CLINICAL VIGNETTE

Burkholderia pseudomallei Infection in a Patient with Cystic Fibrosis

Amos Lichtman, MD, Roxana Cortes Lopez, MD and Patricia Eshaghian, MD

Case Presentation

A 23-year-old female with Cystic Fibrosis (CF) presented to the emergency room for acute onset chest pain, shortness of breath and cough productive of blood tinged sputum. Her symptoms developed during a short flight from Bangkok to Japan, the first leg of her journey returning from a vacation in Thailand. During this vacation she stayed mostly in urban areas, but visited the island of Ko Pha-ngan and swam in the ocean. She was brought directly to the E.D. from the airport.

Her CF was complicated by bronchiectasis, sinus disease, pancreatic insufficiency and prior pneumonia. Vitals were notable for an oxygen saturation of 89% on room air and fever to 38.8C. Physical exam was notable for respiratory distress, spasmodic coughing, and crackles at both lung bases. She was placed on high flow nasal cannula oxygen and admitted to the intensive care unit (ICU). Given her recent long flight and use of oral contraceptives, computed tomography angiography (CTA) of the chest was obtained to rule out acute pulmonary embolism (PE) (Figure 1).

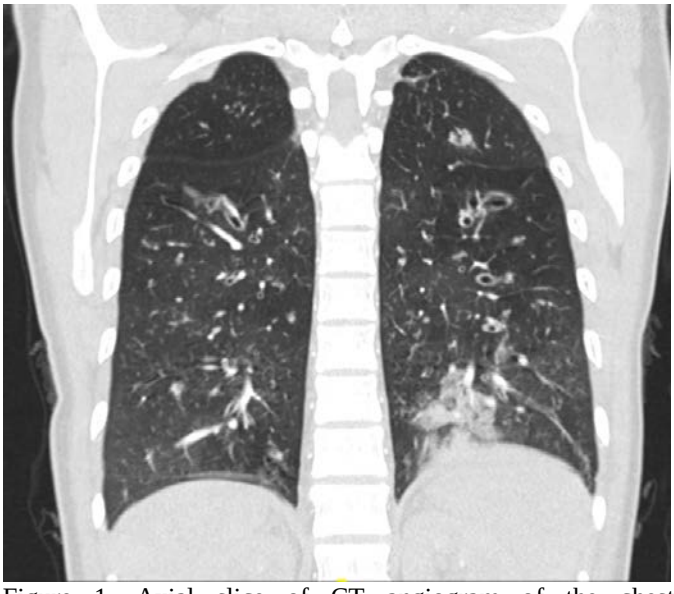

Figure 1. Axial slice of CT angiogram of the chest demonstrating bronchiectasis and right lower lobe infiltrate.

Imaging demonstrated right lower lobe nodular airspace consolidation along with small pneumomediastinum. She was started on ceftazidime-avibactam, doxycyline and trimethoprim-sulfamethoxazole due to prior susceptibility patterns.

Sputum cultures obtained on admission were initially only positive for MSSA, PsA and Steno-trophomonas maltophilia. Viral illness was ruled out with negative respiratory viral panel. Eventually, oxygen requirements improved and her airway clearance regimen was continued. On hospital day 11, however, respiratory cultures returned positive for *Burkholderia pseudomallei*. Infectious disease recommended a three week course of intravenous (IV) Ceftazidime followed by a 3-month course of trimethoprim-sulfamethoxazole to eradicate this organism. She was eventually weaned to room air and was discharged on IV antibiotics. The sputum culture was sent to the CDC for sensitivities, and the *B. pseudomallei* was found to be sensitive to all antibiotics tested (amoxicillin-clavulanic acid, ceftazi-dime, doxycycline, impenem, meropenem, tetraycline, and trimethoprim-sulfamethoxazole). The patient continued to do well on follow-up and pulmonary function tests demonstrated no decrease in baseline FEV1. Sputum cultures obtained after completion of the antibiotic course were negative for *B. pseudomallei*.

Discussion

Burkholderia pseudomallei is a gram-negative bacteria endemic to Southeast Asia and Australia, and is only commonly known to cause infections in residents and travelers to endemic areas. It causes the pulmonary disease known as melioidosis, and is recognized as a potential bioterrorism agent.[1,2] It is likely that the patient was exposed via inhalation of contaminated aerosolized water or percutaneous inoculation from soil during her recent trip to Thailand. Direct human-to-human transmission is very rare. Percutaneous inoculation with hematogenous spread to the lungs and direct inhalation are the most common routes of transmission.[2-4] Patients with cystic fibrosis are likely at increased risk of pulmonary infection with this organism due to their structural lung disease.[1]

Long duration of antibiotic treatment is generally indicated as eradication is difficult, and persistence is associated with an accelerated decline in pulmonary function in patients with cystic fibrosis. Case reports of successful eradication have generally involved induction with a regimen containing IV ceftazadime followed by suppressive therapy for 1-4 months with various regimens, frequently containing oral TMP/SMX.[1,5] Resistance is thought to develop through similar mechanistic patterns as in *Pseudomonas aeruginosa*.[6]

This treatment strategy is similar to that utilized in patients without cystic fibrosis.[7] In these patients, Melioidosis often presents with an acute septic phase, often in patients with diabetes, renal disease, or with no risk factors. Extrapulmonary involvement, including neurologic infection, can occur. Abscess formation is common.[2] After treatment of the acute phase, eradication is necessary even in patients without underlying lung disease.

Our patient's cystic fibrosis was both a risk factor for acquisition of this infection and likely made eradication more difficult. *B. pseudomallei* is intrinsically resistant to many antibiotics, but rarely to first-line therapies. When resistance does develop, it usually does so during treatment.[8] In cystic fibrosis patients, resistance in these patients is thought to develop through similar mechanistic patterns as in *Pseudomonas aeruginosa*.[6] Also similarly to *P. aeruginosa*, *B. pseudomalle*i produces a biofilm which contributes to persistence and resistance to antibiotics, and biofilm disruption represents a potential therapeutic target.[9,10]

Early identification, may help prevent chronic infection and poor outcomes, especially in a traveler returning from an endemic area with structural lung disease, although challenging. Counseling patients with cystic fibrosis about the risks of traveling to endemic areas is important. Further research into the optimal duration and regimen for eradication in patients with cystic fibrosis is needed.

REFERENCES

1. **Geake JB, Reid DW, Currie BJ, Bell SC; MelioidCF Investigators, Bright-Thomas R, Dewar J, Holden S, Simmonds N, Gyi K, Kenna D, Waters V, Jackson M, O'Sullivan B, Taccetti G, Kolbe J, O'Carroll M, Campbell D, Jaksic M, Radhakrishna N, Kidd TJ, Flight W**. An international, multicentre evaluation and description of *Burkholderia pseudomallei* infection in cystic fibrosis. *BMC Pulm Med*. 2015 Oct 9;15:116. doi: 10.1186/s12890-015-0109-9. PubMed PMID: 26453341; PubMed Central PMCID: PMC4600338.
2. **Currie BJ, Ward L, Cheng AC**. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin prospective study. *PLoS Negl Trop Dis*. 2010 Nov 30;4(11):e900. doi: 10.1371/journal.pntd.0000900. PubMed PMID: 21152057; PubMed Central PMCID: PMC2994918.
3. **Hsueh PT, Huang WT, Hsueh HK, Chen YL, Chen YS**. Transmission Modes of Melioidosis in Taiwan. *Trop Med Infect Dis*. 2018 Feb 28;3(1). pii: E26. doi: 10.3390/tropicalmed3010026. Review. PubMed PMID: 30274423; PubMed Central PMCID: PMC6136622.
4. **Brundage WG, Thuss CJ Jr, Walden DC**. Four fatal cases of melioidosis in U. S. soldiers in Vietnam. Bacteriologic and pathologic characteristics. *Am J Trop Med Hyg*. 1968 Mar;17(2):183-91. PubMed PMID: 4869109.
5. **O'Carroll MR, Kidd TJ, Coulter C, Smith HV, Rose BR, Harbour C, Bell SC**. *Burkholderia pseudomallei*: another emerging pathogen in cystic fibrosis. *Thorax*. 2003 Dec;58(12):1087-91. PubMed PMID: 14645982; PubMed Central PMCID: PMC1746554.
6. **Viberg LT, Sarovich DS, Kidd TJ, Geake JB, Bell SC, Currie BJ, Price EP**. Within-Host Evolution of *Burkholderia pseudomallei* during Chronic Infection of Seven Australasian Cystic Fibrosis Patients. *MBio*. 2017 Apr 11;8(2). pii: e00356-17. doi: 10.1128/mBio.00356-17. PubMed PMID: 28400528; PubMed Central PMCID: PMC5388805.
7. **Dance D**. Treatment and prophylaxis of melioidosis. *Int J Antimicrob Agents*. 2014 Apr;43(4):310-8. doi: 10.1016/j.ijantimicag.2014.01.005. Epub 2014 Feb 3. Review. PubMed PMID: 24613038; PubMed Central PMCID: PMC4236584.
8. **Wuthiekanun V, Amornchai P, Saiprom N, Chantratita N, Chierakul W, Koh GC, Chaowagul W, Day NP, Limmathurotsakul D, Peacock SJ**. Survey of antimicrobial resistance in clinical *Burkholderia pseudomallei* isolates over two decades in Northeast Thailand. *Antimicrob Agents Chemother*. 2011 Nov;55(11):5388-91. doi:10.1128/AAC.05517-11. Epub 2011 Aug 29. PubMed PMID: 21876049; PubMed Central PMCID: PMC3195054.
9. **Pakkulnan R, Anutrakunchai C, Kanthawong S, Taweechaisupapong S, Chareonsudjai P, Chareonsudjai S**. Extracellular DNA facilitates bacterial adhesion during *Burkholderia pseudomallei* biofilm formation. *PLoS One*. 2019 Mar 11;14(3):e0213288. doi: 10.1371/journal.pone.0213288. eCollection 2019. PubMed PMID: 30856240; PubMed Central PMCID: PMC6411153.
10. **Limmathurotsakul D, Paeyao A, Wongratanacheewin S, Saiprom N, Takpho N, Thaipadungpanit J, Chantratita N, Wuthiekanun V, Day NP, Peacock SJ**. Role of *Burkholderia pseudomallei* biofilm formation and lipopolysaccharide in relapse of melioidosis. *Clin Microbiol Infect*. 2014 Nov;20(11):O854-6. doi: 10.1111/1469-0691.12614. Epub 2014 Mar 29. PubMed PMID: 24602145; PubMed Central PMCID: PMC4304327.

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