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Case Report Open Access

Aspergillus Lymphadenitis Mimicking Cervical Lymph Node Recurrence in a Breast Cancer Patient

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Abstract

Invasive aspergillosis mostly occurs in severely immune compromised patient and infrequently in an immune-competent host. The usual site of infection is the pulmonary system. Extra pulmonary sites such as isolated lymphadenopathy without systemic symptoms are rare. We present a case of aspergillosis in the cervical lymph node of breast cancer patient six years after completing chemotherapy. Diagnosis was excision biopsy of an enlarged cervical lymph node and the patient was successfully treated with oral Itraconazole for three months without disease recurrence 3 years following completion of medication.

Keywords: Aspergillosis; Lymph nodes; Breast cancer; Immune-competent

Introduction

The Aspergillus species are fungi named after a device used to disperse holy water with a similar structure to the spore. Averagely, humans are exposed to 200–2000 Aspergillus spores (conidia) per day because numerous Aspergillus conidia are found to be airborne in the environment [1]. Even though there are over 1000 species of Aspergillus, approximately 20 of these are linked to opportunistic clinical infection in humans. The commonest types causing clinical symptoms are A.Fumigatus and A.Flavus. Prolonged neutropenia, organ transplantation, patients receiving cancer therapies such as chemotherapy, stem cell transplantation, diagnosis of some haematological cancers and other conditions such as chronic granulomatous disease of childhood, iron overload are considered predisposing factors to clinical invasive aspergillosis [2-8]. Mortality from invasive Aspergillus is reported to be 18% in immunocompromised children [9]. The high mortality persist in spite of the recent developments and improvements in management strategies.

There are three common pathological presentations of aspergillosis: invasive aspergillosis (associated with systemic disease and lymphadenopathy, running a mild or fulminant course), Aspergilloma (characterized by colonization of bullae left after cavitary lung diseases such as tuberculosis leading to life threatening hemoptysis); and allergic broncho-pulmonary aspergillosis characterized by asthma-like presentation with elevated IgE to aspergillus. There are very few reported cases of isolated lymph node disease in the absence of systemic disease. Management includes the use of specific antifungals in parenteral or oral forms depending on the disease severity.

Case Report

A 63-year old female was first seen in January 2007 at the Korle-bu Teaching Hospital, Accra, Ghana following mastectomy and axillary dissection for carcinoma of the right breast. She was initially treated by wide local excision for a malignant lump in the right breast in 2005 but defaulted adjuvant treatment after 3 cycles of chemotherapy (Cyclophosphamide, Adriamycin, 5- Fluorouracil). She developed a recurrent lump in her right breast in 2006 for which she had mastectomy and axillary dissection. Histopathology showed Invasive mucinous carcinoma with positive deep resection margin. She was staged as pR1T3N0M0. ER Positive. PR Positive, Her2 unknown. Her metastatic workup was negative. She subsequently had 6 cycles of adjuvant chemotherapy (Paclitaxel and Capecitabine) followed by radiotherapy to the chest wall, completing in June 2007. The period of chemotherapy and radiotherapy was generally uneventful except for a one week break in chemotherapy treatment for afebrile neutropenia. She completed five years of tamoxifen in 2012. In October 2013, she presented with bilateral enlarged and progressively tender neck swelling of 5 months duration. Examination revealed enlarged left levels IV and V cervical lymph nodes, 3 cm in maximum diameter, hard, mobile and tender. The contra-lateral neck had sub-centimeter tender cervical nodes in levels IV and V. Differential diagnosis of the enlarged nodes included recurrent breast cancer, tuberculosis or HIV Infection was entertained. HIV test using ELIZA was negative. An excision biopsy was recommended on account of a negative metastatic workup including a normal chest X-ray, oral and chest wall and breast examination, low tumor marker levels as well a good clinical performance status. Hematological indices on laboratory test were essentially normal. Histopathology of the lymph node reported multiple granulomata with numerous fungal hyphae with branching and spores consistent with Aspergillus lymphadenitis. Microbiology and cultures were not done. Following a highly probable diagnosis of aspergillus lymphadenitis, she was treated with oral Itraconazole 400 mg daily for three months with complete resolution of cervical lymph nodes by the end of the second week.

Discussion

In spite of their ubiquitous nature, most humans do not develope clinical evidence of infection, antibody- or cell-mediated acquired immunity to aspergillus. The host's response following an encounter

with this microorganism is the key determinant for the development of invasive disease, suggesting that innate immunity is paramount in fighting invasion [10,11]. This is important because humans are exposed to large amounts of conidia a day. Some studies have estimated the mean concentration of Aspergillus conidia in air to be 0.2 to 15 conidia/m^3 and as high as 106 conidia/m^3 in some agricultural settings and decaying biomass [12]. In immune-competent persons, anatomical barriers and phagocytes such as alveolar macrophages and neutrophils prevent the development of invasive aspergillosis by inhibiting the growth of conidia and hyphae. The recognition of inhaled conidia leads to the intracellular degradation of the spores and the secretion of pro-inflammatory mediators which recruit neutrophils to assist in fungal clearance. However, conditions of the host such as stem cell transplant recipients, administration of anticancer drugs or prolonged use of corticosteroids leads to quantitative and qualitative neutrophil impairment. This results in reduced natural immune responses and eventually development of invasive disease.

In the case presented, the last cycle of chemotherapy was six years prior to the development of symptoms. During chemotherapy she received several pulsed doses of dexamethasone for 3-4 days as premedication for chemotherapy and prophylaxis for delayed nausea and vomiting. An accurate diagnosis of invasive aspergillosis is important as an earlier diagnosis is associated with improved patient survival. Microbiological culture of Aspergillus together with histopathologic evidence of tissue invasion by hyphae provides definitive evidence of invasive aspergillosis. A few studies advocate for histological diagnosis alone as proof of infection but these will be considered as probable aspergillosis infection. Biopsy is associated with certain risk such as bleeding and therefore may be withheld in most instances. More recently serum biomarkers such as galactomannan and beta-D-glucan assays, sputum or Broncho alveolar lavage specimens for fungal staining and culture yield highly accurate diagnostic results comparable to invasive biopsy techniques [13]. On microscopy, Aspergillus species have septate hyphae which tend to have dichotomous branching that is progressive and primarily at acute angles of about 45° and are reliably demonstrated by silver stains, e.g., Gridley stain or Gomori methenamine- silver giving the fungal walls a gray-black color [12].

When a high-risk patient develops a probable clinical picture suggestive of aspergillosis infection, initiating empiric treatment is warranted immediately whilst awaiting evidence of diagnosis from diagnostic test to avoid untoward outcomes. Voriconazole, an ozole antifungal is currently the drug of choice for invasive aspergillosis because it has better tolerance and improved survival compared to Amphotericin B [14]. Posaconazole, Amphotericin B, or amphotericin B lipid formulations may also be considered as empiric therapy in critically ill patient, particularly if presenting with sinusitis compatible with mucormycosis, because voriconazole is ineffective for Zygomycetes infection. Caspofungin is also approved for invasive aspergillosis in patients unable to tolerate or progress following initial therapies [15]. Combination therapy can be used as initial therapy in critically ill patients or salvage treatment following failures [16]. Azole antifungals reduce amphotericin-binding sites and in effect diminish its efficacy, therefore concomitant therapy of the two drugs is not advised. Other approved drugs include, Isavuconazole and Itraconazole. Itraconazole is indicated as initial therapy when other drugs are unavailable. This patient received Itraconazole because it was the most affordable medication in oral formulation.

Conclusion

We report a rare case of Isolated Aspergillus lymphadenitis six years following breast Cancer treatment. In a patient with a prior history of malignancy and chemotherapy administration, the possibility of infections including fungi should be entertained as differential diagnoses of new onset lymphadenopathy in the absence of clinical or radiological progression of malignant disease.

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