Capnocytophaga Lung Abscess in a Patient with Metastatic Neuroendocrine Tumor

Raghu Thirumala, MD, MPH1a, Urania Rappo, MD, PharmD2a*, N. Esther Babady, PhD3, Mini Kamboj, MD2 and Mohit Chawla, MD1

1Department of Medicine, Pulmonary Medicine Service and Interventional Pulmonology, 2Department of Medicine, Infectious Disease Service, 3Department of Laboratory Medicine, Microbiology Service, Memorial Sloan-Kettering Cancer Center, New York, NY

aPrimary co-authors

Footnotes: R.T. and U.R. contributed equally to the manuscript. R.T. is currently a Pulmonary and Critical Care Fellow at Lenox Hill Hospital/North Shore-LIJ Health System, NY. U.R. is currently a National Research Service Award Fellow at Weill Cornell Medical College as part of the T32 Fellowship training program in Health Services Research funded by the Agency for Healthcare Research and Quality. Presented in part as a poster at the New York State Thoracic Society Annual Scientific Assembly, West Point, New York, 2010.

*Corresponding author. Mailing address:
Weill Cornell Medical College
Division of Clinical Epidemiology and Evaluative Sciences Research
1300 York Avenue, Box #46
New York, NY 10065
Phone: 646-962-5050
Fax: 646-962-0620
ABSTRACT:

*Capnocytophaga* species are known commensals of the oral cavity of humans and animals (mainly dogs and cats), and are a rare cause of respiratory tract infections. We report a case of cavitary lung abscess caused by *Capnocytophaga* species in a patient with metastatic neuroendocrine tumor.
CASE REPORT:

A 39-year-old man with metastatic well-differentiated neuroendocrine tumor presented with fever and productive cough for two weeks. The patient’s primary tumor was a large right infra hilar lung mass causing obstruction of the bronchus intermedius and extended to the right middle lobe (RML) and right lower lobe (RLL) bronchi. He also had multiple bilobar liver metastases. He had been treated with monthly octreotide injections for symptom control of carcinoid syndrome (hormone hypersecretion), which often occurs in metastatic neuroendocrine tumors. He had also recently been on chemotherapy with oral capecitabine and temozolomide.

Two weeks after planned right hepatic artery embolization for liver metastasis and symptom control, he experienced low-grade fevers with cough productive of foul-smelling melanoptysis, night sweats, malaise and weight loss. The symptoms did not respond to a brief course of azithromycin. A computed tomograph (CT) of the chest revealed a new 8.7 x 6.4 cm cavitary abscess in the right lung. He was empirically treated with oral clindamycin for presumed aspiration pneumonia and anaerobic coverage, but was admitted two days later for progressive symptoms.

His medical history included three episodes of pneumonia that pre-dated the cancer diagnosis, heavy marijuana use for 20 years (quit 1 month prior to his current admission) and occasional alcohol use; he denied cigarette smoking. He had four cats at home, and denied recent travel, sick contacts, exposure to tuberculosis, or prior incarceration; he worked as a salesman for a waste transfer facility.
On admission, he was febrile (38.4˚C) and tachycardic without acute distress. Physical examination revealed an ill-appearing young man with normal dentition; chest exam was remarkable for decreased breath sounds at the right base, egophony, and dullness to percussion on the right. Laboratory values showed elevated WBC 24,800/µL (neutrophils 87%), thrombocytosis of 878 K/µL (normal 160-400), mild hyponatremia 132 mEq/L (136-144), low albumin 2.9 g/dL and high INR 1.83 (0.85-1.17). Admission chest radiograph and a repeat chest CT revealed an increase in the size of the right lung abscess to 10.2 x 8.3 cm (Fig. 1A and 1B). The patient was started on intravenous antibiotics, including piperacillin/tazobactam and vancomycin. A PPD was placed and was negative; sputum samples were also negative for acid-fast bacilli (AFB) on smear and mycobacterial culture remained negative after 42 days. Blood cultures were negative after five days of incubation. Serum Aspergillus galactomannan antigen, β-D glucan and Legionella urinary antigen assays were all negative. Vasculitis panel, including p-ANCA and c-ANCA were negative. On hospital day #2, the patient underwent drainage of the lung abscess with CT-guided placement of a pigtail catheter and 150 mL of thick, tan-colored fluid was aspirated. The abscess fluid was negative for AFB on smear and culture, and the initial gram stain showed 4+ polymorphonuclear cells, 3+ gram positive cocci in chains and 3+ gram negative rods. After 72 hours, culture of the lung abscess fluid grew 4+ yellow-tan colonies with gliding motility on a sheep blood agar (SBA) plate. Gram stain of these colonies revealed thin, fusiform gram-negative bacilli (Fig. 2); no other organisms were recovered in culture. The gram-negative bacillus was identified as *Capnocytophaga* species (99.99%) using the RapID™ ANA II system (Remel, Lenexa, KS) and further classified as human *Capnocytophaga* species based on negative oxidase and catalase tests (feline and canine species are oxidase and catalase positive). In an attempt to further speciate the organism, additional biochemical reactions were
set up including nitrate reduction (negative), esculin hydrolysis (positive), ortho-nitrophenyl-β-D-galactopyranoside (ONPG) hydrolysis (positive) and gelatin hydrolysis (negative). Based on these reactions, three human *Capnocytophaga* species could be excluded including *C. gingivalis* (negative for all reactions), *C. granulosa* (esculin negative) and *C. haemolytica* (nitrate positive), leaving two potential species including *C. ochracea* and *C. sputigena*. The organism tested positive for β-lactamase production by the Cefinase™ disc test.

The patient defervesced with prompt resolution of leukocytosis and clinically improved after a CT-guided drainage catheter was placed into the abscess. The antibiotic regimen was changed to ampicillin/sulbactam to complete six more weeks as outpatient. He was then switched to piperacillin/tazobactam via pump for easier home dosing for two more weeks (total IV antibiotic therapy of nine weeks). The pigtail catheter was removed four weeks after placement. Rigid bronchoscopy at the end of his antibiotic course confirmed complete obstruction of the bronchus intermedius (Fig. 1C), which was palliated via mechanical debulking and laser ablation, to achieve partial patency and regain both RML and RLL ventilation. Therapeutic aspiration of purulent secretions during this procedure grew pharyngeal flora with no evidence of *Capnocytophaga* species, and bronchoscopic biopsy confirmed typical carcinoid.

The patient continued to improve with marked resolution of the abscess on follow-up chest CT as early as 6 weeks after presentation. His metastatic carcinoid showed clinical and radiologic response after a left hepatic artery embolization, systemic chemotherapy, and maintenance monthly octreotide. He required two additional palliative rigid bronchoscopies to gain maximal patency of the bronchus intermedius, RML and RLL with concurrent negative bronchial cultures.
The genus *Capnocytophaga* is a group of long, thin, fusiform, slow growing, facultative anaerobic, gram-negative rods with gliding motility whose growth is optimal in a CO₂-enriched atmosphere, hence the name *Capnocytophaga* (consumption of CO₂) (10). *Capnocytophaga* species are part of the normal oral flora in dogs, cats, and humans, and were once associated with periodontal disease but are now considered commensals in dental plaque of humans (10). In immunocompetent patients, respiratory tract infections occur due to secretions from the oral cavity and are usually polymicrobial (5, 17). In immunocompromised hosts with neutropenia or oral ulcerations, *Capnocytophaga* species can cause severe systemic infections and even death (10, 17).

*Capnocytophaga* infections can have varied clinical presentations, such as periodontal disease (9, 22), respiratory tract infections (3), ophthalmic lesions (1, 6, 18), traumatic pericarditis, mediastinal abscess (16), brain abscess (21), meningitis (12, 20) and peritonitis (10, 15). The species colonizing the human oral tract are *C. ochracea*, *C. sputigena*, *C. gingivalis*, *C. haemolytica* and *C. granulosa* (10). Patients with compromised oral mucosa including those undergoing intensive chemotherapy for the treatment of cancer can develop septicemia, which has sometimes led to multi-organ failure and death (2, 3, 8), endocarditis (4), pyonephrosis (23), osteomyelitis and septic arthritis (10, 24). Significant risk factors include splenectomy and alcoholism (10). Isolation of this organism from lung abscess is rare; we found only one other
case report in the English literature (17). The patient was a 66-year-old man with lung cancer who developed the infection after at least 3 days of hospitalization, was initially treated with cefamandole, and was then treated with drainage, pneumonectomy, cephalothin and tobramycin and recovered; no further details are provided. Like our patient, he had underlying lung cancer, was not immunosuppressed, and recovered after drainage and antibiotic treatment.

The species that colonize the saliva of dogs and cats are *C. canimorsus* and *C. cynodegmi*, and have been found to cause disease after pet contact (mostly cellulitis) and severe sepsis after dog bites, especially in splenectomized or alcoholic patients (10).

*Capnocytophaga* species may be difficult to isolate. Most isolates require more than two days to show growth under anaerobic conditions; in our case, the culture revealed growth after three days of incubation. Drugs of choice for treatment of severe infections include penicillin/β-lactamase inhibitor combination, imipenem, or a third or fourth-generation cephalosporin. Milder infections may be treated with oral clindamycin, doxycycline, or a fluoroquinolone. Beta-lactamase producing strains may be more resistant to cephalosporins and should ideally be treated with penicillin/β-lactamase inhibitor combination or imipenem (19). The frequency of β-lactamase production has varied depending on the study, but appears to be increasing (10). A large survey of the oral flora of hospitalized pediatric oncology patients in France showed that 70% of 440 *Capnocytophaga* isolates produced β-lactamase (11). Smaller series have shown a frequency of β-lactamase production of 75% (18 of 24 bloodstream isolates from febrile neutropenic patients in France), 30% (of periodontal isolates from periodontitis patients in Spain), or 32% (6 of 19 mostly clinical isolates in Canada) (14, 13, 19). Our *Capnocytophaga*
isolate was β-lactamase positive and our patient was treated with ampicillin/sulbactam, followed by piperacillin/tazobactam. Vancomycin and metronidazole have no activity against *Capnocytophaga* species. A case of fluoroquinolone-resistant *C. gingivalis* has been reported (7).

Our patient was not neutropenic and likely developed the cavitary lung abscess after aspiration of oral flora via the RUL bronchus during moderate sedation for his right hepatic artery embolization procedure. He was unlikely to clear the aspirate given the high-grade obstruction of the bronchus intermedius (Fig. 1C). Exposure to his cats at home was likely unrelated since his particular *Capnocytophaga* species is not present in feline saliva.

*Capnocytophaga* species are unusual opportunistic pathogens that are a rare cause of lung abscess; we report the second case in the English language literature (17). Our case is remarkable in the sheer size of the lung abscess, which occurred in the setting of airway obstruction, and the rapidity of resolution after drainage and IV antibiotics with minimal residual parenchymal damage. Clinicians treating patients with cancer should be aware that β-lactamase producing organisms are becoming increasingly common and empiric coverage with vancomycin, cephalosporins or fluoroquinolones may not be adequate in this setting (10, 19). Prompt diagnosis and appropriate treatment are imperative in the management of these infections, as the organism is capable of causing sepsis, multi-organ failure and death in certain patient populations, such as immunosuppressed patients undergoing treatment for cancer.
REFERENCES:


FIG. 1. A chest X-ray (A) and CT scan (B) at admission showing a large, irregular air and fluid intraparenchymal collection up to 10.2 x 8.3 cm, and obliteration of the bronchus intermedius by calcified mass (arrow) with increased necrosis and collapse of the RML and RLL. Initial bronchoscopy (C) showing complete obstruction of bronchus intermedius by tumor (arrow).

FIG. 2. Gram-negative rods identified as human Capnocytophaga species (oil immersion, 1000x magnification)

FIG. 3. Chest CT 10 months after presentation (A): Interval clearing of dense RLL consolidation and decreased size of partially calcified mass in the right hilum. Patent bronchus intermedius (arrow) as viewed on CT (A) and follow-up bronchoscopy (B) after laser ablation and mechanical debulking.