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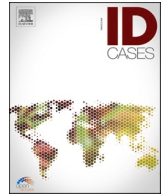
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Case report

A fatal case associated with *Catabacter hongkongensis* bacteremia in lung cancer patient: A case report

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ABSTRACT

Catabacter hongkongensis is a bacterium first isolated in 2007 and has since been detected in the blood of about fifteen patients with disease such as gastrointestinal malignancy, intestinal obstruction, or acute intestinal infection. We describe herein the case of a patient newly diagnosed with metastatic lung cancer, who died from a fatal infection possibly related to *Catabacter hongkongensis* bacteremia. By reviewing all cases reported in the literature, our case report supports that this infection is associated with a very high mortality in cancer patients.

Introduction

Catabacter hongkongensis is a rare Gram-positive anaerobic coccobacillus, first isolated in 2007 in blood cultures from four patients living in Hong-Kong and Canada [1]. Since then, this bacterium has been only reported few times in literature, mostly from Asia (seven cases from Hong-Kong, one from South Korea and one from New-Zealand) [1,4]. Other reports were from North America (two cases from Canada) [1] and Europe (four cases, from Italy, Sweden and France) [5,8]. We describe herein the case of a patient newly diagnosed with metastatic lung cancer, who died from a fatal infection possibly related to *Catabacter hongkongensis* bacteremia.

Case description

A 62-year-old caucasian man was admitted to our Pneumology Unit the 29th of December 2020 for dyspnea, cough, and body condition loss (scale 1 on the Performance Status score). He was recently diagnosed with non-small cell lung cancer ("not otherwise specified" NOS subtype) with no oncogenic mutations but high PD-L1 expression at 80 %. The tumor mass was para-hilar, extended to the right upper lobe and the middle lobe, partially necrotic (82 × 61 mm), with important bilateral

necrotic adrenal metastases (right: 139 × 98 mm; left: 66 × 42 mm). There was no other metastatic lesion. The other antecedents were hypertension, chronic obstructive pulmonary disease and peripheral arterial disease. Importantly, his general health status was preserved, with no organ failure, and a survival estimated well beyond 3 months. The therapeutic project was a combination of both chemotherapy and immunotherapy (immune checkpoint inhibitors, anti-PD1).

At patient's arrival, exertional dyspnea (mMRC scale 3) and productive cough with difficulty in expectoration were described. There wasn't any need for oxygen support. Clinical examination found decrease in right apical vesicular lung sound, a painless palpable mass in the right hypochondrium, without any sign of peripheral hypoperfusion. He underwent a bronchial fibroscopy in order to relieve bronchial obstruction because thoracic CT showed complete upper right lobe atelectasis. After identifying a wild-type *Streptococcus pneumoniae* from bronchoaspiration (total bacteria count > 5 UFC (log10)/mL), we started amoxicillin-clavulanic acid from the 31st/12 to the 7th/01. On January the 4th, the patient had fever (up to 39.3 °C) and chills. He underwent a new fibroscopy and two blood culture samples, aerobic and anaerobic, were collected. His leukocyte count grew from 13.5 G/L (31st/12) to 24 G/L (on the 7th/01). Among seven blood culture samples collected between the 2nd/01 and the

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Table 1
Summary of all *Catabacter hongkongensis* infections reported from the literature.

Ref.	Age/ Gender	State	Case year	Clinical context	Blood culture/ Days or hours to positive	Identification method	Strain	Suspected source of the bacterium	Surgical or medical treatment used	Outcome
2007, Lau et al. [1]	48/M	Hong-Kong	1999	Small bowel obstruction with secondary sepsis	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Cefuroxime + Metronidazole	Recovered after 19 days of hospitalization
2007 Lau et al. [1]	39/M	Hong-Kong	2003	Acute appendicitis with perforation	Anaerobic, 3 days	16S RNA sequencing	HKU17	Intestinal	Emergency laparoscopic appendectomy/Cefuroxime + Metronidazole	Recovered after 2 days
2007 Lau et al. [1]	74/M	Canada	2004	Exchange of biliary stent	Anaerobic, unknown	16S RNA sequencing	CA1	Intestinal	Ciprofloxacin	Recovered
2007 Lau et al. [1]	66/F	Canada	NA	Sepsis/Metastatic lung cancer	Anaerobic, 5 days	16S RNA sequencing	CA2	NA	Cefuroxime + Ciprofloxacin	Died 2 weeks after admission
2012, Lau et al. [2]	91/F	Hong-Kong	2008	Sepsis with liver abscess and suspected carcinoma of the colon	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Ticarcillin-clavulanic acid + gentamicin	Died a month after admission from nosocomial pneumonia
2012, Lau et al. [2]	21/M	Honk-Kong	2009	Acute gangrenous perforated appendicitis	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Emergency laparoscopy with appendectomy/Cefuroxime + Metronidazole	Recovered a month after admission
2012, Lau et al. [2]	81/F	Honk-Kong	2009	Sepsis/metastatic colorectal cancer	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Amoxicillin-clavulanic acid then Piperacillin-Tazobactam	Died 9 days after admission
2012, Lau et al. [2]	76/M	Honk-Kong	2009	Acute calculous cholecystitis	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Cefuroxime + Metronidazole	Recovered after 3 weeks
2012, Lau et al. [2]	81/F	Honk-Kong	2010	Infected tumor/colon adenocarcinoma with liver metastasis	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Cefuroxime + Metronidazole	Died 2 months after admission
2012, Lau et al. [2]	21/M	Honk-Kong	2009	Acute gangrenous perforated appendicitis	Anaerobic, 3 days	16S RNA sequencing	HKU16	Intestinal	Emergency laparoscopy with appendectomy/Cefuroxime + Metronidazole	Recovered a month after admission
2016, Choi et al. [3]	77/M	South Korea	NA	Acute cholecystitis	Anaerobic, 3 days	16S RNA sequencing	NA	Intestinal	Endoscopic retrograde biliary drainage/Cefodizime + Metronidazole	Recovered
2012, Smith et al. [4]	47/M	New-Zealand	NA	Acute appendicitis with perforation/Perianal abscess	Anaerobic, 4 days	16S RNA sequencing	HKU16	Intestinal	Laparoscopy and pelvis wash out/Cefuroxime + Metronidazole, Amoxicillin-clavulanic acid	Recovered
2015, Torri et al. [5]	55/M	Italia	NA	Septic shock/Road accident with multiple pelvic fractures and splenic hematoma	Anaerobic, 82 h	16S RNA sequencing	HKU16	NA	Ceftazidime + Gentamicin then vancomycin + meropenem	Recovered
2016, Kaden et al. [6]	83/M	Sweden	NA	Fever and chills without any focal infection symptoms: viral infection suspected	Anaerobic, 80 h	16S RNA sequencing	ABBA15k	NA	No antibiotic treatment	Recovered
2011, Elsendoorn et al. [7]	52/M	France	NA	Intestinal perforation peritonitis with pneumoperitonitis	Anaerobic, 3 days	16S RNA sequencing	NA	Intestinal	Amoxicillin-clavulanic acid + gentamicin/Laparotomy, complete colectomy with rectum closure end and ileostomy	Recovered
2021, Cabrol et al. [8]	80/W	France	NA	Abdominal abscess fistulized to a sigmoid tumor	Anaerobic, 67 and 74 h	16S RNA sequencing	NA	Intestinal	Piperacillin-Tazobactam and Vancomycin	Died after 1 month
2021, Mandin et al.;	62/M	France	2021	Septic shock/Non-small cell lung cancer with adrenal metastases without any intraperitoneal involvement	Anaerobic, 65 h	16S RNA sequencing	NA	Pulmonary or Intestinal	Amoxicillin-clavulanic acid then Piperacillin-Tazobactam + Amikacin	Died 23 days after admission

NA = Not available, F = female, M = male.

11th/01, only one anaerobic blood bottle culture collected the 04th/01 (during amoxicillin-clavulanic acid treatment) was positive after 65 h, revealing Gram-positive coccobacilli from direct microscopic analysis. We decided to continue amoxicillin-clavulanic acid because the patient was stable, with no new fever episode. In the meanwhile, a central venous catheter was placed on December the 31st and he underwent his first chemo-immunotherapy cycle (Carboplatin-Pemetrexed-Pembrolizumab) on January the 5th with granulocyte colony-stimulating factor for 5 days. Despite different assays, no identification could be performed using MALDI-TOF MS (VITEK® MS, bioMérieux) using the V3.2 database, thereby justifying molecular and sequencing methods. *Catabacter hongkongensis* was then identified using the 16S RNA partial sequencing method as previously described (with no subculture available for antibiotic susceptibility testing) [9]. On the 11th/01, that is seven days after Gram-positive coccobacilli observed on the anaerobic blood sample, **respiratory status declined with oxygen flow rate of 1 L/min needed and he became hypotensive (blood pressure 89/59 mmHg) with oliguria, poor peripheral perfusion (pale and mottled skin) and hyperlactatemia (4.1 mmol/L) despite vascular filling (500 mL of saline solution (NaCl 0,9 %) administered in twenty minutes).** Intravenous antibiotic therapy, associating piperacillin-tazobactam and amikacin, was initiated and he was therefore transferred to the Intensive Care Unit to get vasopressive support. Piperacillin-tazobactam was continued until the 21st/01. His clinical condition was stable thanks to these therapies but he underwent a septic shock 23 days after, with no other bacteria isolated in any other sample (6 blood cultures samples pairs between the 12th/01 and 27th/01, urine cultures the 11th/01 and 21st/01, BAL the 25th/01). To note, only one blood sample was positive for *Staphylococcus haemolyticus* but was considered as a contaminant. On the 21st/01, considering this new clinical impairment, the intravenous antibiotic treatment was switched for imipenem/cilastatin association, maintained until his death on the 27th/01.

Discussion

According to literature, little is known about *Catabacter hongkongensis*' epidemiology. *Catabacter hongkongensis* is a motile, catalase-positive, strictly anaerobic, nonsporulating, Gram-positive coccobacillus. It was first described by Lau et al., 14 years ago as a new family of bacteria named *Catabacteriaceae*, based on its unique phenotypic and genotypic characteristics [1]. *Catabacter hongkongensis* is the only species of *Catabacter* genus.

We review the characteristics of other patients described in literature with *Catabacter hongkongensis* bacteremia in Table 1. *Catabacter hongkongensis*' growth is slow and tedious with a median detection time in blood culture of 72 h [8]. This long period time to positivity (given the fact that blood bottle samples usually are incubated 5 days excepted in case of endocarditis suspicion) added to this bacteria's growth difficulty might explain the fact that it is mis- or underdiagnosed. To date, half of case reports were from Hongkong patients [1,2,10]. This is the only fifth case described in Europe, and the third in France, since its first description in 2007 [6–8]. Several reports also described the detection of *Catabacter* spp in environmental sources, such as urban aerosols in the United States [11], mangrove sediment in China [12], or from rice paddy field soil in Japan [13]. *Catabacter hongkongensis* has also been described as a commensal intestinal bacteria of an aquatic herbivorous mammal in Japan [14].

Our case supports that *Catabacter hongkongensis* bacteremia is associated with a very high mortality rate in patients suffering from advanced malignancies. Including this case, all patients with malignancies died from this infection (six cases reported worldwide up to now). It is important to highlight that our patient was just diagnosed for a metastatic malignancy and previously had a good condition. Importantly, most cases occurred in patients with gastrointestinal malignancies (primary tumor or metastasis), intestinal obstructions or infections. Thus, the main hypothesis sustained being a gastrointestinal

translocation. In our situation, the patient's symptoms were mostly respiratory due to bronchial obstruction. However, he also had huge bilateral adrenal metastases. These necrotic lesions (both in the thorax and in the abdomen) may be the source of the bacterium. Given the very few number of cases described worldwide, further epidemiological and metagenomic studies are required to better understand the reservoir, phylogeny, virulence factors, pathogenicity, and eventually contamination way(s). Previous case reports described that some strains could be resistant to penicillin and cephalosporin [1,3,7], two antibiotics commonly used in primary intention. Importantly, *Catabacter hongkongensis* was mostly sensitive to metronidazole and vancomycin treatment [1,6,8].

Conclusion

This new observation of fatal septic shock associated with a *Catabacter hongkongensis* bacteremia highlights that this infection is associated with a poor prognosis in neoplastic patients, with a 100 % mortality among reported cases. Obviously, publication bias could explain this high mortality rate. However, identification of Gram-positive coccobacilli in anaerobic blood samples should not be considered as a contamination especially in neoplastic patients, with necrotic tumors. The rarity of this infection and the long delay of culture may defer the introduction of adapted antibiotics.

CRedit authorship contribution statement

Conceptualization: EPT and VM. Data curation: VM. Formal analysis: SC, PB. Methodology: EPT, Supervision: EPT and PB. Validation: EPT, PB, JB, SD, AG, ALC, SC. Writing – original draft: VM. Writing – review & editing: EPT, PB, JB, SD, AG, ALC, SC.

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Ethical approval

Ethical Approval in accordance with local regulations.

Consent

No consent needed for this paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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