Radiologic Diagnosis / *Radyolojik Tanı*

DOI: 10.5578/ced.20239710 • *J Pediatr Inf 2023;17(3):e207-e209*

Bölüm Editörü: Prof. Dr. Mithat Haliloğlu

What is Your Radiologic Diagnosis?

Radyolojik Tanınız Nedir?

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Cite this article as: Güner O, Özer G. What is your radiologic diagnosis? J Pediatr Inf 2023;17(3):e207-e209.

A 13-year-old girl who was followed up with the diagnosis of biphenotypic T-cell leukemia was admitted to our hospital with complaints of fever and shortness of breath after completing the second course of chemotherapy protocol. on physical examination, body temperature was measured as 38.1°C, and during auscultation diminished respiratory sounds over the mid-lower zone of the left lung was detected. Tests revealed; absolute neutrophil count of 5/mm^3, erythrocyte sedimentation rate level of 24 mm/h, C-reactive protein was 5.16 mg/dL, and procalcitonin 0.19 ng/mL. Nodular opacity was observed in the perihilar region of the middle zone of the left lung on the chest X-ray of the patient whose clinical diagnosis was considered compatible with neutropenic fever (Figure 1). On the thoracic computed tomography (CT) examination, nodular consolidation was detected in the superior segment of the left lung lower lobe with a ground-glass halo around it (Figure 2).

Since the patient was currently under posaconazole prophylaxis whose galactomannan antigen tests (1.14 TU/mL) performed to determine the causative agent found high, was currently under posaconazole prophylaxis, liposomal amphotericin B was started for the patient, considering azole resistance in the agent. The agent was not able to be isolated from the culture of the sputum sample taken from the patient. Because the patient was thrombocytopenic, a tru-cut biopsy was performed from the lesion by the interventional radiology team after thrombocyte suspension had been administered. The biopsy result turned out as "necrotic lung tissue containing fungal hyphae and spores".

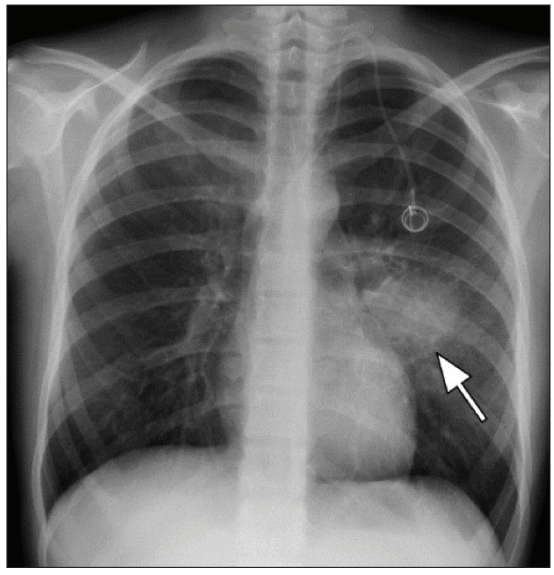

Figure 1. Posteroanterior chest X-ray shows a large nodular opacity (white arrow) in the perihilar region in the middle zone of the left lung.

On the control chest X-ray and thoracic CT scan obtained six weeks after the patient had been followed up with liposomal amphotericin B, peripheral cavitation consistent with "air-crescent sign" that developed in the interim period was detected in the nodular lesion which was observed in the superior segment of the left lower lobe (Figure 3).

What is your diagnosis with these information on the patient's history, examination and radiological findings?

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Received: 05.08.2023 **Accepted:** 23.08.2023 **Available Online Date:** 08.09.2023

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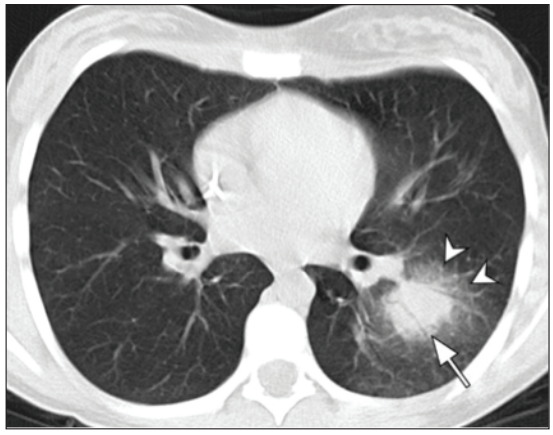

Figure 2. Transverse thoracic CT section shows nodular consolidation (white arrow) with air bronchograms in the superior segment of the left lung lower lobe and "halo sign" (arrowheads) with ground glass opacity around it.

Diagnosis: Nodular Infiltration in the Lower Lobe of the Left Lung Consistent with Angio-Invasive Pulmonary Aspergillosis

Short Discussion

Aspergillus spp. are mold fungi which are found widespread in nature, and the infection they cause is called aspergillosis. Although *A. fumigatus* is frequently identified as the causative agent, especially in pulmonary involvement, *A. flavus, A. terreus, and A. niger* are also among the agents that cause infections in humans (1). Clinical and radiological findings of aspergillosis depends on the immunity of the host, the presence of underlying lung disease, and the virulence of the agent (1,2). Pulmonary aspergillosis is classified under four subtypes: (a) aspergilloma (saprophytic form), (b) allergic bronchopulmonary aspergillosis, (c) chronic pulmonary (semi-invasive) aspergillosis, and (d) invasive aspergillosis (1,3).

Aspergilloma (fungus ball) is defined as the appearance of a mass that occurs due to the accumulation of fungal hyphae, fibrin, mucus and cellular debris in preexisting cavitary lesions in the lung (2,3). It often develops in cavities formed secondary to tuberculosis infection (3,4). The movement of the fungus ball in the cavity can be demonstrated by supine and prone radiographs (5). The crescent-shaped air appearance observed between the ball of the fungus and the cavity wall is defined as the "Monod sign" and should not be confused with the "air-crescent sign" observed in angioinvasive aspergillosis (2).

Allergic bronchopulmonary aspergillosis (ABPA), is a clinical entity secondary to hypersensitivity reaction against *Aspergillus* spp. in patients with asthma and cystic fibrosis (2). On radiographs, gloved finger-like perihilar opacities representing mucus plugs in the lumens of the central bronchi of the upper lobes, transient pulmonary infiltrates and in the later stages central bronchiectasis are observed. (2,4). Although highly attenuated mucus plugs on CT are pathognomonic for ABPA radiologically, hypodense plugs are more common (2,4).

Chronic pulmonary (semi-invasive) aspergillosis is frequently seen in patients with underlying parenchymal lung disease or mild immunosuppression (1,4). Radiography and CT examinations reveal cavitary lesions predominantly in the upper lobes, consolidation and pleural thickening (2). Similar to invasive aspergillosis, cavitary lesions showing "air-crescent sign" or nodular infiltrates can be observed, but the relatively slow clinical course of weeks to months is useful in differentiating these two entities.

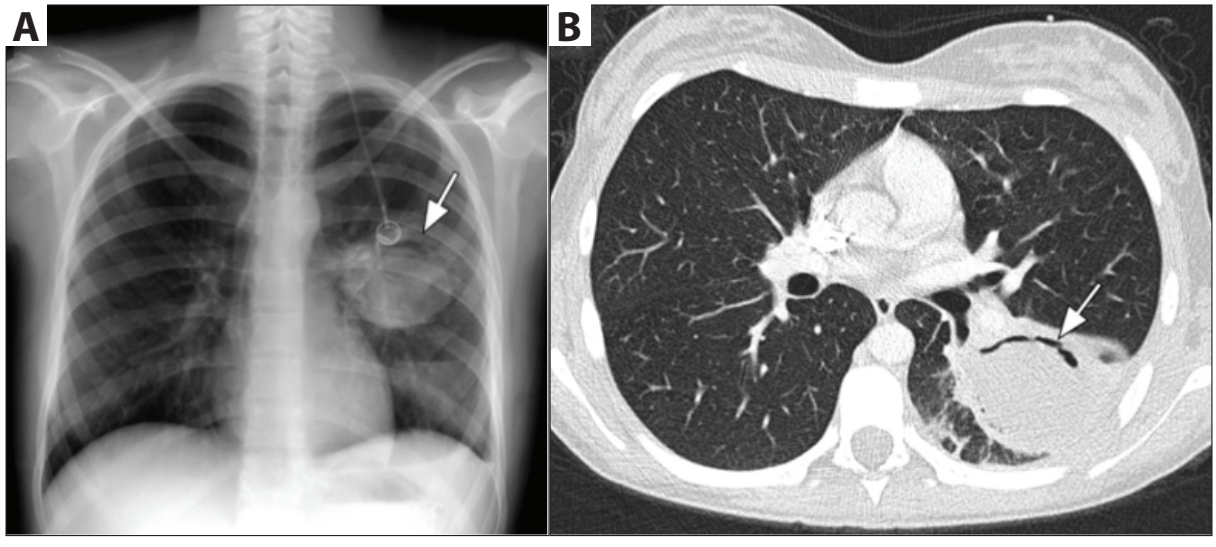

Figure 3. A. On the control posteroanterior chest radiograph taken six weeks later, there is a lucency (white arrow) consistent with the "air-crescent sign" in the nodule in the middle zone of the left lung. **B.** Transverse thoracic CT section shows the cavitary area (white arrow) representing the air-crescent sign.

Invasive pulmonary aspergillosis is a clinical entity that occurs in conditions that cause severe immunosuppression such as hematopoietic stem cell transplantation, solid organ transplantation, hematological malignancies, chemotherapy and high-dose corticosteroid use, rapidly progressing within days, and hematogenous spread to other organs can be observed (1,4). While it may present with fever, cough, pleuritic chest pain, dyspnea and hemoptysis, the clinical presentation may be subtle due to insufficient inflammatory response in patients with severe immunosuppression (4,5). It is classified under two subtypes: of airway-invasive pulmonary aspergillosis and angioinvasive pulmonary aspergillosis.

Airway-invasive pulmonary aspergillosis can occur in three different ways as tracheobronchitis, bronchiolitis and bronchopneumonia. In tracheobronchitis, there is thickening of the trachea and bronchial walls on CT examinations, and localized ulcerations and airway obstruction can be seen in the progressive stages (2,3). Bronchiolitis, centrilobular nodular opacities and tree-in-bud appearance are detected on CT. In the differential diagnosis of these findings, endobronchial tuberculosis spread and nontuberculous mycobacterial infections should be kept in mind (3). Bronchopneumonia, on the other hand, manifests itself with non-specific findings in the form of patchy peribronchovascular consolidations on imaging (2,3).

Angioinvasive pulmonary aspergillosis develops due to the invasion of fungal hyphae into small-medium sized pulmonary artery branches and their occlusion (3). As a result, necrotic hemorrhagic nodules or pleural-based hemorrhagic infarcts occur (3). Characteristic imaging findings are nodules with "halo sign" and pleural based wedge-shaped infiltrates; however, it may also present as nonspecific infiltrates or mass-like lesions (2,3,5). The halo sign is defined as a ground-glass opacity representing the hemorrhage around the lesion surrounding the pulmonary nodule (2). Although it is characteristic for angioinvasive pulmonary aspergillosis, it is not specific because it can be seen in many different pathologies including fungal infections such as pulmonary mucormycosis and cryptococcosis, primary lung tumors, hemorrhagic pulmonary metastases, pulmonary involvement of vasculitides such as granulomatous polyangiitis, and organizing pneumonia (2-6). In addition, the absence of the halo sign does not exclude the diagnosis, since it appears and disappears in the early period of the disease process, often within the first week (2). "Air-crescent sign" is another classic radiological finding of angioinvasive pulmonary aspergillosis and is defined as a crescent-shaped air appearance that separates the sequestrum within the necrotic nodule from the adjacent intact parenchyma. It usually occurs in the late period in parallel with the improvement of neutropenia 2-3 weeks after the commencement of treatment (3,5).

In our patient, imaging findings suggested angioinvasive aspergillosis. The diagnosis was confirmed by the detection of fungal hyphae and spores in the tru-cut biopsy specimen obtained the lesion by interventional radiology and high aspergillus antigen level. The patient's symptoms and radiological findings regressed with liposomal amphotericin B treatment.

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