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Authors

Wong, Brian K.
Scott, DAavid J.

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CLINICAL VIGNETTE

PNEUMOTHORAX: An Unusual Presentation of Aspergillosis

Brian K. Wong, MD and David J. Scott, MD

Introduction

Aspergillus is a common fungal organism isolated in respiratory culture that is acquired by inhalation of airborne spores, with a wide variety of clinical presentations. This is most often found in the setting of the immunosuppressed patient. We wish to report an unusual case of pneumothorax caused by formation of a bronchopleural fistula with subsequent identification of Aspergillus spp.

Case Report

A 66-year-old female with an 8-year history of ulcerative colitis presented to the emergency department with dyspnea and nonproductive cough for 5 days prior to admission. She denied any chest pain, fever, chills, or night sweats. There was no history of recent travel, and no known exposure to birds, cats, or other pets. The patient denied any insect bites. She resided in the high desert between Mojave and Bakersfield.

The patient's ulcerative colitis was controlled on rectal mesalamine, until she experienced a flare characterized by nausea, vomiting, and bloody diarrhea. She was placed on oral prednisone 60 mg daily, with improvement in symptoms, but had significant gastric upset. Azathioprine 50 mg orally was started and prednisone was slowly tapered. The patient was evaluated for tuberculosis and coccidiomycosis prior to the initiation of therapy, which were both negative. Over the next three weeks, she had frequent emergency department visits for nausea and anorexia, which the patient attributed to her medications and was treated with antiemetics and hydration. Her symptoms improved with discontinuation of azathioprine and tapering of prednisone dosage, but she had persistent abdominal cramping and diarrhea.

Physical examination in the emergency department revealed a tachypneic anxious female with oxygen saturation of 90% on 15 liter/min non rebreather mask. The temperature was 36.7C, pulse 100/min and regular, and the blood pressure 97/69 mmHg. Auscultation revealed few bibasilar crackles. Cardiac examination was unremarkable. Skin was without rash. Neurologic exam was normal.

Laboratory data demonstrated WBC 13.4 Hgb 11.4 Hct 34.5% platelet count was normal. Coagulation studies were normal. Electrolytes Na 136 K 4.2 Cl 98 CO2 25 BUN 21 Cr 0.8. Liver function, lactate, and troponin were normal. Arterial blood gas PO2 62 PCO2 34 pH 7.45 on non rebreather mask.

CT pulmonary angiogram was negative for pulmonary embolism. Diffuse ground glass infiltrates bilaterally were noted. No lymphadenopathy, effusions, or mass lesions were identified. Echocardiogram revealed normal left ventricular function with ejection fraction 80%. No valvular dysfunction or pericardial effusion was identified.

The patient was placed on empiric antibiotic coverage consisting of levofloxacin, piperacillin-tazobactam, and vancomycin. Trimethoprim-sulfamethoxazole was initiated for possible Pneumocystis infection. Diagnostic bronchoscopy was performed the following day. Alveolar lavage studies were negative for Pneumocystis, and other cultures were nondiagnostic. Legionella antigen, influenza, and respiratory syncytial virus antigens were negative.

The patient's respiratory status deteriorated requiring intubation and mechanical ventilation on the third hospital day. Repeat chest radiographs showed worsening bilateral infiltrates and increasing positive end expiratory pressure (PEEP) to 10 cm H2O. Oxygen concentrations were required to maintain arterial oxygen saturation. Open lung biopsy was performed on the right upper and lower lobes. Pathology revealed nonspecific findings consistent with acute lung injury. Multiple stains for Pneumocystis, fungal, and acid fast bacilli were negative.

The patient over the next four days appeared to improve and had reduction in her PEEP to 6 cm H20 and inspired oxygen concentration to 55%. There was initially no evidence of air leak from the chest tubes until the fifth postoperative day. An intermittent leak was then noted. Chest radiographs showed both lungs expanded without evidence for pneumothorax. Tracheostomy was performed without complication on the twelfth hospital day.

Chest radiographs remained essentially unchanged. The patient was able to tolerate short weaning trials. WBC increased over the next three days from 10,000 to 19,000. Repeat cultures of blood and urine were negative. Tracheal aspirate revealed usual oropharyngeal flora and rare

Aspergillus. This was felt to represent contaminant or colonization as surgical tissue cultures were negative. Micafungin was initiated.

The air leak over the next six days worsened and became continuous. The patient developed an estimated 20% pneumothorax, which persisted despite placement of a second chest tube. Oxygenation worsened requiring 85% oxygen to maintain adequate arterial oxygen saturation. On the 18th day of hospitalization, the patient had repeat right thoracotomy. Operative findings revealed no discernable air leak at the sites of the original lung biopsy. A nodular enlargement 5 cm from the biopsy site was identified as site of the bronchopleural fistula. Frozen section and subsequent formal sections revealed extensive fibrosis with inflammatory exudate and disruption of the pleural surface with fungal aggregates consistent with Aspergillus.

The patient returned to the ICU with minimal air leak from the chest tubes and resolution of the pneumothorax. Voriconazole, 300mg IV q12h was started. However the air leak worsened and the patient became hemodynamically unstable requiring pressor support. There was no recurrent pneumothorax. Palliative care consultation was requested, and the patient was taken off life support and expired on the 25th hospital day.

Discussion

Aspergillosis is defined as an allergic or infectious disease process that is caused by fungus in the genus Aspergillus. Pulmonary manisfestations are most commonly described, but extra-pulmonary involvement as a consequence of invasive aspergillosis of the lungs was seen in more than 50% of patients in one retrospective autopsy review.[1] There are more than three hundred species of Aspergillus identified. Only a few have been found to cause infections in humans. Aspergillus fumigatus is most often implicated and was once responsible for more than 90% of infections.[2] More recent epidemiological studies have identified A. flavus, A. niger, and A. tereus as causing invasive disease, although A. fumigatus was again responsible for the majority of cases.[3]

Invasive disease is most often seen in the setting of immune suppression and neutropenia. Organ transplantation, solid or hematopoietic, are most often at highest risk.[4] Case reports of chronic obstructive pulmonary patients in the intensive care setting on high dose corticosteroids have been documented.[5]

Pneumothorax as a presenting symptom of aspergillosis is rare with scattered cases reported in the literature.[6,7] Pathologic findings of fungal hyphae with tissue necrosis of the peripheral lung tissue and subsequent rupture of the pleural surface has been demonstrated.[8] An alternative postulated mechanism theorizes fungal hyphae causing partial obstruction of bronchioles, causing a “check valve” effect that subsequently causes formation of subpleural blebs.[9]

Mycetoma formation in emphysematous bulla or old cavitary disease due to tuberculosis or lung abscess has also been described.[10,11]

Diagnosis of invasive aspergillosis by respiratory culture is problematic as Aspergillus conidia (spores) are commonly inhaled into the upper respiratory system and frequently do not cause clinical disease. Tissue invasion documented on biopsy specimens that are most confirmatory of this entity are frequently associated with significant risk of morbidity and mortality given the usual critical nature of the patient’s illness on presentation. Galactomannan, a significant component of Aspergillus cell walls, can be detected by immunoassay in both serum and bronchoalveolar lavage fluid, which may be helpful to support the diagnosis.[12]

Treatment of invasive aspergillosis recommendations from both the American Thoracic Society and Infectious Diseases Society of America are similar in recommending voriconazole as front line therapy.[13,14] A lipid formulation of amphotericin B is suggested in patients intolerant to voriconazole or experience hepatotoxicity.

Conclusion

Pneumothorax in a patient with invasive aspergillosis is a relatively rare occurrence. More commonly seen in hematopoetic and solid organ transplant patients, this can be seen in other patients undergoing immunosuppressive therapy.

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