

Role of CT in the Diagnosis and Follow up of Pediatric Oncology Patients with Fungal Infection

Thesis

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Radio-Diagnosis*

By

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List of Abbreviations

Abb.	Full term
<i>ALL</i>	<i>Acute Lymphoid Leukemia</i>
<i>AML</i>	<i>Acute Myeloid Leukemia</i>
<i>BAL</i>	<i>Bronchoalveolar Lavage</i>
<i>BAL-GM</i>	<i>Bronchoalveolar Lavage-Galactomannan</i>
<i>BDG</i>	<i>(1, 3)-β-d Glucan</i>
<i>BSIs</i>	<i>Blood Stream Infections</i>
<i>CCPA</i>	<i>Chronic Cavitary Pulmonary Aspergillosis</i>
<i>CSF</i>	<i>Cerebrospinal Fluid</i>
<i>CVC</i>	<i>Central Venous Catheter</i>
<i>EORTC/MSG</i>	<i>European Organisation for Research and Treatment of Cancer / Mycosis Study Group)</i>
<i>ESCMID</i>	<i>European Society of Clinical Microbiology and Infectious Diseases</i>
<i>ETT</i>	<i>Endotracheal Tube</i>
<i>FDA</i>	<i>Food and Drug Administration</i>
<i>GM</i>	<i>Galactomannan</i>
<i>GM EIA</i>	<i>Galactomannan- Enzyme Immunoassay</i>
<i>GMS</i>	<i>Grocott's Methenamine Silver Stained</i>
<i>GVHD</i>	<i>Graft Versus Host Disease</i>
<i>HSCT</i>	<i>Haemopoietic Stem Cell Transplantation</i>
<i>IA</i>	<i>Invasive Aspergillosis</i>
<i>IAI</i>	<i>Invasive Aspergillus Infection</i>
<i>IFI</i>	<i>Invasive Fungal Infection</i>
<i>IQR</i>	<i>Inter Quartile Range</i>
<i>MDCT</i>	<i>Multi Detector Computed Tomography</i>
<i>NAC</i>	<i>Non-Albicans Candida</i>
<i>PCR</i>	<i>Polymerase Chain Reaction</i>
<i>SPSS</i>	<i>Statistical Package for Social Science</i>
<i>SVC</i>	<i>Superior Vena Cava</i>

ABSTRACT

Background: Invasive fungal infections are rare in pediatric population, but have a high morbidity and mortality rates despite the development of antifungal treatment. It ranges from superficial, mucosal to invasive infection.

Aim of the Work: To assess the value of CT in the diagnosis of invasive fungal infection and differentiating it from other causes of infection or metastatic deposits in patients with childhood cancer and persistent fever in spite of antibacterial treatment and to assess the radiological response after treatment with antifungal drugs.

Patients and Methods: Our study was done over one year period from October 2017 through October 2018, included 22 immunocompromised pediatric patients from EL-Demerdash tertiary hospital, included (8 male, and 14 female) with age range (14m- 16 yrs.).

We identified immunocompromised patient of having underlying malignancy or auto-immune deficiency. We included all patients with fever, neutropenia and high CRP, in whom we suspected chest or paranasal sinus infection.

Results: In our case group; the most common underlying disease was ALL-B cell (n=6, 40%), followed by ALL-T cell (n=2, 13.3%), AML (n=2, 13.3%), aplastic (n=3, 20%), hepatoblastoma (n=1, 6.7%) and auto-immunodeficiency (n=1, 6.7%).

Analysis of the radiological data showed that macronodules was the most significant finding to suggest fungal rather than bacterial infection (53.3% vs. 0% respectively, $p=0.015$), followed by consolidation (40% vs. 57.1%, $p=0.45$) and ground glassing (26.7% vs. 14.3%).

Cavitary lesions, pleural effusion and lung abscess were associated only with fungal disease, yet it is not considered significant enough in our study as a reliable sign to suggest fungal infection

Conclusion: Increase number of hospitalized pediatric patients with fungal infection is a rising problem, with no specific criteria for early diagnosis among this population causing delay of the proper treatment. In our study hematological malignancy was the most common underlying disease with macronodules being the most specific finding to suggest fungal infection in pediatrics.

Keywords: Pediatric Oncology Patients - Fungal Infection – Candida – Aspergillus

INTRODUCTION

Invasive fungal infections are rare in pediatric population, but have a high morbidity and mortality rates despite the development of antifungal treatment. It ranges from superficial, mucosal to invasive infection.

In the past few decades, there has been a considerable increase in the frequency of invasive fungal infection. This increase is directly related to the increased number of immunocompromised patients, due to the use of chemotherapy, immunosuppressive drugs, stem cell transplantation, and solid organ transplantation (*Ankrah et al., 2016*).

The most common fungi responsible for invasive fungal infections are *Candida* and *Aspergillus*. The incidence of invasive candidiasis is higher in the pediatric age group, with the highest risk in neonates. *Candida* infections in older children are more similar to those in adults. In contrast, Invasive aspergillosis is rare in neonates, but occurs more frequently in older children (*Brissaud et al., 2012*).

The most affected organs in order of frequency, are: lungs (70%), skin (20%), central nervous system (brain, spinal cord), and sinuses (18%) (*Hurtado et al., 2013*).

Early detection of Invasive fungal infection is of high importance, as the prognosis depends strongly on the appropriate use of antifungal early (*Georgiadou et al., 2011*).

In haemato-oncological patients, the chest x-ray is false negative in 45–50%. Therefore, the use of thin-slice chest CT (<3 mm) is indicated in immune- compromised patients when searching for a focus of infection (**Gompelmann et al., 2011**).

CT is not useful in acute fungal sinusitis but in a chronic stage where it can evaluate changes in the bone. In case of bone destruction, intraorbital extension, intracranial extension, or both occur rapidly, with soft tissue inflammation and abscess formation. As a result, a low dose CT scan should be adopted for repeated imaging as bone destruction can be subtle. MRI with gadolinium enhancement is better than CT to assess intracranial and intraorbital extension in three planes (axial, sagittal, and coronal) (**Schelenz et al., 2015**).

AIM OF THE WORK

To assess the value of CT in the diagnose of invasive fungal infection and differentiating it from other causes of infection or metastatic deposits in patients with childhood cancer and persistent fever in spite of antibacterial treatment.

To assess the radiological response after treatment with antifungal drugs.

Chapter 1

ANATOMY OF THE CHEST

Thoracic cavity is enclosed by 12 pairs of ribs that connect in the posterior thorax to the vertebral bodies of the spinal column. In the anterior thorax, the first 7 pairs of ribs are attached to the sternum. The 8th, 9th, and 10th ribs are attached to each other by costal cartilage. The 11th and 12th ribs, known as floating ribs.

Inferiorly, it is separated from the abdominal cavity by diaphragm. And superiorly, the thorax communicates with the root of the neck and the upper extremity.

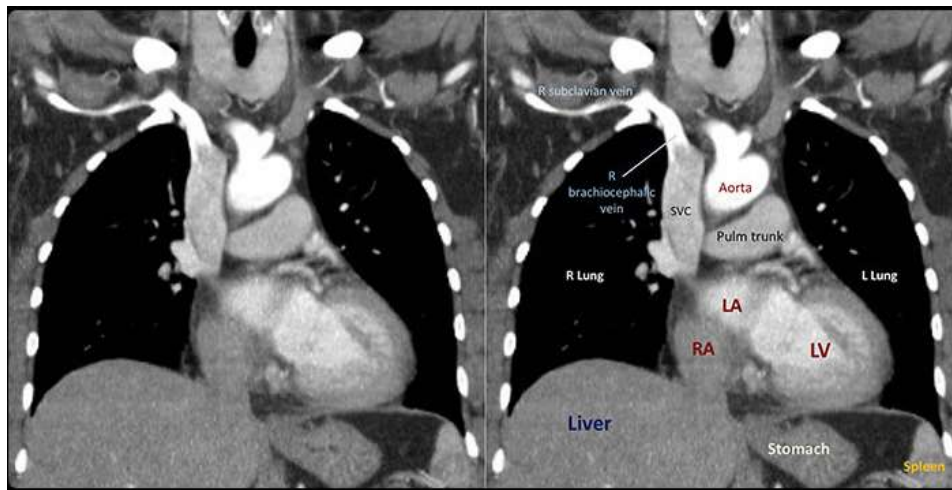


Figure (1): MDCT chest with contrast, coronal view, pulmonary window.

Anatomically its divided into two pulmonary cavities each contain lung with its covering pleura, and the mediastinum in the pleural cavity.

Each lung occupies a hemithorax. The right lung is formed of three lobes (the upper, middle, and lower). The left is formed by two lobes (the upper and the lower), with the lingula considered part of the left upper lobe.

The upper and lower lobes, on each side, are separated from each other by the oblique fissure. On the right, the middle lobe is divided from the upper by the horizontal fissure.

The lungs are lined by two layers of pleura, which are continuous at the hila. The parietal pleura cover the inner surface of the chest wall and the visceral layer is closely applied to the lung surface. Normally, small amount of pleural fluid is present within the pleural cavity to facilitate the smooth movement of one layer over the other during breathing (**Butler et al., 2007**).

The mediastinum is divided by the plane of Ludwig (artificial plane runs from the sternal angle “angle of Louis “to T4 –T5 vertebra) into superior and inferior mediastinum.

The superior mediastinum contains the major vessels supplying the upper extremity, the neck, and the head.

The inferior mediastinum, between the transverse thoracic plane and the diaphragm, is further divided into the anterior, middle, and posterior compartment. The middle mediastinum is the space containing the heart and pericardium. The anterior

mediastinum is the space between the pericardium and the sternum. The posterior mediastinum extends from the pericardium to the posterior wall of the thorax (*Iaizzo et al., 2015*).

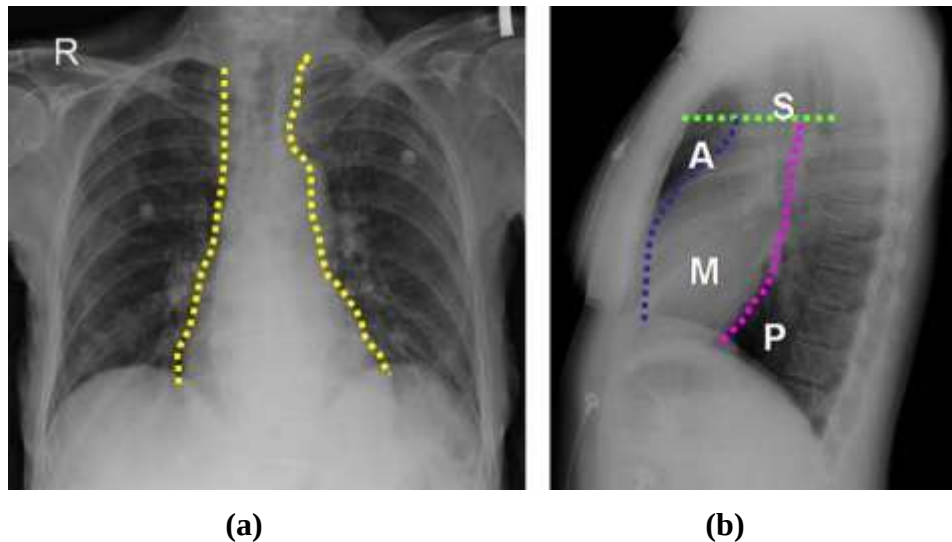


Figure (2): X-ray chest (A); P-A view, shows hilum (lined by yellow dots) (B); lateral view plane of ludwing (green line), separates mediastinum into S: superior mediastinum and inferior mediastinum which subdivided into: A: anterior mediastinum, M: middle mediastinum and P: posterior mediastinum.

Radiologically the mediastinum can be divided into three parts, the anterior division lies in front of the anterior pericardium and trachea, the middle division within the pericardial cavity but including the trachea, and the posterior division lies behind the posterior pericardium and trachea.

Some structures such as the thoracic aorta and the mediastinal lymph nodes are present in all three divisions (*Sutton, 2002*).

All the anatomical structures within the mediastinum are surrounded by fatty connective tissue.

If adequate mediastinal fat is present, the major vascular structures of the mediastinum, the trachea and the oesophagus can be accurately identified.

Axial CT section at the level of the sterno-clavicular joint will show the trachea as a horse shoe-shaped structure lying centrally. Surrounding it in a clockwise direction the brachiocephalic trunk, the left common carotid artery, the left subclavian artery and the oesophagus.

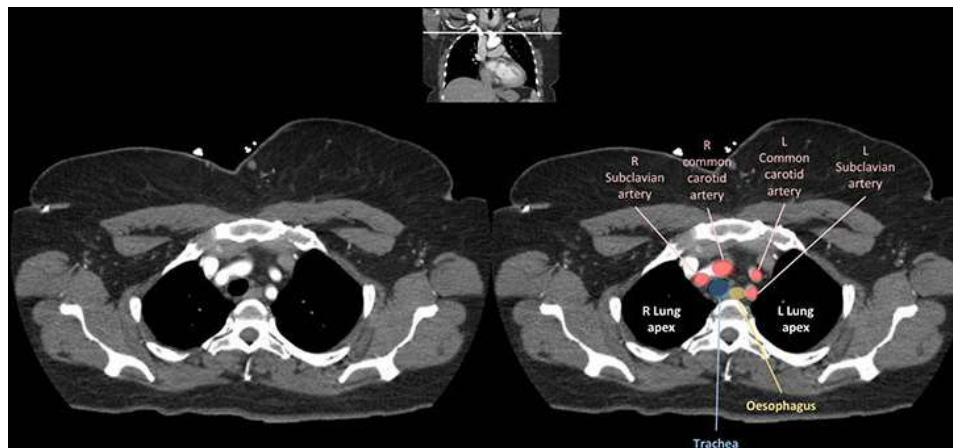


Figure (3): MDCT chest with contrast, axial view, pulmonary window at the level of aortic arch branches.

Anteriorly lies the right and left brachiocephalic veins, which on lower sections they join to form the superior vena cava (SVC).