



Case report

Fatal hemorrhagic pneumonia: Don't forget *Stenotrophomonas maltophilia*



Cristina Gutierrez^{a,*}, Egbert Pravinkumar^a, Dave Balachandran^b, Virginia Schneider^a

^a Department of Critical Care, Division of Anesthesiology and Critical Care, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

^b Department of Pulmonary Medicine, Division of Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

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ABSTRACT

We present a case of fatal hemorrhagic pneumonia secondary to *Stenotrophomonas maltophilia* in a patient with acute myeloid leukemia. *S. maltophilia* is commonly a non-virulent pathogen. However, in the immunocompromised, it is generally associated with bacteremia after central venous catheter placement or pneumonia. Hemorrhagic pneumonia is a rare presentation of this bacteria, with only 31 cases reported in the literature, and has 100% mortality within 72 hours. Rapid recognition and early suspicion should be key in the treatment of these patients.

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1. Case report

A 59 year old man with history of acute myeloid leukemia in remission and undergoing chemotherapy treatment in preparation for stem cell transplant, presented to the emergency department with fever. At the time he was found to be febrile, tachypneic and hypoxic on room air. Laboratory work up was significant for neutropenia which was present for at least 23 days, a normal coagulation profile and mild thrombocytopenia (56,000 K/ μ L). A chest-X ray showed a left lung base infiltrate suggestive of pneumonia (Fig. 1a). He was admitted to the hospital and started on antibiotics for health care associated bacterial pneumonia and fluconazole for possible fungal infection. Within 36 hours of admission he was transferred to the Intensive Care Unit (ICU) with frank hemoptysis, respiratory failure and refractory shock. Chest X-ray at the time showed progression of the pulmonary infiltrates on the left upper and middle lobes (Fig. 1b). A bronchoscopy performed to further assess the source of bleeding revealed no endobronchial lesions, but there was evidence of profuse hemorrhage from the posterior basal segment of the left lower lobe (Fig. 2). Bronchoscopic interventions such as instillation of epinephrine, cold saline and thrombin

solution, were unsuccessful to stop the bleeding. The patient's respiratory status continued to deteriorate requiring PEEP of 15 and 100% FiO₂ and later on was initiated on APRV mode, but still unable to tolerate FiO₂ less than 100%. ABGs at the time continued to show severe hypoxemia and respiratory acidosis (7.27/42/63/89%). Admission blood cultures and bronchial washing revealed gram-negative rods that were later identified as *Stenotrophomonas maltophilia*. Upon recognition of the bacteria trimethoprim/sulfamethoxazole (TMP-SMX) was initiated. Despite aggressive support, the patient continued to deteriorate and died within 24 h of ICU admission (Fig. 1c).

2. Discussion

The differential diagnosis of pathogens causing pneumonia in the immunocompromised host are extensive. The predominant organisms in the non-neutropenic phase of patients with hematological malignancies include *Streptococcus pneumoniae*, *Haemophilus influenzae*, and community-acquired respiratory viruses such as influenza, parainfluenza, respiratory syncytial virus, and adenovirus [1]. Common gram negative organisms include *Serratia*, *Pseudomonas*, *Acinetobacter*, *Citrobacter* and *enterobacter(1)*. When neutropenia has less than 1 week of onset common pathogens for pneumonia are *Pseudomonas aeruginosa*, *Enterobacteraceae*, *S. pneumoniae*, Influenza virus and RSV infections. After the second week of neutropenia organisms such as *Serratia*, *Pseudomonas*, *Acinetobacter*, *Citrobacter*, *Enterobacter* and mold are more common (1). In prolonged neutropenia the organisms are similar to those in

* Corresponding author. Department of Critical Care, Division of Anesthesiology and Critical Care, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 0112, Houston, TX, 77030, USA.

E-mail addresses: CGutierrez4@mdanderson.org (C. Gutierrez), EPravink@mdanderson.org (E. Pravinkumar), DBalachandran@mdanderson.org (D. Balachandran), vfschnei@mdanderson.org (V. Schneider).

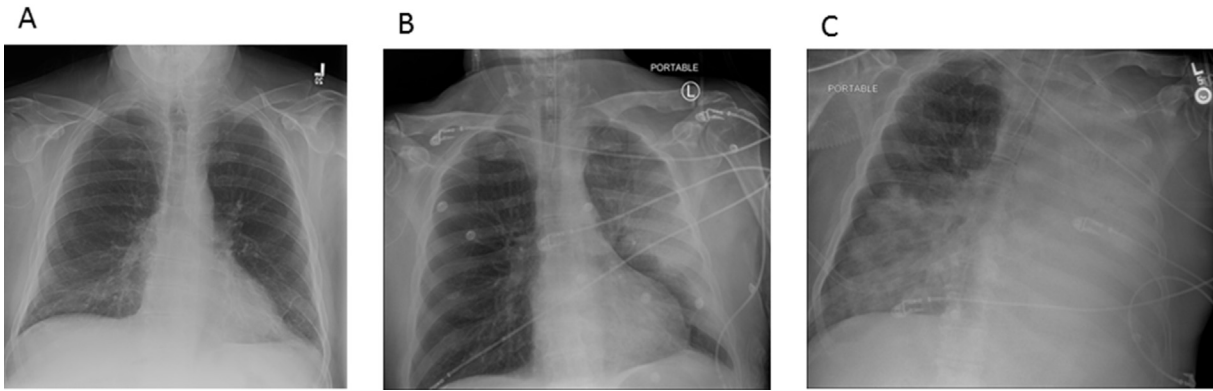


Fig. 1. Progression of chest X-ray in a patient with *S. maltophilia* hemorrhagic pneumonia. **a.** Portable chest X-ray on admission. **b.** Post-intubation portable chest X-ray, 36 hours after admission to the hospital. **c.** Portable chest X-ray 72 hours after hospital admission.

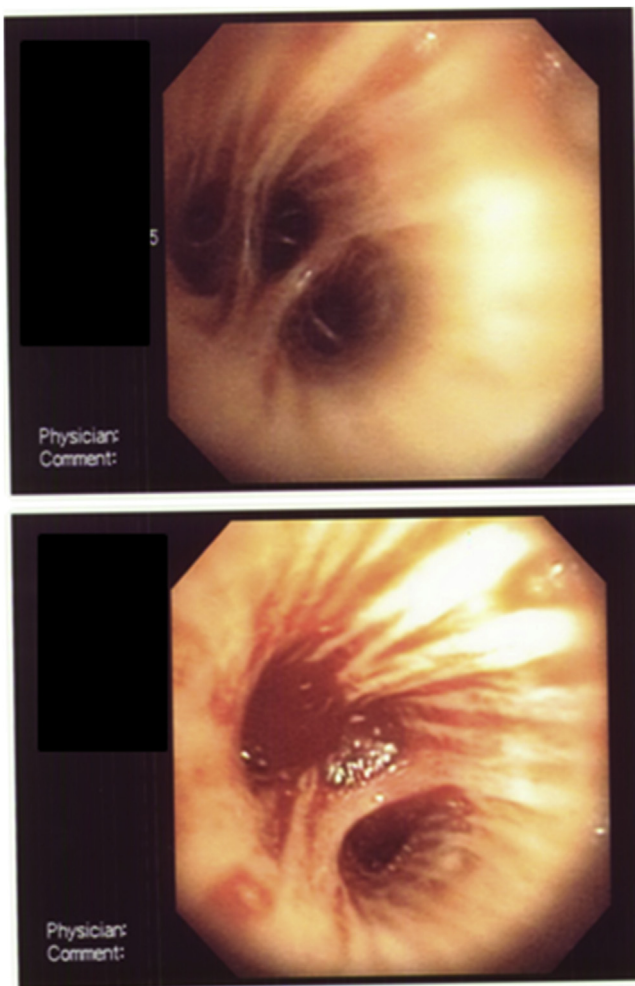


Fig. 2. Evidence of active bleeding during bronchoscopy from posterior basal segment of the left lower lobe.

the second week but are mainly multi drug resistant organisms.

S. maltophilia is usually a non-virulent, gram-negative bacillus found as an airway colonizer in the immunocompetent host [2–5]. Since the 1990s however, this bacteria has emerged as an important nosocomial pathogen [2–5]. In immunocompromised patients, *S. maltophilia* commonly causes pneumonia and bacteremia

associated with central venous catheter infections [2,3,5]. Other sites of infection include the eye, soft tissues, joints, meninges, endocardium and urinary tract [4]. In immunocompromised patients, and specifically cancer patients, risk factors for infection include neutropenia, prolonged ICU stay, prior use of broad spectrum antibiotics and mechanical ventilation [6]. If a patient has any of these risk factors mortality ranges between 14 and 77%; moreover, mortality is higher when bacteremia is secondary to central venous catheter placement and when the patient has required mechanical ventilation [3,4]. When *S. maltophilia* pneumonia develops in a patient without risk factors, it is usually a mild lobar pneumonia and can be treated as an outpatient [6,7]. On the contrary, in the presence of any risk factors, patients can develop a disease severe enough to require ICU admission, and carries a mortality as high as 50% [6,7].

Hemorrhagic pneumonia is a rare presentation of *S. maltophilia*. To our knowledge, only 31 cases are reported in the literature and they are all in patients with hematological malignancies [3,5]. The exact mechanism by which *S. maltophilia* causes hemorrhage is unknown. A study by Windhorst et al., suggests that StmPr1, a protease of the subtilase family, is secreted by the bacteria leading to tissue invasion, destruction and hemorrhage [8]. Hemorrhagic pneumonia by *S. maltophilia* develops in patients who have recently received chemotherapy or a hematopoietic stem cell transplant [5]. Eighty-four percent of these patients have bacteremia, and their clinical presentation is severe with 100% mortality within 72 hours of diagnosis [5,9]. Due to its severity and rapid progression, early suspicion is important; however, efforts for surveillance and prophylaxis are so far limited. In a systematic review of the literature surveillance sputum cultures were positive in only 30% of patients who developed hemorrhagic pneumonia [3]. Also, despite prophylaxis with quinolones or co-trimoxazole, mortality was unchanged for patients who developed hemorrhagic pneumonia [3,5]. While immunosuppression is a significant risk factor for *S. maltophilia* infection, it is important to recognize that other infectious causes for hemoptysis such as aspergillomas and tuberculosis should be considered in this population [10].

S. maltophilia is resistant to third generation cephalosporins, β -lactams, carbapenems and aminoglycosides, all of which are commonly used as initial therapy for pneumonia in the immunocompromised [3–6]. While the mechanism of resistance is not completely understood, it is believed that low membrane permeability and chromosomally encoded efflux pumps cause resistance to beta-lactamases, aminoglycosides and quinolones [4,6]. Another limitation to adequate treatment of this pathogen is that *in-vitro* results of susceptibility for *S. maltophilia* are not standardized; this

leads to discrepancy when reporting results and can impact treatment efficacy [4,6]. TMP-SMX is considered the drug of choice. Dosing, while not clinically studied, should be similar as in pneumocystis treatment [3–5]. Increasing resistance to TMP-SMX is reported, and it is now debated whether synergistic double coverage therapy should be recommended for initial treatment. Combination therapy should include TMP-SMX and addition of quinolones, colistin, ticarcillin-clavulanate, ceftazidime or aztreonam [4–7]. When considering quinolones, moxifloxacin has shown to have better *in-vitro* activity against *S. maltophilia* when compared to ciprofloxacin [11]. Data on the efficiency and clinical response of combination therapy is scarce and no clinical studies are available [4,6].

3. Conclusion

Commonly, invasive fungal pneumonia is suspected in immunocompromised patients with hemorrhagic pneumonia; however, *S. maltophilia* should be considered in the differential diagnosis in patients with risk factors. Heightened clinical suspicion and early treatment may lead to increased survival.

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