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Two rare cases of pleural infection due to *Prevotella* species

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Sir,

Prevotella species are anaerobic bacteria that form part of the oral microbiota and upper respiratory and genitourinary tracts. They are usually associated with oral infections, but it can be also observed in some other infections such as skin and soft tissue, and pleuropulmonary infections. Until now, there are only few reports on pleural infection published in the literature caused by *Prevotella* species and obtained in pure culture [1-7]. We here present two additional and uncommon cases of pleural infection caused by *Prevotella* species and a review of the cases previously published.

Case 1.- A 60-year-old man was admitted due to chest pain, general malaise and vomiting. Blood analysis showed increased levels of glucose (198 mg/dL), urea (200 mg/dL), creatinine (1.53 mg/dL), procalcitonin (65.26 ng/mL), AST (437 U/L), and ALT (308 U/L). A physical exam showed cervical edema, and a cervico-thoracic CT scan showed great quantity of gas affecting cervical region and mediastinum (Figure 1) along with a pleural effusion. A diagnosis of mediastinitis was established and a thoracotomy was performed along with drainage of pleural effusion as well. Treatment with piperacillin-tazobactam and linezolid was started.

Case 2.- A 47-year-old woman was admitted due to drowsiness and inability to emit language and open the eyes. Blood analysis showed increased levels of glucose (150 mg/dL), sodium (105 mEq/L), C-reactive protein (42.7 mg/L) and decreased levels of potassium (3.10 mEq/L), chlorine (80 mEq/L) and white cell count ($3.44 \times 10^3/\text{mm}^3$). A brain CT scan was performed showing no abnormalities. The patient was admitted to the ICU and treatment with fluid and electrolyte



Figure 1 | Cervical CT scan showing a big quantity of gas corresponding to a mediastinitis.

replacement was initiated. A hormonal study was performed showing increased levels of TSH (31.59), antibodies anti-peroxidase (>1000 U/ml) and decreased levels of thyroxine (<0.28 ng/dL). Moreover, the antinuclear antibodies were positives. The patient was diagnosed of systemic lupus erythematosus and myxedematous coma. Later, a chest ultrasound revealed a left pleural effusion; drainage was then performed.

Both pleural fluids were sent to the microbiology laboratory for culture. The two samples were inoculated onto both aerobic and anaerobic blood agar (Becton Dickinson), chocolate agar (Becton Dickinson), and thioglycolate broth (Becton Dickinson), incubating all media at 37° C for 5 days. Gram staining of both fluids exhibited abundant Gram-negative rods. On the second day of incubation, numerous

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Table 1		Main characteristics of <i>Prevotella</i> pleural infections.							
Case (year of publication) [reference]	Age (years)/ sex	<i>Prevotella</i> species	Identification method	Underlying conditions and/or risk factors	Possible source of infection	Clinical manifestations	CRP (mg/L)	Treatment	Outcome
1 (2013) [2]	17/M	<i>Prevotella</i> spp	PCR (16S rRNA)	NR	NR	Fever, cough, chest pain	NR	Antibiotics + drainage	Cure
2 (2015) [5]	76/M	<i>Prevotella</i> spp	PCR (16S rRNA)	DM	NR	Fever, chest pain	147.4	Antibiotics + drainage	Cure
3 (2018) [3]	88/M	<i>Prevotella dentalis</i>	MALDI-TOF MS PCR (16S rRNA)	CRD DM	Lung	Chronic pleural effusion	194.1	Antibiotics + drainage	Died
4 (2020) [5]	42/M	<i>Prevotella oris</i>	NR	DM	Lung	Chest pain, left upper limb weakness, cough	399	Antibiotics + drainage	Cure
5 (2021) [6]	12/M	<i>Prevotella pleuritidis</i>	Next-generation sequencing-based clinical metagenomics	DM	Lung	Fever, cough, chest pain, dyspnea	NR	Antibiotics + drainage	Cure
6 (2021) [7]	49/M	<i>Prevotella</i> spp	PCR (16S rRNA)	NR	Lung	Asthenia, fever, weight loss, dyspnea	87.5	Antibiotics + thoracoscopic surgery	Cure
7 (2022) [PR]	60/M	<i>Prevotella oris</i>	MALDI-TOF MS PCR (16S rRNA)	Mediastinitis	Lung	Chest pain, general malaise, vomiting	Normal	Antibiotics + drainage	Died
8 (2022) [PR]	47/F	<i>Prevotella denticola</i>	MALDI-TOF MS PCR (16S rRNA)	Autoimmune disease	NR	Drowsiness, inability to emit language	42.7	Antibiotics + drainage	Cure

M: male; F: female; NR: not reported; CRP: C-reactive protein; PR: present report; DM: diabetes mellitus; CRD: chronic respiratory disease.

colonies of microorganisms were observed in pure culture on anaerobic blood agar alone in both samples. MALDI-TOF MS (Bruker Biotyper, Billerica, MA) results identified the strains as *P. oris* and *P. denticola* (log scores of 2.20 in case 1 and 2.14 in case 2). Biotyper software version 9 was used (8468 msp) for analyses. The two strains were sent to the Centre of Genomic and Oncologic Research (GENYO, Granada, Spain) for 16S rRNA gene sequence analysis using a previously reported method [8]. Fragments of 1,363 bp (case 1) and 1,357 bp (case 2) were obtained. The strain from case 1 showed 99.42% similarity with the *P. oris* strain NCTC 13071 GenBank sequence (accession n° LR134384.1) and the strain from case 2, 99.2% similarity with the *P. denticola* strain SEQ210 17855 GenBank sequence (accession n° JN867285.1). 16S rRNA gene sequences of the isolates were submitted to GenBank (accession number OM909079 for case 1 and ON248549 for case 2).

The gradient diffusion strip method (Etest bioMérieux) was used for antimicrobial susceptibility testing based on 2022 EUCAST criteria [9]. MIC values for the strain isolated in case 1 were benzylpenicillin (0.125 mg/L), piperacillin-tazobactam (<0.016 mg/L), clindamycin (0.047 mg/L), meropenem (0.012 mg/L), and metronidazole (0.19 mg/L). Values for the strain isolated in case 2 were benzylpenicillin (8 mg/L), piperacillin-tazobactam (0.032 mg/L), clindamycin (>256 mg/L), meropenem (0.047 mg/L), and metronidazole (1 mg/L). In case 1, the patient rapidly developed to septic shock and dead after 6 days. In case 2, the patient was prescribed i.v. meropenem (500 mg/8 h) for 20 days and was discharged after 40 days.

Pleural infections caused by anaerobic bacteria are usually of polymicrobial nature, presented as mixed infections containing aerobes and anaerobes. We here reported two cases of pleural infection due to *P. oris* and *P. denticola* in pure culture. Table 1 shows the main characteristics of patients with pleural infections due to *Prevotella* spp.

The introduction of MALDI-TOF MS for routine analyses in clinical laboratories has improved the identification of anaerobic bacteria and may help to detect new species. Last years, antimicrobial resistance is increasing among anaerobic bacteria worldwide. *Prevotella* species have been traditionally considered susceptible to penicillin, but an increasing rate of resistance to this drug has been documented over recent years, ranging from 33% to 60%, especially in *P. bivia* [10,11]. Thus, empirical treatment with penicillin cannot be recommended in infections caused by *Prevotella* species. Regarding to metronidazole, some studies reported resistance of some *Prevotella* strains to this drug [12,13]. The above findings indicate that *Prevotella* species cannot be considered as usually susceptible to antibiotics. Antimicrobial resistance of *Prevotella* spp. and other anaerobes is an emerging problem that warrants closer antimicrobial surveillance, increased resistance testing, and the stringent monitoring of treatment failures.

This is a report of two additional cases of *P. oris* and *P. denticola* as cause of pleural effusion and indicates that *Prevotella* species can produce infections in pure culture at this location. These case reports and recent observations of

antimicrobial resistance among *Prevotella* species highlight the need for caution when treating these infections with antibiotics and for the susceptibility testing of Gram-negative anaerobes in all cases.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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