Invasive pulmonary aspergillosis presenting as thoracic mass causing obstruction of the superior and inferior vena cava in an immunocompetent patient: a diagnostic dilemma

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Invasive pulmonary aspergillosis (IPA) is a disease of immunocompromised patients, but its prevalence is increasing in immunocompetent persons. Patients usually present with non-specific symptoms, sometimes consistent with bronchopneumonia. We discuss the case of a 19-year-old boy who presented with constitutional respiratory symptoms along with signs of obstruction of the superior and inferior vena cava. A chest radiograph was suggestive of a thoracic mass raising suspicion of bronchogenic carcinoma/benign mass, sarcoidosis and tuberculosis, but a diagnosis of invasive aspergillosis was established. The patient showed excellent clinico-radiological improvement with administration of voriconazole. Invasive pulmonary aspergillosis may also present with atypical findings and should be considered in differentials when investigating a case even if the patient does not have a risk factor.

Aspergillus is a ubiquitous fungus belonging to the ascomycete molds. The Aspergillus genus of molds was probably first described by Micheli in 1729.1 Aspergillus infection is acquired by inhalation of airborne spores and may cause a variety of pulmonary diseases that may be life threatening especially in the presence of underlying lung disease and compromised immune status. The manifestations of infection range from chronic necrotizing aspergillosis in patients with chronic lung disease and/or mildly compromised immune systems to invasive pulmonary aspergillosis (IPA) in severely immunocompromised patients.

Invasive pulmonary aspergillosis was first described in 1953 by Rankin as disseminated aspergillosis.2 Its incidence is increasing due to widespread use of chemotherapy and immunosuppressive agents.3,4 The radiological presentation varies from multiple nodules or a mass with or without a halo sign, cavitation, focal ground glass haziness, bronchopneumonia and a diffuse interstitial process.5 We report a case with an unusual presentation of IPA as a thoracic mass causing obstruction of both the superior venal cava (SVC) and inferior vena cava (IVC) in a young immunocompetent person.

CASE

A 19-year-old male was admitted to our respiratory medicine ward with a feeling of heaviness on the right side of his chest, weight loss, the appearance of tortuous swelling on the anterior abdominal wall and shortness of breath. Cough, expectoration, hemoptysis, wheeze, fever, anorexia and night sweats were absent. The patient denied any significant medical or surgical history, including allergies and had an insignificant family history. He was a nonsmoker, non-alcoholic and not drug addicted. There were no skin lesions, or ear, nose, throat and ophthalmic complaints. There was no history of exposure to dust.

A general physical examination and vitals were within normal limits except for a tortuous swelling over the anterior abdominal wall (venous prominence), which increased on bending forward (Figure 1). A chest ex-
amination showed decreased movement and markedly reduced breath sounds on the right hemithorax with slightly engorged neck and thoracic veins. Examination of other systems found nothing abnormal.

Laboratory tests showed Hb 9.5 g/dL, total leukocyte count 12,800/µL with neutrophils 90% and a platelet count of 244,000/µL. The serum biochemistry profile including liver function tests, random blood sugar, renal function tests, alkaline phosphatase, serum calcium and serum ACE were unremarkable. HIV serology was negative. ECG and ultrasonography of the abdomen was normal. Spirometry showed a mild restrictive pattern. Chest radiograph posterior-anterior view showed a right-sided homogeneous opacity involving the upper and midzone with blunting of both the cardiophrenic and costophrenic angle on the same side (Figure 2). A contrast-enhanced computerised tomography scan (CECT) of the chest showed a right hilar mass with collapse of the right upper lobe, with complete occlusion of the SVC and IVC along with moderate pleural effusions (Figure 3).

Pleural fluid analysis was suggestive of exudative pleural effusion (cell counts of 90% lymphocytes and protein 5.0 g/dL with low ADA 30 IU/l) negative for acid fast bacilli (AFB) and malignant cells. On fiber optic bronchoscopy, complete occlusion of the right upper lobe bronchus due to extrinsic compression with minimal mucosal irregularity/nodularity was observed. Further bronchial washing, broncho-alveolar lavage and transbronchial needle aspiration (TBNA) samples were sent for AFB smear and culture, cytopathological examination, KOH smear and fungal culture. Reports were negative for tuberculosis and malignancy. KOH smear from the TBNA sample was positive for fungal hyphae, which on methamine silver nitrate staining showed acute angle branching septate fungal hyphae suggesting Aspergillus fumigatus (Figure 4). Further culture on Sabouraud agar confirmed the species as Aspergillus fumigatus (Figure 5).

We made a final diagnosis of a right-sided aspergillus mediastinal mass with right upper lobe collapse, SVC and IVC obstruction. Following initiation of therapy with voriconazole (intravenous initially for a week followed by oral), the patient had marked relief of symptoms and improvement in clinical as well as radiological (chest X ray and CECT thorax) parameters within 15 days (Figures 6a, 6b) and was discharged on oral voriconazole. The patient was followed up for six months while on treatment and had significant improvement.

DISCUSSION

Aspergillus spp are ubiquitous fungi, widely distributed in the environment and commonly isolated from organic as well as inorganic compounds. The organism may cause a variety of pulmonary diseases including invasive pulmonary aspergillosis (IPA) in severely immu-
nocompromised patients. Invasive aspergillosis means the presence of aspergillus organisms deep in the basement membrane of the bronchial tree, which may develop acutely and chronically. IPA is a common cause of morbidity and mortality in persons with classical risk factors. Chronic necrotizing aspergillosis, a variant of IPA seen in patients with chronic or persistent pulmonary disease, is locally invasive.

Risk factors for invasive pulmonary aspergillosis:
- Persistent neutropenia (<500 cells/mm$^3$) for >10 days or neutrophil dysfunction
- Solid organ transplantation or hematopoietic stem cell transplantation
- Prolonged administration of immunosuppressive agents (steroids, ciclosporin and other cytotoxic therapy)
- Hematological malignancy like leukemia
- AIDS patients with CD4 count <50 cells/mm$^3$
- Prolonged hospitalization with parenteral nutrition (incidence≈0.3% to 19%)
- Use of multiple antibiotics for long duration

None of these factors were present in our patient. He was immunocompetent with a good build and well nourished. The mode of transmission of fungal spores to the human host is by inhalation to the lungs where it can present with a wide spectrum of clinical syndromes. IPA may start in other locations such as the sinuses, gastrointestinal tract, skin and brain. Symptoms are nonspecific and mimic bronchopneumonia (fever nonresponsive to antibiotics, cough, sputum production and dyspnea, sometimes pleuritic chest pain and hemoptysis. Our patients had vague and nonspecific symptoms with signs of superior and inferior obstruction of the vena cava.

The chest radiograph of IPA is not of much use in the early stages of disease as changes are nonspecific, but in later stages it varies from a single to multiple pulmonary nodules with or without cavitation, bronchopneumonia, pleural-based infiltrates suggestive of pulmonary infarctions and very rarely, pleural effusions. Parameswaran K et al$^3$ reported a case of bilateral hilar lymphadenopathy with IPA. A mediastinal mass due to aspergillus has not been reported yet that is also large enough to cause SVC and IVC obstruction. A high-resolution CT scan of the chest (HRCT) is more useful than a radiograph of the chest. The typical CT scan “halo sign,” “air crescent sign” and “monad sign” sometimes suggest aspergillus infection. These signs help in early diagnosis and can improve outcomes.

Along with an unusual clinical and radiological presentation, the diagnosis of IPA is difficult, so a high

![Figure 3. Contrast-enhanced CT scan of the chest showing a right hilar mass with collapse of the right upper lobe, with complete occlusion of the superior vena cava and inferior vena cava along with moderate pleural effusion.](image3.png)

![Figure 4. Methamine silver nitrate staining showing acute angle branching with septate fungal hyphae suggesting Aspergillus.](image4.png)

![Figure 5. Culture on Sabourouds agar showing aspergillus fumigatus.](image5.png)
index of suspicion for invasive disease is necessary in immunocompromised patients. Histopathological confirmation by examining lung tissue of thoracoscopic or open lung biopsy remains the “gold standard” in the diagnosis of IPA. The presence of septate, acute, branching hyphae invading the lung tissue samples, along with a positive culture for Aspergillus diagnostic of IPA confirms the diagnosis. Histopathological examination excludes alternative diagnoses (malignancy or other infectious diseases). The detection of Aspergillus antigens (galacromannan) in body fluids is a recent advance in the diagnosis of IPA, but is not available at our centre.

The treatment of IPA is as difficult as diagnosis. Despite the introduction of several new antifungal drugs, mortality remains high. Conventional amphotericin B is still the first-line therapy for patients with invasive aspergillosis, but it can cause serious side effects. A new broad spectrum antifungal voriconazole is currently the treatment of choice in patients with IPA. Patients receiving voriconazole had a higher favorable response rate and survival at 12 weeks. The duration of treatment ranges from 6 months to one year. Surgical treatment is reserved for patients who do not tolerate antifungal therapy or have residual localised but active lesions, despite adequate antifungal therapy.

CONCLUSION
This patient had an unusual presentation of invasive aspergillosis as a thoracic mass (anterior mediastinal mass) with obstruction of the superior and inferior vena cava and a right-side pleural effusion in an immunocompetent young adult. When it was treated with voriconazole for six months, the patient had almost complete resolution of the disease. One should keep a high index of suspicion for IPA even if the patient has no classical risk factors and presents with an atypical presentation. Confirming the diagnosis early may reduce morbidity and mortality.
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