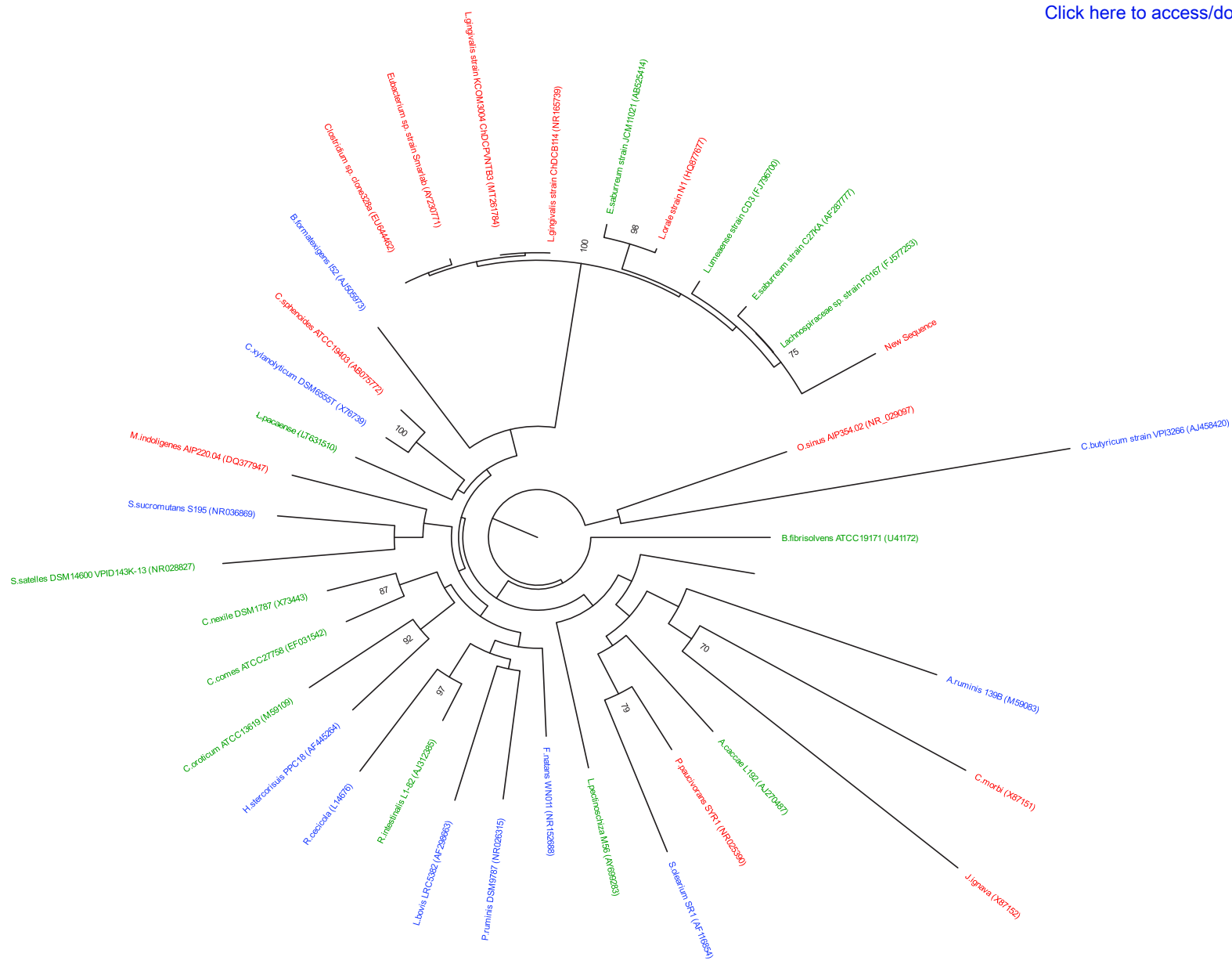


Figure 2.

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Classification	<i>L. umeaense</i>	<i>L. orale</i>	<i>L. Saburreum</i>	<i>L.gingivalis</i>	<i>L. umeaense</i>
Phylum	Bacillota				
Family	Lachnospiraceae				
Genus	Lachnoanaerobaculum				
Reference Strain (Accession number)	CD3:22 (NR_116814)	N1 (NR_118086)	CCUG 28089 (NR_104684)	ChDC B114 (NR_165739)	OR_186325
Isolation	Biopsy of the proximal small intestine of a girl with celiac disease	Saliva of a healthy young man	-	Human subgingival plaque from a gingivitis lesion	Bacteremia of an immunocompromised patient in the context of hematological diseases.
Reported bacteremia	No	Yes	No	Yes	Present description (1 st description)
Morphology	Spores in the shape of sticks, spread out and circular.				
- Cell shaped	No				
- Motility	Positive (easy fading)				
- Gram stain	Obligate anaerobes				
Oxygen tolerance	Obligate anaerobes				
Diameter	1-3mm	1.5 - 3mm	1 - 2mm	/	1-3mm
Edges	Erode edges	Rhizoidal edges and pyramidal centers	Erode edges	/	Erode edges
Hemolysis on blood agar	Non-haemolytic	Non-haemolytic	Non-haemolytic	/	Non-haemolytic
Culture and growth conditions	37°C				
- Temperature	37°C				
- pH	6.5-7.0	6.5-7.0	7.0-7.5	/	-
DNA G+C content	35%	38%	37%	35.9%	/
Enzyme production	Saccharolytic and non-proteolytic	Saccharolytic and non-proteolytic	Saccharolytic and non-proteolytic	Saccharolytic and non-proteolytic	/
Butyric acid	+	+	+	/	/

Acetic acid	+	+	+	/	/
Lactic acid	/	+	+	/	/
H ₂ S	+	+	+	/	/
NH ₃ ⁺	+	+	+	/	/
Urease	-	+	-	/	/
Indole	-	+	+	/	/
α-galactosidase	+	+	+	/	/
β-galactosidase	+	+	+	/	/
α-glucosidase	+	+	+	/	/
β-glucosidase	+	+	+	/	/
β-glucuronidase	+	+	+	/	/
α-fucosidase	/	/	+	/	/
Pyroglutamic acid arylamidase	/	+	+	/	/
Fatty acid	C14 : 0, C16 : 0 and C18 : 1v7c dimethyl acetal	C14 : 0, C16 : 0 and C18 : 1v7c dimethyl acetal	C14 : 0, C16 : 0 and C18 : 1v7c dimethyl acetal	C _{16:0} (30.7%), C _{14:0} (17.7%), iso-C _{19:0} (14.9%), C _{17:0} 2OH (12.0%)	/
Antibiotic susceptibility testing profiles					
Antibiotic susceptibility	/	Penicillin, Piperacillin, Ceftriaxone, Cefepime, Imipenem, Meropenem, Clindamycin, Metronidazole	/	Ampicillin/Sulbactam Piperacillin/ tazobactam Cefotaxime, Ceftriaxone, Cefmetazole, Imipenem, Meropenem, Clindamycin, Metronidazole	Co-amoxiclav, piperacillin-tazobactam, imipenem, clindamycin, rifampicin, linezolid and metronidazole
Intermediate susceptibility or Resistant	/	Moxifloxacin, Levofloxacin, Ciprofloxacin	/	Moxifloxacin	Moxifloxacin