A Rare Presentation of Multiple Fungal Balls in Type 1 Diabetes Mellitus with Old Pulmonary Tuberculosis

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Abstract: Aspergillosis is the collective term used to describe all the disease entities caused by more than 50 pathogenic and allergic species of Aspergillus, A. fumigatus being the most responsible specie for invasive and chronic aspergillosis. The primary risk factors being profound neutropenia and glucocorticoid use. We are reporting a rare case of bilateral multiple fungal balls in a 22-year-old Type I diabetic patient with prior history of pulmonary tuberculosis.

I. Introduction

Aspergillosis is the name given to a wide variety of diseases caused by fungal infection of the genus Aspergillus. The majority of cases occur in people with underlying illnesses such as tuberculosis or chronic pulmonary disease (COPD), steroid abuse and may occur with otherwise healthy immune systems. Most commonly, aspergillosis occurs in the form of chronic pulmonary aspergillosis (CPA), aspergilloma or allergic bronchopulmonary aspergillosis (ABPA). Some forms are intertwined; for example, ABPA and simple aspergilloma can progress to CPA. The most frequently identified pathogen is Aspergillus fumigatus—a ubiquitous organism that is capable of living under extensive environmental stress. It is estimated that most humans inhale thousands of Aspergillus spores daily, but they do not affect most people’s health due to effective immune responses. The mortality rate is 50% if infection is treated but 100% when diagnosis is missed.

II. Case Report

A 22 years old female with 1 ½ year history of type I Diabetes mellitus presented to the emergency department with C/o decreased food intake since 1-week excessive thirst and increased frequency of urination for one week. Vomiting (5 – 6 episodes) for 2 days. Abdominal pain with loose motions for 1 day. Past history of Anti tuberculous therapy for pulmonary TB and extra pulmonary TB lymph node for 10 months. On examination patient is conscious and coherent. Pulse rate 120 / min, BP 110/70 mm/Hg, cardiovascular system – S1, S2 present, respiratory system – bilateral coarse crepitation’s present, per abdomen – tenderness present in epigastrium, CNS – no abnormal detected.

Investigations:

- HB – 10 grms/dl, TC – 14,800 /mm³, DC – P⁹⁰L₁₈ E₂M₆₀, ESR – 20 mm/hr, sputum – AFB – Negative, VCTC – Negative, FBS – 340 mg/dl, PPBS – 410 mg/dl, urine ketone bodies – Negative, serum electrolytes – Na⁺ – 123 mmol/l, K⁺ – 2.8 mmol/l, Cl⁻ – 90 mmol/l.

CT Chest:

- Bilateral upper lobe Bronchiectasis changes with multiple continuous lesions.
- Few cavities with fungal ball (mycetoma).

Ultrasound abdomen:

- Bilateral hydro uretero nephrosis
- Bladder wall thickening
- Bilateral grade – 1, RPD changes.

Chest X ray showed non homogenous opacity in left upper zone. CT chest showed B/L upper lobe cavity with intra cavity hyperdense nodules with crescent sign. Nodules are varying in position and non-enhancing, probably ASPERGILLOMA.

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Patient was treated with inj. Piperacillin – Tazobactum for 5 days and tablet. Itraconazole 200mg twice daily with strict glycaemic control and other supportive management with proper nutrition. Patient condition improved symptomatically.
III. Discussion

Infections due to Aspergillus species result in significant morbidity and mortality. Most infections are attributed to Aspergillus fumigatus, followed by Aspergillus flavus and Aspergillus terreus. Fungal pneumonia is an infectious process in the lungs caused by one or more endemic or opportunistic fungi. Fungal infection occurs following the inhalation of spores, after the inhalation of conidia, or by the reactivation of a latent infection. Haematogenous dissemination frequently occurs, especially in an immunocompromised host. Aspergillus presents as a spectrum of clinical syndromes like Invasive pulmonary aspergillosis, chronic necrotising aspergillosis, Aspergilloma (fungal ball), allergic bronchopulmonary aspergillosis.¹

Invasive pulmonary aspergillosis usually occurs in severely immunocompromised patients.² The expanded use of glucocorticoids accounts for increasing number of fungal infections reported in mildly or non-immunocompromised hosts.³ Other most common risk factors include neutropenia, acute leukaemia, and relapsing disease, ADE protocol of chemotherapy and nosocomial infections.

Genetic predisposition: With regard to predisposition through stem cell transplants, certain toll-like receptor (TLR) polymorphisms (e.g., TLR 4 haplotype S4) in an unrelated stem cell donor can increase the risk of invasive aspergillosis in the transplant recipient. Similarly, TLR1 and TLR6 polymorphisms in the recipient have been associated with susceptibility to invasive aspergillosis after allogeneic stem cell transplantation.⁴

Complications of fungal pneumonia include (1) disease dissemination to other sites (i.e., brain, meninges, skin, liver, spleen, kidneys, adrenals, heart, and eyes) and sepsis syndrome and (2) blood vessel invasion, which can lead to pulmonary haemoptysis, infarction, myocardial infarction, cerebral emboli, cerebral infarction, or blindness. Others include Bronchopleural or tracheoesophageal fistulas, chronic pulmonary symptoms, Mediastinal fibrosis (histoplasmosis), Broncholithiasis (histoplasmosis), Pericarditis and other rheumatologic symptoms.⁵

The endemic fungal pneumonias are generally self-limited in healthy hosts. Patients with fungal pneumonias may develop chronic pulmonary (e.g., cavitation, pleural effusions, bronchopleural fistulas) or extra pulmonary complications. In patients with AIDS, the mortality rate is as high as 70%. Aspergillosis in patients who are neutropenic (from either leukaemia chemotherapy or bone marrow transplantation) has a mortality rate of 50-85%. More often, in the case of aspergillosis, the cause of mortality in patients who are immunocompromised is disseminated disease.⁶ Endemic fungal disease affects men (75-95%) more often than women; oestrogen-mediated inhibition of mycelium-to-yeast transformation may be responsible for the male predominance.

History findings in persons with fungal pneumonia may include, fever, cough (usually non-productive), chest discomfort, dyspnoea, enlarged mediastial adenopathy, haemoptysis, hypersensitivity or allergic reactions. In individuals who are neutropenic or immunocompromised, persistent fever (even before pulmonary findings) may be an early sign of infection, especially if the fever is unresponsive to broad-spectrum antibiotics. Hypersensitivity or allergic reactions include allergic bronchial asthma (Aspergillus species, Candida species), allergic bronchopulmonary mycoses (Aspergillus species, Candida species), bronchocentric granulomatosis (necrotizing granulomatous replacement and eosinophilic infiltration of bronchial mucosa in infection with Aspergillus species), and extrinsic allergic alveolitis (malt worker's lung, farmer's lung).

Various antigen detection assays, such as galactomannan enzyme immunoassay for detection of Aspergillus invasive infections, are now in clinical use. Polymerase chain reaction (PCR)–based assays are also available for detecting various pathogens, including Aspergillus, Histoplasma, and Candida species. For Aspergillus species antigen, galactomannan ELISA assay findings may be positive in the blood very early prior to clinical suspicion of invasive fungal infection and may be of use in monitoring and pre-emptive treatment in high-risk populations.

Using a galactomannan platelia Aspergillus enzyme immunoassay approved by the US Food and Drug Administration (FDA), investigators showed that 2 consecutive samples with an optical index of 0.5 provided the highest test accuracy (specificity, 97.5%; sensitivity, 92.1%; positive predictive value, 87.5%; negative predictive value, 98.5%). Testing in bronchoalveolar lavage (BAL) fluid increased the sensitivity compared with
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