

An Unusual Cause of Neutropenic Fever: Spontaneous *Pantoea agglomerans* Bacteremia in an Adult

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Abstract Neutropenia is a serious complication found in immunocompromised patients, particularly those with cancer and human immunodeficiency virus (HIV). The etiology of neutropenia is multifactorial and can be caused by the direct effects of HIV infection, cytotoxic antineoplastic therapy, and malignancy. The main complication of neutropenia is a bloodstream infection caused by gram-positive bacteria (GPB) and gram-negative bacteria (GNB). GPB, specifically *S. epidermidis*, tend to affect cancer patients more often than GNB. However, GNB such as *Pseudomonas aeruginosa* have been associated with more serious infections. We report a case of neutropenic fever caused by a GNB, *Pantoea agglomerans*, in a 47-year-old Afro-Caribbean man with HIV and metastatic salivary adenocarcinoma. *Pantoea agglomerans* is a non-spore forming rod typically isolated from plants, fruits, and fecal matter, and is rarely pathogenic in humans. In the current literature, cases of *P. agglomerans* have been documented primarily in the pediatric population secondary to penetrating wound trauma. To our knowledge, this is the first case of spontaneous neutropenic fever secondary to *P. agglomerans* bacteremia in an Afro-Caribbean adult male.

Keywords: *pantoea agglomerans*, bacteremia, immunocompromised state, HIV, neutropenic fever, malignancy

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1. Introduction

Neutropenia is a common condition associated with cancer patients, characterized by a clinically significant reduction in the number of neutrophils. In accordance with the most current guidelines by the Infectious Disease Society of America (IDSA) and the American Society of Clinical Oncology (ASCO), neutropenia can be defined by an absolute neutrophil count (ANC) of < 1500 cells/ μ L. Severe neutropenia is further defined by an ANC is < 500 cells/ μ L, or if the ANC is expected to decrease to < 500 cells/ μ L over the next 48 hours. [1] Neutropenia can also be associated with inherited/congenital disorders or acquired conditions, such as medication adverse effects, infections, malignancies, and nutritional deficiencies. Neutropenic fever (NF) can be a serious complication in neutropenic patients. NF is defined as the first febrile episode following a chemotherapy-induced neutropenia. IDSA defines this as a single oral temperature of $\geq 38.3^{\circ}\text{C}$ (101°F) or a temperature of $\geq 38.0^{\circ}\text{C}$ (100.4°F) sustained over a one-hour period. All patients presenting with NF should be empirically treated with broad-spectrum antibiotics, regardless of their calculated risk for infection. [1,2] Bacteremia caused by GNB are among the most common infections seen in neutropenic patients, and carries a high mortality risk. [3]

The following is a case of an unexpected opportunistic bacteria, *Pantoea agglomerans*, causing NF. It is the first case to our knowledge of NF secondary to spontaneous *P. agglomerans* bacteremia in an Afro-Caribbean adult male.

2. Case Report

A 47-year-old Afro-Caribbean man with AIDS (CD4 155, HIV-1 viral load < 20), stage 4 adenocarcinoma of the left submandibular gland with metastases to the lung & CNS, and Asthma-COPD overlap syndrome (ACOS) who presented with fever, abdominal pain and hematochezia for three days. Two days prior to presentation, he had a temperature of 101°F , chills, generalized malaise, a gradual-onset throbbing headache and odynophagia. He took acetaminophen for the fever prior to arrival. The patient had recently undergone induction chemotherapy 3 days ago with docetaxel and trastuzumab and had received filgrastim due to neutropenia.

The patient had a complicated oncologic history, which included resection of the left submandibular gland in 2017 with adjuvant chemotherapy and radiation, left lung metastasectomy in 2018 and a right cerebellar metastasectomy in 2019 with adjuvant radiation therapy, which was complicated by cerebellar herniation into the cranial defect. Other past medical history included pulmonary

embolism, *Pneumocystis jirovecii* pneumonia, and status post treatments for latent tuberculosis and syphilis.

His family history was positive for maternal breast cancer. Social history unveiled that he was residing in a shelter, had a 20 pack-year smoking history (had quit for 20 years), drank alcohol socially and did not use illicit drugs. The patient reported good compliance with his medications which included tramadol, bicitegravir, emtricitabine, tenofovir alafenamide, darunavir, cobicistat, dapson and apixaban.

In the emergency department, the patient was afebrile with a pulse of 95 beats per minute, blood pressure of 95/52 mmHg and oxygen saturation of 98% on ambient air (Table 1). He appeared ill, cachectic, and uncomfortable. The physical examination was significant for surgical scars on the right lateral neck and left mandible, oral-pharyngeal thrush, hyperactive bowel sounds and periumbilical tenderness. No neck masses were appreciated. Cardiopulmonary exam was unremarkable. Neurologic exam was grossly intact, with no focal deficits, A&O x3. Labs were significant for white blood cell count of 0.36 per μL with an ANC of 28. The blood levels of electrolytes, calcium, total bilirubin, lipase and alkaline phosphatase were within range (Table 2.) A computed tomography (CT) of the abdomen with intravenous (IV) contrast was performed, which showed submucosal edema and wall thickening of the colonic loops diffusely, consistent with signs of acute colitis (Image A). Blood cultures were drawn, he was given 2

liters of normal saline, 2 grams cefepime and subsequently admitted to the hospital. He was also placed on neutropenic precautions.

He continued on IV fluids and empirically started piperacillin and tazobactam while awaiting the results of the blood cultures. Fluconazole and nystatin were also administered to treat the oropharyngeal thrush. The stool culture was negative for *Salmonella*, *Shigella*, *Aeromonas*, *C. difficile* toxin A and B and ova and parasite. There were no additional episodes of hematochezia, but odynophagia persisted despite therapy instituted and viscous lidocaine. He remained hemodynamically stable with the exception of one hypotensive episode which responded to 1 liter of normal saline. Blood cultures were found to be positive for *P. agglomerans*, sensitive to ceftriaxone. Per ID recommendations, the patient's antibiotic coverage was switched to 2 grams IV ceftriaxone, given every 24 hours for a total of 5 days. Serum electrolytes, liver and kidney functions remained unremarkable, the neutrophil count was noted to improve over the hospital course (Table 2). The odynophagia improved enough to tolerate a full diet by the end of admission, and the abdomen was soft and nontender to palpation. He was discharged on hospital day 10 and given prescriptions for fluconazole for 21 days and cefpodoxime, to complete the full 14-day course of antibiotics. He was set to follow up with outpatient oncology for the management of his stage IV adenocarcinoma.

Table 1. Vitals

	On admission	12 hours post admission	Day 2	Day 4	At discharge
Blood pressure (mmHg)	95/52	71/41	96/57	96/62	120/74
Temperature ($^{\circ}\text{F}$)	100.1	100.4	99.2	98.0	97.8
Heart Rate (bpm)	95	89	93	84	85
Respiratory Rate	18	18	18	18	16
Oxygen Saturation (%)	95	90	93	93	90

Table 2. Laboratory Data

	Reference range	On admission	Day 2	Day 4	At discharge
Blood					
Hematocrit (%)	(42.0-52.0)	40.6	37.0	34.2	39.1
Hemoglobin (g/dl)	(14.0-18.0)	13.4	12.4	12.6	12.9
WBC (/nL)	(4.5-10.9)	0.36	2.62	9.91	6.30
Differential count					
Neutrophils (%)	(38.7-60.3)	7 (m)	60.3	74.3	70.9
Granulocytes (%)	(0-0)	-	4.2	11.3	
Bands	(0.0-10.0)	1 (m)	7	3	
Metamyelocytes			2		
Lymphocytes (%)	(22.4-49.0)	65(m)	11.8	5.3	14.6
Monocytes (%)	(2.4-9.2)	18(m)	21.4	8.2	9.4
Eosinophils (%)	(0.0-8.6)	8 (m)	0.4	0.1	0.0
Basophils (%)	(0.0-1.0)	0	1.9	0.8	0.5
Platelet count		88	73	88	146
Red cell count (/pL)	(4.2-6.1)	4.43	4.16	3.96	4.39
Urea nitrogen		14	12	10	9
Creatinine		0.84	1.04	1.11	1.05
Glucose		98	83	89	90
Alanine aminotransferase		26	21	20	45
Aspartate aminotransferase		27	20	24	46
HIV viral load		<50			
CD4 T-lymphocyte count		145			

m: manual count was performed.



Image 1. Computed tomography of the abdomen with contrast (A Moderate, diffuse submucosal edema and wall thickening of the colonic loops. The ascending, transverse and descending colonic loops are decompressed)

3. Discussion

P. agglomerans is a Gram-negative bacteria (GNB) of the *Enterobacteriaceae* family. It is a non-spore forming rod found in the environment, normally isolated from plant and fecal matter. *P. agglomerans* can be a pathological or a commensal organism that colonizes the normal gut microbiota. Human infection is unusual in immunocompetent patients. [5] *P. agglomerans* disease is associated with pediatric blood infections secondary to penetrating wounds. [4,5] *P. agglomerans* has also been documented in nosocomial bacteremia, especially through the contamination of intravenous fluids, blood products, anesthetic propofol, and parenteral nutrition. [6-10] Overall, it is an unusual opportunistic infection. Our patient was found to have spontaneous *P. agglomerans* bacteremia in the setting of absolute neutropenia. There are only three other documented cases of spontaneous *P. agglomerans* bacteremia in adults. [11]

Bloodstream infections are the most common complication in neutropenic patients and carry a high morbidity and mortality risk. Microbes such as *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, *Actinobacter* species and *Escherichia coli* are among the responsible for fulminant bacteremia. Rare opportunists, such as *Citrobacter sps* and *Candida non-albicans*, have also been documented. [3]

The present case demonstrates that immunosuppression and increased intestinal permeability secondary to acute colitis, unexpected gut flora can translocate into the blood and result in profound bacteremia. Our patient's recent chemotherapy induction and subsequent neutropenia most likely precipitated this acute illness. Clinicians should take note of the association of *P. agglomerans* bacteremia in the setting of neutropenic fever. The potential for hospital-wide outbreaks of *P. agglomerans* must also be emphasized, given the nature of the microorganism and its affinity for growth in the hospital setting. [12]

P. agglomerans bacteremia is a well-documented childhood illness, especially in the scope of septic arthritis, osteomyelitis, colon cancer and bloodstream infections. The majority of acute illnesses were associated with penetration of soft tissues and bone via plant thorns. [4]

P. agglomerans bacteremia secondary to chemotherapy-induced immunosuppression is not uncommon, however cases reported are limited to pediatric population. One reported case described an adult male with *P. agglomerans* bacteremia secondary to colon cancer. [13] Immunocompromised patients are at an intrinsically higher risk for developing bacteremia compared to individuals with a robust immune system; this is especially true for patients who have an indwelling catheter. [14] Spontaneous *P. agglomerans* infections are much less common. [11]

P. agglomerans poses a particular risk for fatal nosocomial infections. Of note, one infant suffered from necrotizing enterocolitis which compromised the integrity of the intestinal barrier, natural *P. agglomerans* colonies present in the infant's colon were able to disseminate.¹⁵ Ironically, oncology clinics pose an infection risk for neutropenic patients, and it is not uncommon for infectious outbreaks to occur; *P. agglomerans* infections have been linked back to a contaminated pharmacy sink used for preparing chemotherapy. [6]

P. agglomerans in essence is an environmental bacterium. As such, it has an astonishing ability to thrive on anything derived from nature. This can include a variety of items found in health care settings, such as flower arrangements brought in by family, fresh fruit or even plant-based medical supplies such as cotton swabs and cotton-based gauzes. These items pose a hazard as they can serve as a nidus for infection, allowing for re-infection, or worse; potentially establish colonization of a hospital unit. [12] The neutropenic diet may be used to cut down on infection in neutropenic patients, despite the lack of scientific evidence. [16,17] This diet in theory may cut down on dietary microbial load, thus limiting the colonization in the bowel and subsequently reducing the rate of systemic dissemination.

It is crucial for clinicians to be aware of the possibility of spontaneous *P. agglomerans* bacteremia in neutropenic patients, its unique association with colonization of hospital units and its ability to contaminate hospital-associated materials. It is also important to note that *P. agglomerans* outbreak in the hospital setting have been well documented, and this microbe warrants extra precautions and considerations when caring for neutropenic patients.

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