The spectrum of imaging findings of invasive pulmonary aspergillosis in children with hematologic malignancies

Poster No.: C-2260
Congress: ECR 2014
Type: Educational Exhibit
Authors: A. Bechir\textsuperscript{1}, A. Achour\textsuperscript{2}, R. Haifa\textsuperscript{1}, Y. Ben Youssef\textsuperscript{1}, H. Zaghouani\textsuperscript{1}, K. Chakib\textsuperscript{3}, K. Abderrahim\textsuperscript{1}, \textsuperscript{1}Sousse/TN, \textsuperscript{2}Sousse, Tunisia/TN, \textsuperscript{3}Sousse, DEPARTMENT OF RADIOLOGY, FARHAT HACHED HOSPITAL, SOUSSE/TN
Keywords: Lung, Haematologic, CT-High Resolution, Computer Applications-General, Haematologic diseases
DOI: 10.1594/ecr2014/C-2260

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

- Description and illustration of clinical, histological and imaging findings seen with the spectrum of invasive pulmonary aspergillosis encountered in children with cancer.

- Representative cases demonstrate the clinical applications of CT in the evaluation and management of invasive fungal disease.
Background

Aspergillus is an important cause of opportunistic pathogens in immunocompromised children. It may cause respiratory or systemic infections, and can cause life-threatening complications. High risk children are allogeneic bone marrow recipients, and those with hematologic malignancies, aplastic anemia or chronic granulomatous disease. Profound and prolonged neutropenia and corticosteroid therapy are the most important predisposing factors. Invasive respiratory aspergillosis in immunocompromised children is associated with significant morbidity and mortality. Invasive aspergillosis (IA) in children is different from that in adults in terms of signs, symptoms, associated specific findings, and difficulties in early diagnosis.

In the study, we analyzed the clinical manifestations and imaging findings of invasive pulmonary aspergillosis of immunocompromised children in hematology.
Findings and procedure details

PATIENTS AND METHODS:

We retrospectively studied 12 cases of IA diagnosed in our hospital's hematology unit between July 2006 and November 2012. The patients were 5 to 14 years of age (mean 8 years) with 6 male and 6 female patients. They presented with acute myeloid leukemia (AML) in 6 cases, acute lymphoblastic leukemia (ALL) in 5 cases, and acute biphenotypic leukemia in one case. They were hospitalized in standard rooms without any air filtration system. The patients underwent thoracic X-ray and thoracic CT SCAN in every case. A weekly blood test with the Aspergillosis hemagglutination®, Fumouze Diagnosis was performed for all patients. Screening for Aspergillus antigen was performed with ELISA double sandwich on serum in 12 cases, on broncho-alveolar lavage (BAL) in 2 cases.

12 patients were treated by standard amphotericin B regimen then switched to voriconazole. The treatment was initiated in case of clinical symptoms and positive antigenemia in all cases.

RESULTS:

A total of 12 patients have been described. All our patients were given an aplasia inducing chemotherapy regimen. At diagnosis of 9 patients were neutropenic with less than 500 elements/mm3 in 9 cases and less than 100 elements/mm3 in 6 cases. The duration of neutropenia ranged from 4 to 65 days (mean 28 days). Symptoms suggesting IA appeared after the 6th day of aplasia in 9 cases. The clinical signs suggestive API was dominated by the presence of fever in all patients, cough in 8 cases, a chest pain in 5 cases of hemoptysis in 2 cases, a earl the pulmonary auscultation in 5 cases and dyspnea in 4 cases.

The thoracic X-ray showed isolated or multiple nodules in 3 cases, systematized opacities in 2 cases, diffuse reticulo-nodular infiltrates in 4 cases, and a decreased pulmonary transparency in one case. A thoracic CT scan revealed opacities with excavation in..... cases, nodules associated with a halo sign in four cases, and isolated or multiple nodules in ..... cases.

The mycological diagnosis of sputum was negative on direct examination in every case whereas culture allowed isolating *Aspergillus* in ..... cases. Direct examination of BAL was negative in two cases. The aspergillar species isolated in sputum were *A. flavus* in..... cases, *A. niger* in..... cases, and *A. nidulans* in.... case. Aspergillus seroconversion was observed in..... cases. Screening for galactomannan in serum was positive in all cases.
The test was positive for the only BAL tested, and this positivity was concomitant with that of serum.

According to EORTC/MSG criteria, the 12 cases of IA in our series were classified as probable IPA in 11 cases, possible IPA in one case. The outcome was death in 1 case.

**DISCUSSION:**

Invasive fungal infections represent an increasingly major cause of morbidity and mortality among immunocompromised individuals. The reasons of increasingly number of patients with IA being reported in the past few years have been attributed to several factors: more intensive immunosuppressive therapies for GVHD and rheumatologic diseases, increased use of unrelated donor transplantations, more intensive preparative regimens to avoid rejection or relapse, and an increase of early post-transplantation survival because of better control of bacterial and cytomegalovirus infection.

Early detection of IA is difficult due to the lack of sufficiently sensitive and specific diagnostic tools.

Conventional diagnosis of IA is dependent on culture and histopathologic examination of the tissue(s) involved. Microscopy and culture of sputum and bronchoalveolar lavage samples, and blood culture are insufficiently sensitive for proper diagnosis. Most IA cases are detected only at autopsy and biopsy from the infected tissue which is not always available in patients with a severe underlying condition. Therefore, diagnosis depends on a combination of clinical and radiologic signs, and clinical experiences. A serum enzyme-linked immunosorbent assay (ELISA) has been developed for the detection of circulating galactomannan (GM), which is a major constituent of Aspergillus cell wall.

The clinical symptoms and signs associated with IA may be associated with fever, cough, pleuritic pain, and hemoptysis. The occurrence of fever despite appropriate antibiotic therapy over 96 hours in neutropenic patients with hematologic malignancies surrogates the possibility of IA.

Leukocyte reconstitution led to overwhelmingly inflammatory response in the infected lung with local necrosis of pulmonary parenchyma. Life threatening pulmonary bleeding with hemoptysis is regarded as a poor prognostic sign in IA.

In patients with defects in their defense mechanisms, the aspergillus spores will undergo germination and turn into invasive hyphae. Histologic analysis demonstrates invasion and occlusion of small and medium-sized pulmonary arteries by fungal hyphae.

**Imaging findings:**
Radiologic evaluation has a foundational role in IA diagnosis; however, there have been recent advances in noninvasive alternate markers of many diseases.

Plain radiographs reveal poorly defined pulmonary nodules, pleural-based nodular mass and/or air-space segmental or lobar consolidation. Multiple findings and signs have been described (figure 1).

The "CT Halo" is characterized by the presence of ground-glass low attenuation surrounding a non-specific pulmonary mass or mass-like infiltrate. In severely neutropenic patients, the halo sign is highly suggestive for IPA and examination, the halo of ground glass attenuation results from alveolar hemorrhage. The halo sign has been demonstrated in a number of other conditions associated with pulmonary hemorrhagic nodules such as lung metastasis from hypervascular tumors, pulmonary Kaposi sarcomas or Wegener granulomatosis. The halo has also been described in patients with eosinophilic pneumonia, tuberculosis, Mycobacterium avium complex and cytomegalovirus with a limited number of patients (figures 2 and 3).

The "hypodense sign" was described as the central hypodensity within pulmonary lesions, also proposed as the other early sign seen in IPA. The hypodense sign has proven to be a precursor of the crescent sign, anticipating it by a range of 2-19 days (figure 4).

The "air crescent" sign was recognized as a crescent shaped or circumferential area of air within a parenchymal consolidation or nodular opacity. Pathology reveals hyphal from the fungus invades the pulmonary vasculature resulting in pulmonary hemorrhage, arterial thrombosis anfilled the space from the resorption of the necrotic tissue periphery of the lesion. This appearance is usually seen during a convalescent stage (figure 5).
Fig. 1: Patient with AML and febrile neutropenia. Chest radiograph demonstrated faint patchy opacity in RUL.

© hematology, Ibn El Jazzar, Farhat Hached Sousse - Sousse/TN
**Fig. 2:** (a, b) CT scan in lung window axial planes. There were focal consolidations in both upper lobes with peripheral ground glass densities

© hematology, Ibn El Jazzar, Farhat Hached Sousse - Sousse/TN
**Fig. 3:** CT scan in lung window revealed pulmonary nodule. Crescent air density is noted within the nodule consistent with the air Crescent sign.

© hematology, Ibn El Jazzar, Farhat Hached Sousse - Sousse/TN
Fig. 4: CT scan with contrast in soft tissue window showed segmental consolidation. Hypodense sign was demonstrated as focal low density within the lesion

© hematology, Ibn El Jazzar, Farhat Hached Sousse - Sousse/TN
**Fig. 5:** CT scan in lung window revealed pulmonary nodule. Crescent air density is noted within the nodule consistent with the air crescent sign.

© hematology, Ibn El Jazzar, Farhat Hached Sousse - Sousse/TN
Conclusion

Pulmonary aspergillosis is a potentially fatal infection especially in immunocompromised patients. Various radiographic findings including CT signs have been described. The comprehensive pictorial review aims to provide the practicing radiologist a summary of the imaging diagnostic criteria for this clinically significant diagnosis. In an appropriate clinical setting, knowledge of imaging findings of pulmonary and thoracic aspergillosis will be helpful to establish the diagnosis, which leads to proper treatment especially for pediatric patients.
References


4- Saghrouni F, Ben Youssef Y, Gheith S and all. Twenty-nine cases of invasive aspergillosis in neutropenic patients. Médecine et maladies infectieuses. 41, 2011; 657-662.


