Case Report of Acute Invasive Aspergillosis in an Immunocompetent Patient

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Introduction: *Aspergillus* is a genus of fungus that infects people with various sources of immunosuppression including neutropenia, long-term use of glucocorticoids, or history of use of immunosuppressive medications. [1,2] Exceptions to these groups include those with high exposure rate (construction workers), underlying lung disease (COPD, and asthma), or prior history of tuberculosis. [1,2] The incidence of an *Aspergillus* infection in patients without these aforementioned risk factors are extremely low (2% in a non-compromised host). [3]
Aspergillus can cause several disease states affecting the upper and lower respiratory tracts, including allergic bronchopulmonary aspergillosis, allergic aspergillus sinusitis, aspergilloma, chronic pulmonary aspergillosis, invasive aspergillosis, and cutaneous aspergillosis. [4] Here, we present a case of an acute flare up of invasive aspergillosis in a chronic pulmonary aspergillosis patient with multiple aspergillomas in an immunocompetent patient without traditional risk factors.

Timeline:

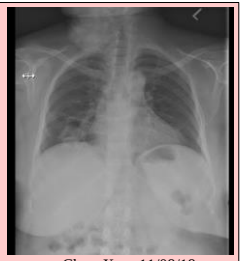
11/28/17 – 12/14/17	First Hospitalization: Dx: RLL Invasive Aspergilosis, *E Coli* Bacteremia, TB ruled out, 28 day course of Ertapenem and Antifungal therapy
10/19/18 – 11/1//18	Second Hospitalization: Dx: Multiorganism pneumonia with Aspergilloma, TB ruled out, 1 week ceftriaxone and 9 days dual antifungal course, with 90 day Voriconazole course discharge plan.
12/27/19	PCP Follow Up: Voriconazole Desquamatization / nail yellowing noted, referred to Dermatology.
1/29/19	Infectious Disease Follow Up: CT Chest with persistent Aspergillomas, patient refusing lobectomy.

Patient Information:
A 66 year-old Bangladeshi female with a past medical history of hypertension, asthma, hypothyroidism, cavitary lung lesion, diabetes mellitus type 2, presents to the JHMC ED on 10/19/2018 with a chief complaint of shortness of breath (SOB) and hemoptysis. Symptoms began 5 years ago in Bangladesh, but she has since immigrated to the United States 2 years ago. Symptoms have worsened recently and are associated with nasal congestion, throat soreness, generalized chest pain and generalized weakness. History of present illness is significant for a cavity lesion in the right lower lobe and ESBL- *E. coli* bacteremia which were previously treated. Additionally, she has a known case of *Aspergillus* mycetoma and has refused surgical intervention. She has had multiple work ups of tuberculosis in the past, all of which have been negative. She is married and has never smoked tobacco, and denies alcohol or illicit drug. All other systems reviewed and were negative.

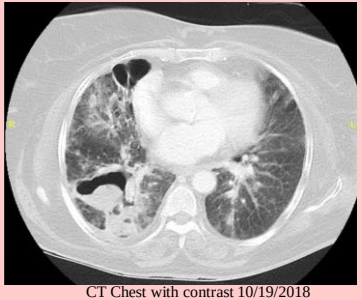
Clinical Findings:
The patient presents in moderate distress due to the hemoptysis and SOB. Vital signs were significant for tachycardia (122 bpm) and a fever of 102.4°F. Physical exam was significant for mild-moderate respiratory distress, cervical lymphadenopathy, rales in the right middle and lower lung fields, and use of accessory muscles of respiration. All other vital signs and physical exam findings were unremarkable.

Diagnostic Assessment:
Daily CBC and BMP were trended. Initial screening focused on pulmonary assessment including *S. Pneumoniae* / *Legionella* urine antigens, blood, urine and sputum cultures (including fungal, acid fast bacilli, aerobic and anaerobic bacteria). Chest X Rays were trended for improvement. Hospital course evolved to include CT Chest with contrast, Bronchoalveolar Lavage (BAL) and fungal testing including (1-3) – beta-D-glucan 97 (meaning fungal infection likely) and serum galctomanan (meaning aspergillus infection likely) 1.27, as well as inflammatory marker of procalcitonin and CRP.

Imaging:



Chest Xray 11/08/18



CT Chest with contrast 10/19/2018

Therapeutic Interventions:
On presentation, the patient was septic requiring IV fluid resuscitation and broad spectrum antibiotic/fungal coverage including Doxycycline 100mg IV q12hrs, Meropenem 1 gm IV q8hrs, Vancomycin 1gm IV q12hrs, and Caspofungin 50mg IV q24hrs. Airborne isolation precautions were in place until Sputum cultures returned negative x 3 for AFB. Bronchoalveolar Lavage was completed with complications of desaturation and hemoptysis, requiring stabilization in ICU. On day 5 of hospitalization Infectious Disease recommended initiating Voriconazole 6mg/kg IV x 1day, followed by 4 mg/kg/IV PO maintenance dose for dual fungal therapy as the patient remained febrile. Cultures from BAL grew *K. pneumonia* allowing for narrowing of IV antibiotics to Ceftriaxone 2gm IV daily for 7 days and continuation of dual antifungal therapy. The patient's hemoptysis resolved and was discharged home on day 12 of hospitalization to complete a 90 day course of Voriconazole 200mg PO q12hrs.

Follow-Up and Outcomes:
The patient continues to recover and follow up with pulmonology and PCP. The patient continues to refuse lobectomy. Repeat CT chest without contrast significant for improvement with persistent cavitation. TB Quantiferon testing remains negative. The patient experienced yellowing of nails and desquamatization of palms and sole which could be a result of long-term use of Voriconazole. The patient was sent to dermatology for consultation.

Discussion:
Our case report reveals the challenges associated with long term care in a patient with chronic aspergillosis with multiple cavitary lesions in the context of non-immunosuppression without neutropenia.

The most typical presentation of invasive aspergillosis occurs in patients with immunosuppression or prolonged neutropenia, however patients with underlying lung disease acquiring invasive aspergillosis have been reported multiple times. [6,7,8] Increased susceptability to fungal infection is seen in patients with underlying lung disease secondary to multiple risk factors including frequent hospitalizations, use of broad-spectrum antibiotics, comorbidities favoring fungal growth such as diabetes mellitus and abnormal structure and function of the lung with decreased ability to resist fungal infections. [6,7,8]

Our patient presented with a number of these unconventional risk factors as well as a history of prior *Aspergillus* infection and signs / symptoms of tuberculosis (with endemic region history), which complicates the diagnostic and management approach. CT chest, tuberculosis work up and a broad treatment regiment are required in a patient with a complex pulmonary history [4, 9].

Positive (1,3)-beta D-glucan and galctomanan serum studies aided diagnosis toward fungal origin, however confirmation of fungal culture with BAL is required [5]. While our BAL confirmed multi-organism pneumonia and allowed for tailoring of antibiotics, the side effects of the procedure were significant, requiring intensive care unit management.

The patient's noncompliance with recommended lobectomy for 5 years has complicated and worsened her treatment course and prognosis, requiring multiple hospitalizations, recurrent pneumonias, unresolved fungal infection and long-term Voriconazole treatment. Long-term voriconazole use has its own complications including most seriously vision changes, myalgia, easy bruising, arrhythmia, skin reactions, jaundice and edema [10]. Patients requiring this therapy should be followed routinely with liver function tests, dermatologists and ophthalmologists [10].

In conclusion, aspergillosis in this patient with atypical presentation and limited management options provides significant diagnostic and therapeutic challenges, however with careful management and follow up, our patient can attain functional status.

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