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Review

Pulmonary fungal infection: Imaging findings in immunocompetent and immunocompromised patients☆

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Abstract

Histoplasmosis is the most common endemic mycosis in North America, and is followed by coccidioidomycosis and blastomycosis. Although the majority of these infections in immunocompetent persons are self-limited, some patients can develop severe pneumonitis or various forms of chronic pulmonary infection. Cryptococcoci, Aspergillus, Candidas, and Mucorals are ubiquitous organisms, which may affect immunocompromised patients. Specific imaging findings can be expected, depending on the organisms involved, underlying patients' conditions (immune status), and specific situations after immune depleting procedures.

Keywords: Fungi; Lung diseases; Lung infection

Contents

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1. Introduction

Fungal infections may be observed in immunocompetent hosts and immunocompromised patients. In immunocompetent hosts, *Histoplasma capsulatum, Coccidioides immitis, Paracoccidioides brasiliensis*, and *Blastomyces dermatitidis* are important causative organisms, whereas in immunocompromised patients Aspergillus, Candida species, Cryptococci, *Pneumocystis jiroveci*, and the species causing mucormycosis are important pathogens. In this pictorial essay, the authors describe a spectrum of pulmonary fungal infections, and their clinical, pathologic and imaging findings, and discuss differences in their appearances in immunocompetent and immunocompromised patients.

1.1. Aspergillosis

1.1.1. Aspergilloma (fungus ball)

Aspergilloma is a saprophytic form of infection in immunocompetent patients. A fungus ball can be defined as a conglomeration of interwined fungal hyphae admixed with mucus and cellular debris within the pulmonary cavity or ectatic bronchus. The most common underlying cause is tuberculosis, which is associated in approximately 25–50% of cases. Radiographs show a round mass of soft-tissue density within a cavity. Typically, masses are separated from cavity walls by an air space, which results in the air-crescent sign. The most characteristic CT finding is of a round soft-tissue intracavitary mass (Fig. 1). Moreover, fungus balls usually move, when a patient changes position. Aspergilloma is often associated with thickening of the cavity wall and adjacent pleura. This pleural thickening may be the earliest radiographic sign before any visible mass-forming changes are observed within a cavity.

1.1.2. Allergic bronchopulmonary aspergillosis (ABPA)

This aspergillosis is an uncommon pulmonary disorder that usually occurs in asthmatic patients. ABPA may also occur in patients suffering from cystic fibrosis or Kartagener's syndrome and in patients who underwent lung transplantation. Pathogenically it is believed to involve both types I and III allergic reactions. Inhaled Aspergillus spores have a propensity to germinate and proliferate in the proximal airways of asthmatics, which often show evidence of asthma-associated mucosal injury. The resulting fungal hyphae induce mucus production and additional mucosal injury, and eventually lead to bronchiectasis.

Pathologically, segmental and proximal subsegmental bronchi are distended with mucus that contains numerous eosinophils and scattered, typically fragmented fungal hyphae. Adjacent bronchial walls show fibrosis and chronic inflammation with abundant eosinophils. Although there may be focal ulceration of airway epithelium, tissue invasion by the fungus is not seen. Bronchioles distal to ectatic bronchi may also be distended with mucus or may show replacement of their epithelium by a granulomatous inflammatory infiltrate and filling of their lumens by necrotic debris (bronchocentric granulomatosis). Patchy filling of alveolar airspaces by eosinophils

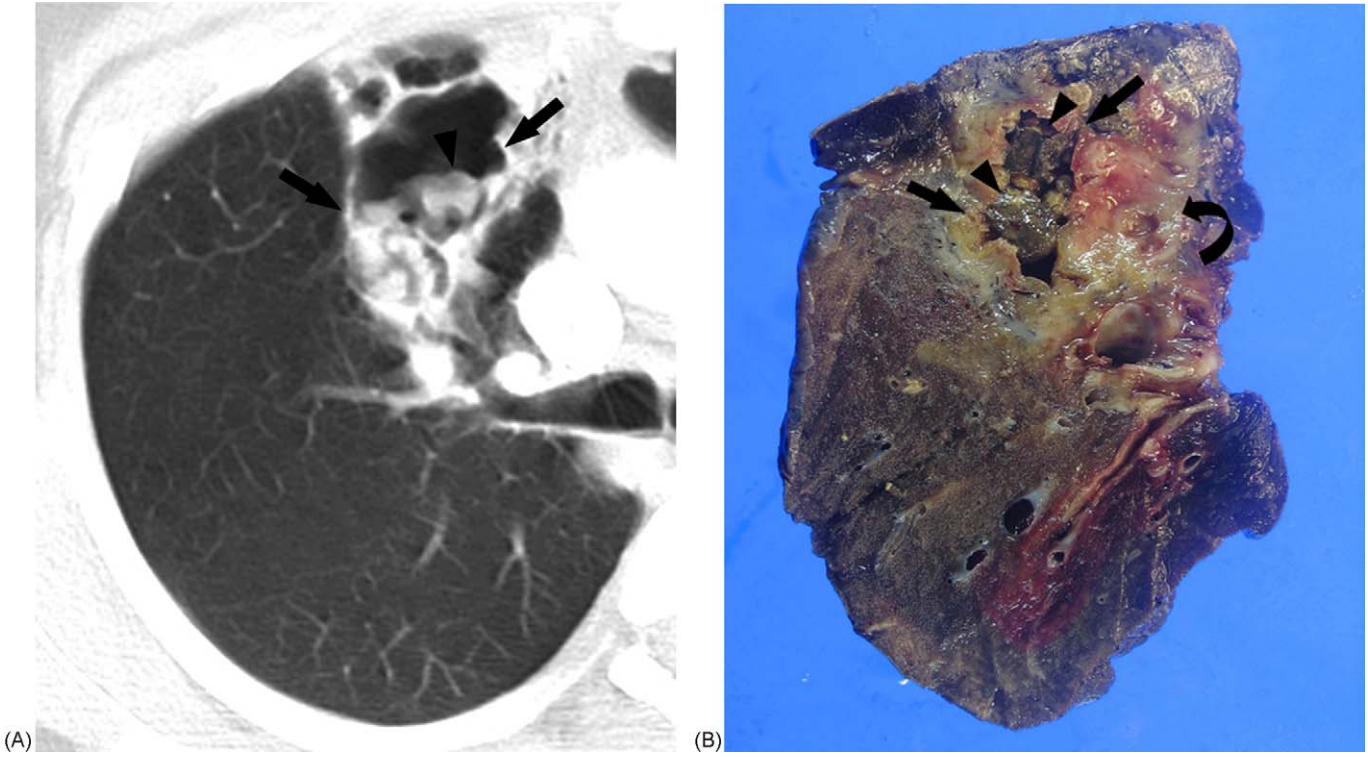

Fig. 1. Aspergilloma in dilated bronchus in a 34-year-old woman. (A) Lung window transverse CT (5.0-mm section thickness) scan obtained at level of right upper lobar bronchus shows dilated bronchus (arrows) containing soft-tissue nodule (arrowhead) in right upper lobe. (B) Photograph of lobectomy specimen shows a dilated bronchus (arrows) containing multiple brownish nodules of fungal balls (arrowheads). Also note dilated bronchi with inflammatory change (curved arrow) in surrounding lung.

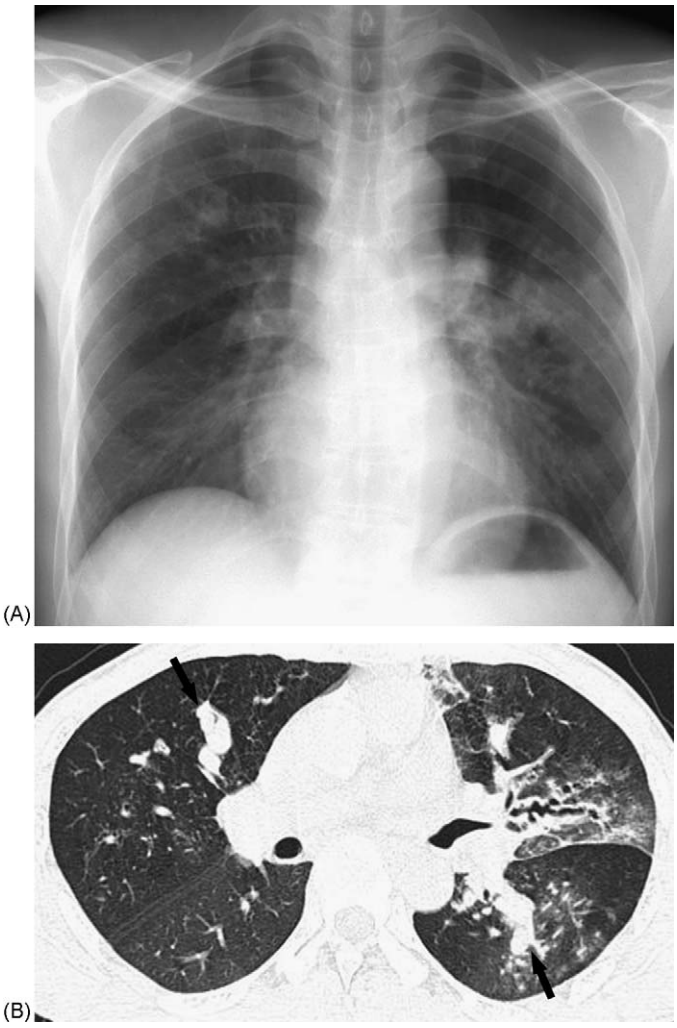

Fig. 2. Allergic bronchopulmonary aspergillosis in a 43-year-old asthmatic man. (A) Chest radiograph shows multiple round nodular lesions and opacity in both lungs. (B) Lung window transverse CT (1.0-mm section thickness) scan obtained at level of bronchus intermedius shows central bronchiectasis, mucoid impaction (arrows), small nodules, and ground-glass opacities in both lungs. (Courtesy of Dr. Mi Young Kim, Department of Radiology, Inje University Ilsan Paik Hospital, Ilsan, Korea).

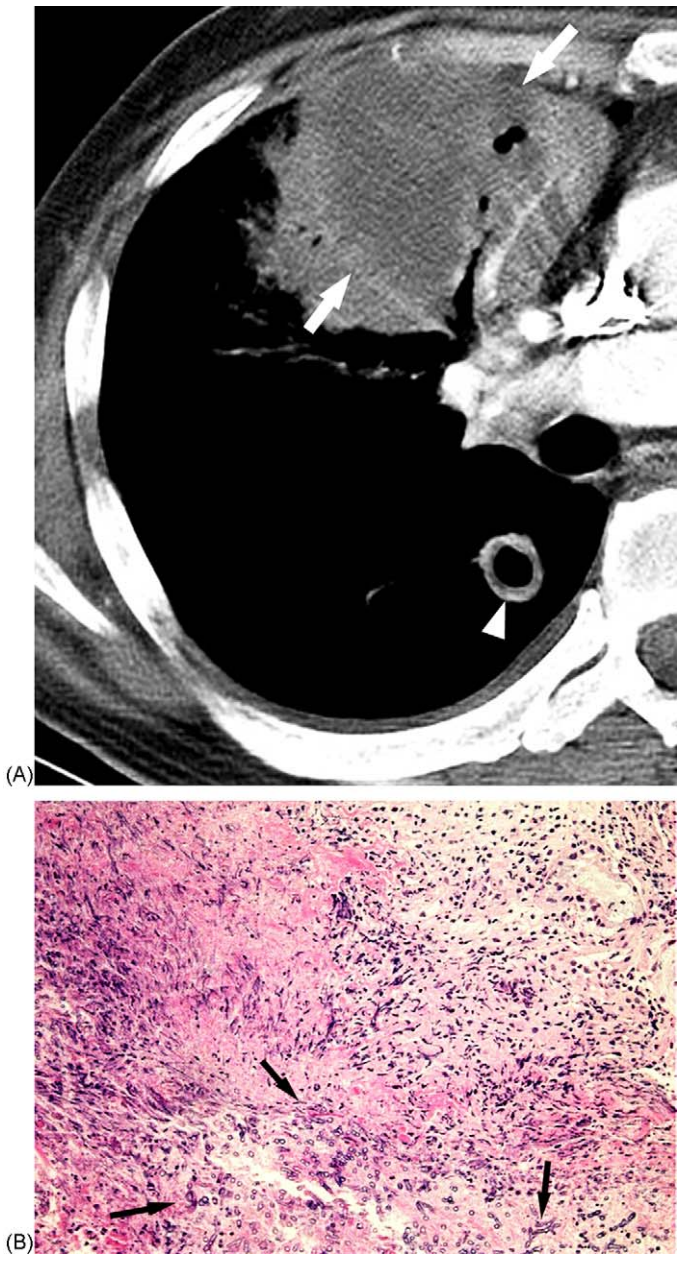

Fig. 3. Semi-invasive pulmonary aspergillosis in a 45-year-old man who underwent bone marrow transplantation for chronic myelogenous leukemia. (A) Mediastinal window transverse enhanced CT (5.0-mm section thickness) scan obtained at level of bronchus intermedius shows consolidation (arrows) containing central necrotic low-attenuation area in right middle lobe. Also note a cavitary lesion (arrowhead) in right lower lobe. Right pleural effusion is associated. (B) Photomicrograph of core biopsy specimen from consolidative lesion shows a necrotizing granuloma containing fungal hyphae (arrows) (H and E, 40×).

(eosinophilic pneumonia) may be observed in adjacent lung parenchyma [1].

Acute (transient) radiographic findings consist of consolidation (80%), mucoid impaction (30%), and atelectasis (20%) (Fig. 2). Chronic (permanent) findings consist of over-inflation, tubular or ring shadows, vascular deficiency, and lobar shrinkage [2]. HRCT findings include bronchiectasis (segmental airways; central or cystic in nature), mucous plugging, atelectasis, peripheral consolidation or ground-glass opacity, mosaic perfusion, and air trapping on expiration (Fig. 2) [3].

1.1.3. Semi-invasive aspergillosis (chronic necrotizing pulmonary aspergillosis, CNPA)

This type is the chronic granulomatous form of aspergillosis, and arises in mild immunologic compromise conditions and is a progressive form of localized disease [4]. Patients generally, are poorly nourished due to alcoholism, diabetes, chronic granulomatous disease, or connective tissue disorders. Clinical symptoms include a cough, sputum, fever, and hemoptysis, usually of several few months duration. Its time course differs from that of invasive aspergillosis, in which the rate of progression depends on the degree of immunosuppression, and its symptom usually has a duration of 2 or 3 weeks. Histologically, there is often a mixture of fibrosis and acute or organizing pneumonia. Foci of necrotizing granulomatous inflammation containing

fungal hyphae may be seen in parenchyma (Fig. 3) or in relation to large or small airways (bronchocentric granulomatosis).

Radiographic findings include consolidation, or a progressive cystic infiltrate, which subsequently forms a thick-walled cavity and aspergilloma with upper lobe predominance [5]. Pleural thickening is frequently seen. CT findings include bronchopneumonia (Fig. 3) and cavitary consolidation containing an aspergilloma [6]. CNPA shows the presence of tissue invasion and destruction, whereas aspergilloma usually forms within preexisting cavity without tissue invasion.

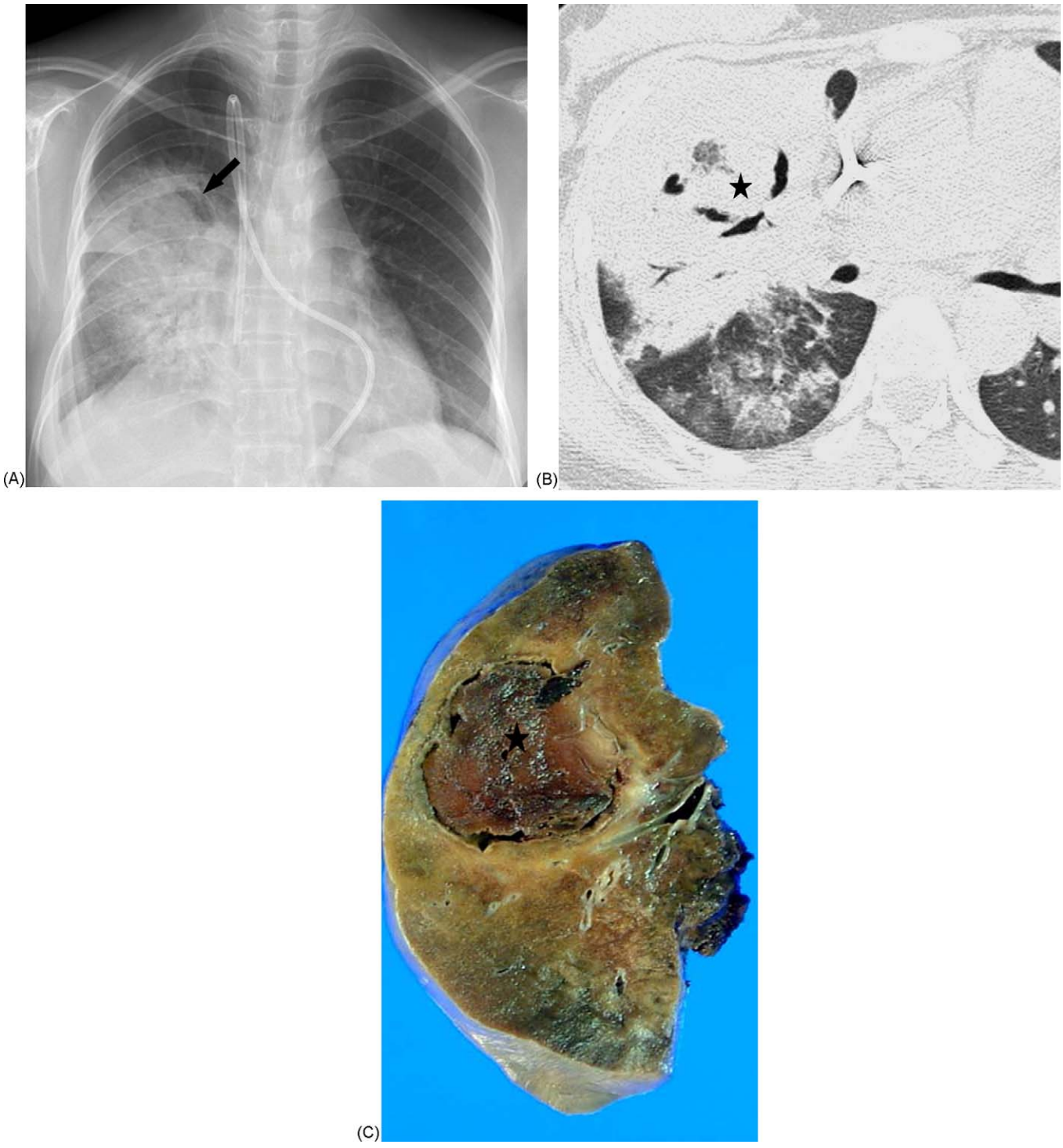

Fig. 4. Invasive pulmonary aspergillosis showing crescent sign in a 25-year-old woman who underwent allogeneic bone marrow transplantation for acute promyelocytic leukemia. Patient was recovering from neutropenia with absolute neutrophil count 760, when given images were obtained. (A) Chest radiograph shows large area of parenchymal consolidation containing air-crescent (arrow) in right lung. Central venous line is inserted. (B) Lung window transverse CT (1.0-mm section thickness) scan obtained at level of right upper lobar bronchus shows cavitary consolidation containing intra-cavitary soft-tissue nodule (asterisk), so-called lung ball, in right upper lobe. (C) Photograph of right upper lobectomy specimen shows a lung ball (asterisk) consisting of necrotic tissue and fungal organisms.

1.1.4. Invasive pulmonary aspergillosis

Invasive pulmonary aspergillosis is the most common opportunistic pulmonary fungal infection, followed by candidiasis and mucormycosis. Major risk factors include severe or prolonged neutropenia (absolute neutrophil count <500), prolonged corticosteroid therapy, graft-versus-host disease after allogeneic bone marrow transplantation, and late-stage AIDS. Affected patients have non-specific fever, cough, and dyspnea symptoms, although symptoms suggestive of pulmonary embolism such as a pleuritic chest pain and hemoptysis may also occur. Systemic dissemination to central nervous system, kidney, and gastrointestinal tract occurs in 25–50% of patients. Mortality rates are high (50–70%), and outcome depends on early antifungal therapy, severity of underlying disease, and speed of granulocyte recovery. Infection begins when aerosolized spores are inhaled into distal airways and airspaces. In the absence of an effective host immune response, spores mature into hyphae that can invade pulmonary arteries, which results in pulmonary arterial thrombosis, hemorrhage, lung necrosis, and systemic dissemination.

Invasive pulmonary aspergillosis characteristically manifests on radiographs as multiple, ill-defined 1–3-cm peripheral nodules that gradually coalesce into larger masses or areas of consolidation. Lobar or diffuse pulmonary consolidation is common, but less specific. Cavitation in a nodule or mass (40%) produces the air-crescent sign (Fig. 4), and intracavitary content in invasive aspergillosis consists of infarcted lung tissue (lung ball). Cavitation occurs after granulocyte recovery, and usually indicates a good prognosis. An early CT finding, is a rim of ground-glass opacity surrounding the nodules (CT halo sign) (Fig. 5). This finding is non-specific and has also been described in patients with tuberculosis, mucormycosis, and Wegener's granulomatosis [7,8]. In the appropriate clinical setting, however, the CT halo sign is highly suggestive of angioinvasive aspergillosis. HRCT may also demonstrate patchy areas of consolidation, often with a peribronchial distribution. Pleural effusion is uncommon, and adenopathy is rare. Chest wall or mediastinal invasion can occur.

Airway invasive aspergillosis accounts for about 15–30% of cases of invasive disease [9]. It is characterized histologically by liquefactive necrosis and a neutrophilic infiltrate that is centered about membranous and respiratory bronchioles. Its most common radiographic presentation consists of patchy unilateral or bilateral areas of consolidation. HRCT demonstrates centrilobular nodules and branching linear opacities (tree-in-bud pattern), and patchy areas of consolidation, often with a peribronchial distribution (Fig. 6). These findings histologically correspond to foci of necrotizing bronchitis and bronchiolitis, typically associated with a neutrophilic inflammatory reaction. In such situations, Aspergillus organisms can be observed to have infiltrated airway walls and immediately adjacent parenchyma [9].

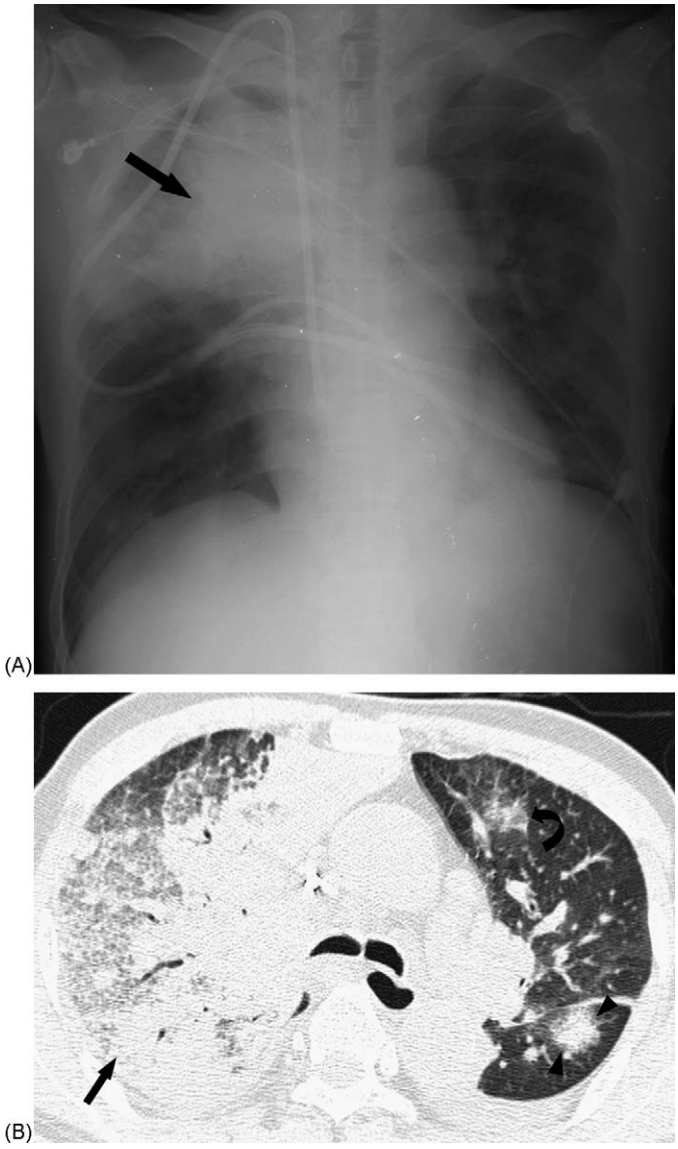

Fig. 5. Invasive pulmonary aspergillosis in a 47-year-old man who received induction chemotherapy for acute myelogenous leukemia. Absolute neutrophil count was 0 when given images were obtained. (A) Chest radiograph shows lobar consolidation (arrow) in right upper lobe. Also note parenchymal opacities in left lung. Central venous line is inserted. (B) Lung window transverse CT (1.0-mm section thickness) scan obtained at level of main bronchi shows lobar parenchymal opacity in right upper lobe (arrow). Also note solid nodule with surrounding ground-glass opacity (halo sign) (arrowheads) and nodular ground-glass opacity (curved arrow) in left lung. Left pleural effusion is associated.

1.2. Candidiasis

Candida albicans is the most frequently isolated member of Candida species in both oval budding yeast and pseudohyphae forms. Pulmonary infection is invariably seen in debilitated or immunocompromised patients, and usually accompanies widespread infection of the urinary tract, gastrointestinal tract, liver, spleen, or central nervous system [4].

Radiographic findings include nodules and patchy unilateral or bilateral airspace consolidation [10,11]. HRCT findings include nodules, ground-glass opacities and patchy consolidation [12]. The parenchymal abnormalities may have smooth or irregular margins and be surrounded by a halo of ground-glass opacity due to hemorrhage. These findings histologically correspond to foci of necrotizing bronchopneumonia, with an abundance of neutrophils. In hematopoietic stem cell transplant

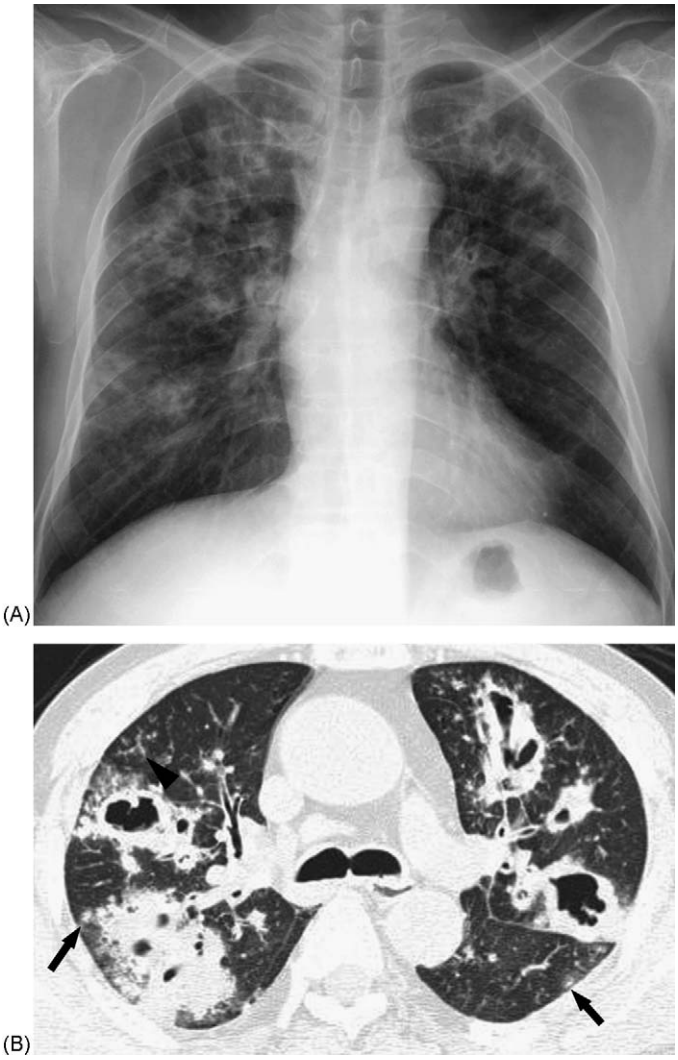

Fig. 6. Airway invasive aspergillosis in a 59-year-old man who underwent corticosteroid therapy for 6 years due to degenerative arthritis. (A) Chest radiograph shows multi-focal parenchymal opacities along dilated bronchi in bilateral upper and middle lung zones. (B) Lung window transverse CT (1.0-mm section thickness) scan obtained at level of main bronchi shows bronchial dilatation, wall thickening, and peribronchial consolidation and ground-glass opacity in both lungs. Also note small centrilobular nodules (arrows) and tree-in-bud opacities (arrowhead) in both lungs. (Courtesy of Dr. Yeon Joo Jeong, Department of Radiology, Pusan National University Hospital, Pusan, Korea).

patients, the most common HRCT findings are multiple nodular opacities (observed in up to 88% of patients; 15 of 17 patients), often associated with consolidation (Fig. 7). Nodules may be an isolated CT finding in 35% of patients. Air-space consolidation is identified in 65% of patients, ground-glass opacity in 35%, and ground-glass opacity halos surrounding nodules in 33% [13].

1.3. Mucormycosis

Pulmonary mucormycosis is relatively rare, and an often fatal, opportunistic infection caused by fungi of the class Zygomycetes, order Mucorales. The main risk factors are diabetes, hematologic malignancy, renal insufficiency, organ

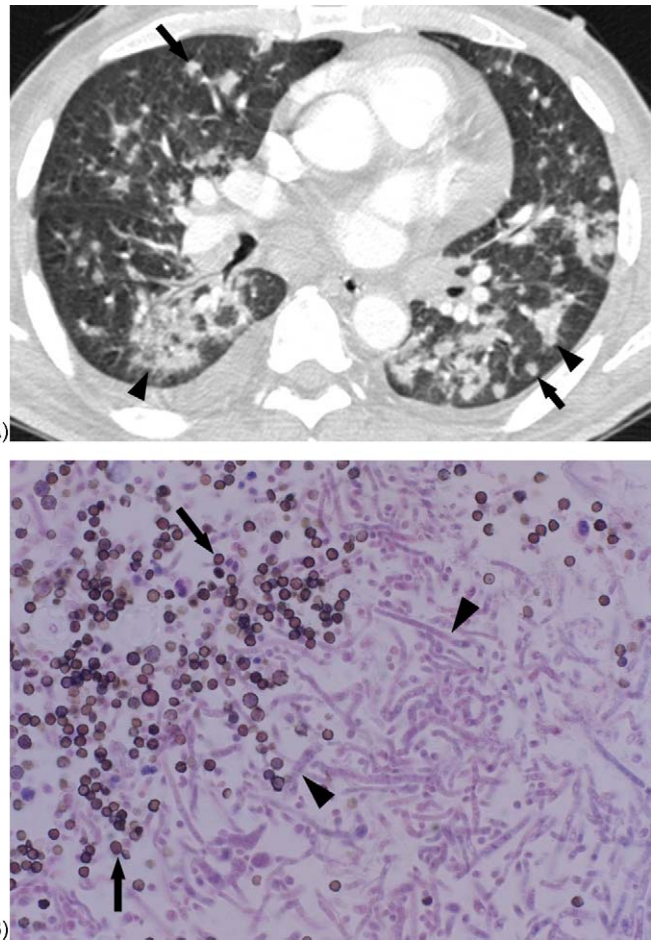

Fig. 7. Disseminated candidiasis in a 31-year-old man with acute myelogenous leukemia. (A) Lung window transverse CT (5.0-mm section thickness) scan obtained at level of basal truncal bronchus shows multiple small nodules (arrows) in both lungs, mixed with parenchymal opacities (arrowheads). Also note bilateral pleural effusions. (B) Photomicrograph of bronchial biopsy specimen shows multiple yeasts (arrows) and pseudohyphae form fungi (arrowheads) (Gomori-methenamine silver staining, 100×).

transplantation, and metabolic acidosis. Pathologically, confluent pneumonia or pulmonary infarction and hemorrhage due to large vessel thrombosis are seen. Less commonly, cavitation or abscess formation is observed. The overall mortality rate of pulmonary mucormycosis is 45%, and patients treated using a combined medical-surgical approach have better outcomes than those treated conservatively. Thus, this relatively rare but often fatal disease should be suspected in immunocompromised patients who fail to respond to antifungal therapy.

Chest radiographs show lobar or multi-lobar consolidation, and solitary or multiple masses or nodules. Cavitation is frequent. Hilar or mediastinal adenopathy is observed in fewer than 10% of patients, and pleural effusion in up to 19% of patients [14,15]. CT findings include focal or diffuse consolidation, single or multiple nodules or masses (Fig. 8). CT may demonstrate additional findings including bronchial occlusion (endobronchial mucormycosis) (Fig. 9), a halo sign (central coagulation necrosis and surrounding hemorrhage) (Fig. 8), or a pulmonary artery pseudoaneurysm [15,16].

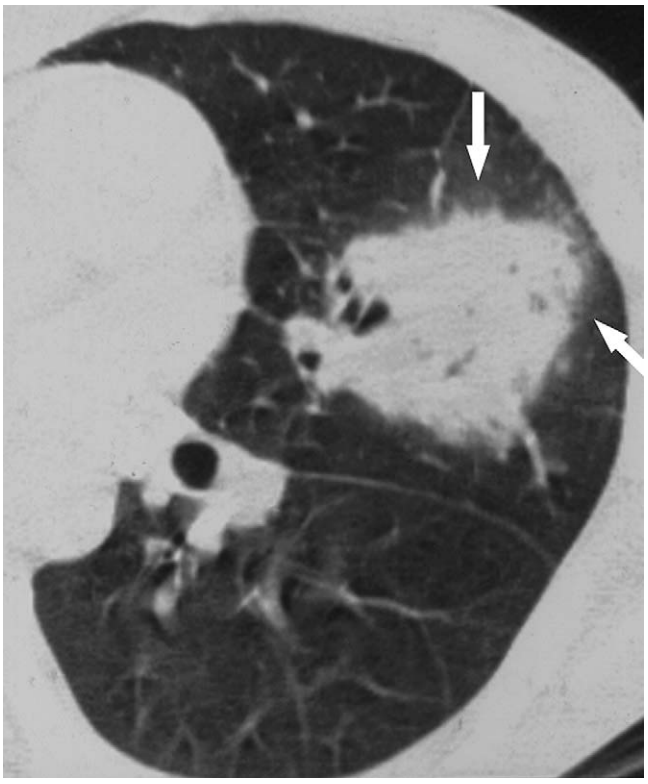

Fig. 8. Pulmonary mucormycosis in a 32-year-old man with non-Hodgkin's lymphoma. Lung window transverse CT (5.0-mm section thickness) scan obtained at level of left basal truncal bronchus shows consolidation and surrounding ground-glass opacity (arrows) in left upper lobe.

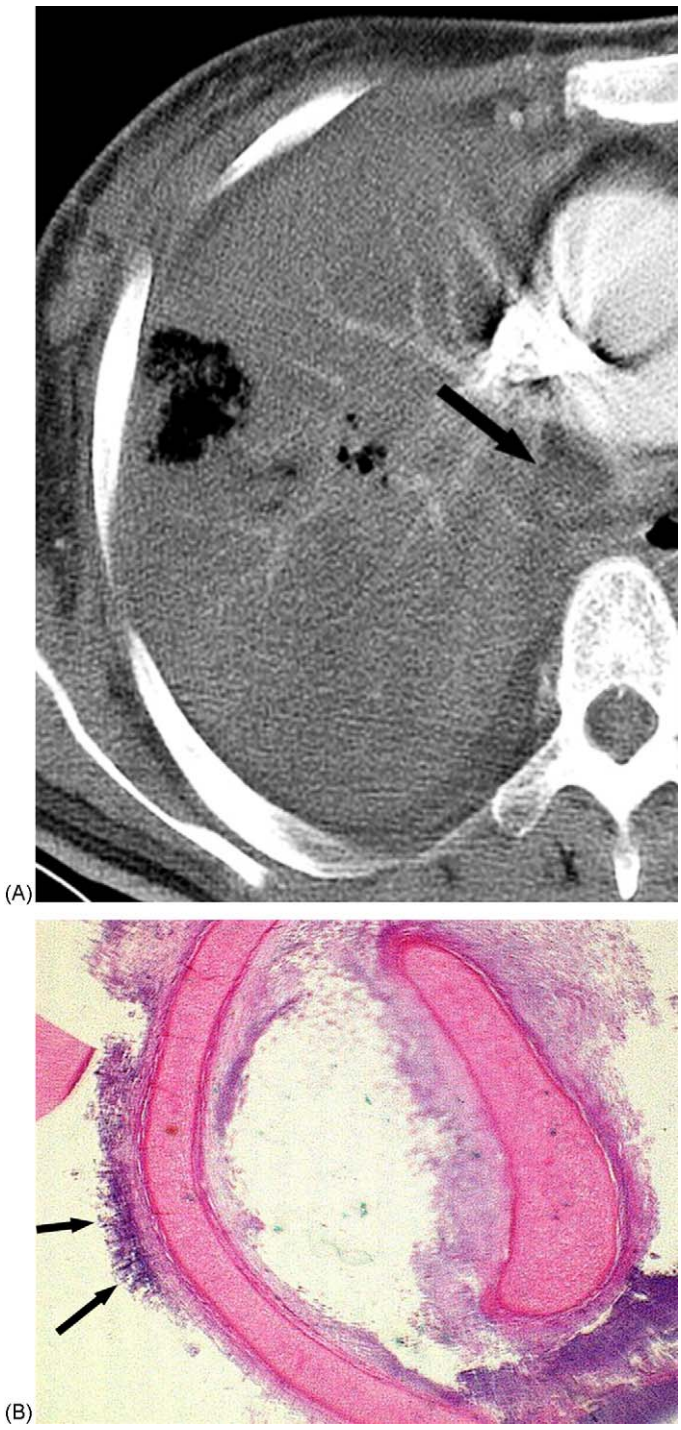

Fig. 9. Airway mucormycosis in a 45-year-old woman with diabetes. (A) Mediastinal window transverse CT (5.0-mm section thickness) scan obtained at level of right inter-lobar pulmonary artery shows low-attenuation lesion obstructing proximal bronchus intermedius (arrow) and volume expanding lobar consolidation in right upper lobe. Bronchoscopy showed complete obstruction of bronchus intermedius by a smooth endobronchial nodule originating from anteromedial portion of the bronchus (not shown here). (B) Photomicrograph of pneumonectomy specimen shows chronic active bronchial inflammation with fungal organism invasion (arrows) to the bronchial wall. (H and E, 1×).

1.4. Cryptococcosis

Cryptococcosis is caused by *Cryptococcus neoformans* (*C. neoformans*), which shows a worldwide distribution in soil, and especially in soil containing pigeon or avian droppings. *C. neoformans* is a thin-walled, non-mycelial, budding yeast, which is characterized by a thick polysaccharide capsule best seen by Mucicarmine staining. Cryptococcosis occurs predominantly in immunocompromised patients but also in immunocompetent hosts. The lungs, central nervous system, blood, skin, bone, joints and prostate are the sites principally involved. About 30% of patients are asymptomatic, whereas in the remaining patients symptoms range from a mild cough and low-grade fever to acute respiratory distress syndrome. About 50–60% of symptomatic infections are related with AIDS. The disease can spread rapidly throughout lungs and disseminate to extrapulmonary sites, especially the meninges in immunocompromised patients.

Histopathologically, immunocompetent patients show granulomatous response, such as non-caseating granulomas or extensive caseation. In immunocompromised patients, intact alveolar spaces become filled with yeast. Radiographic findings include solitary or multiple nodules, segmental or lobar consolidation, cavitation within nodules (10–15%), hilar and mediastinal LAP, and pleural effusion. CT most commonly shows nodules (Fig. 10) or focal areas of consolidation (Fig. 11) in immunocompetent patients [17,18]. Nodules are often multiple, small,

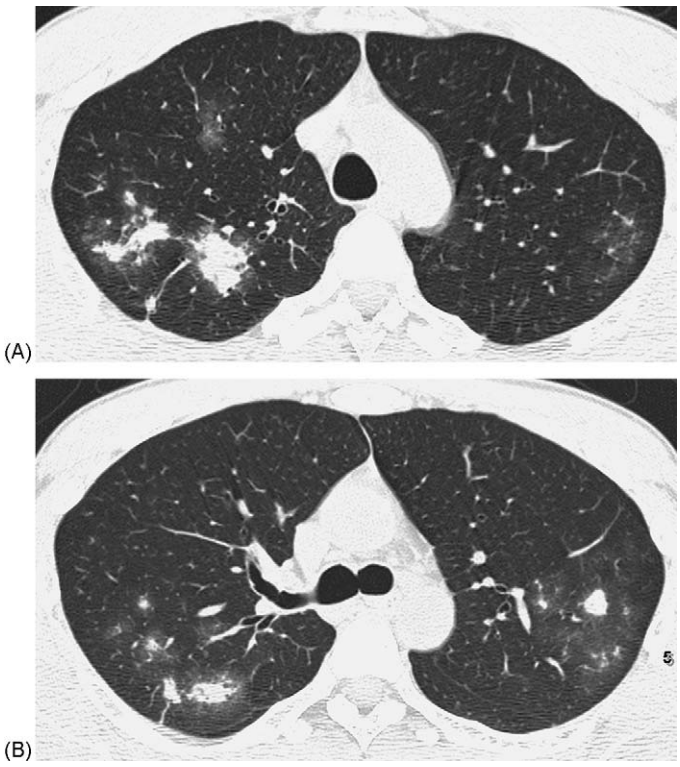

Fig. 10. Cryptococcosis in a 39-year-old military officer serving in frontier. (A and B) Lung window transverse CT (1.25-mm section thickness) scans obtained at levels of aortic arch (A) and main bronchi (B), respectively, show multiple poorly-defined nodules with surrounding ground-glass opacity (halo sign) in both lungs.

and well-defined with middle and upper lung zone predominance [17]. In the immunocompetent, cryptococcal infections are commonly localized in the lung and patients are asymptomatic; whereas, in the immunocompromised, cryptococcal infections often cause symptomatic pulmonary infections and often disseminate to the CNS, skin, and bones. In AIDS patients, mediastinal and hilar lymph node enlargement is common, whereas nodules are uncommon [19].

1.4.1. Pneumocystis jiroveci pneumonia or Pneumocystis pneumonia (PCP)

Pneumocystis jiroveci pneumonia or *Pneumocystis* pneumonia (PCP) is a form of pneumonia caused by a yeast-like fungal microorganism called *Pneumocystis jiroveci* (sometimes spelled *jirovecii*, formerly known as *Pneumocystis carinii*). It is relatively rare in people with normal immune systems but common among people with AIDS. PCP can also develop in patients who are taking immunosuppressant medications (e.g., patients who have undergone solid organ transplantion) and in patients who have undergone bone marrow transplantation. The most common histopathology consists of finely vacuolated eosinophilic material within alveolar airspaces accompanied by a variably severe infiltrate of lymphocytes and plasma cells in the adjacent interstitium. The foamy material consists of solitary and encysted organisms (detected with special stains as round or helmet-shaped structures) admixed with host-derived material such as surfactant and fibrin. Other histologic reaction patterns include granulomatous inflammation and diffuse alveolar damage [20–22].

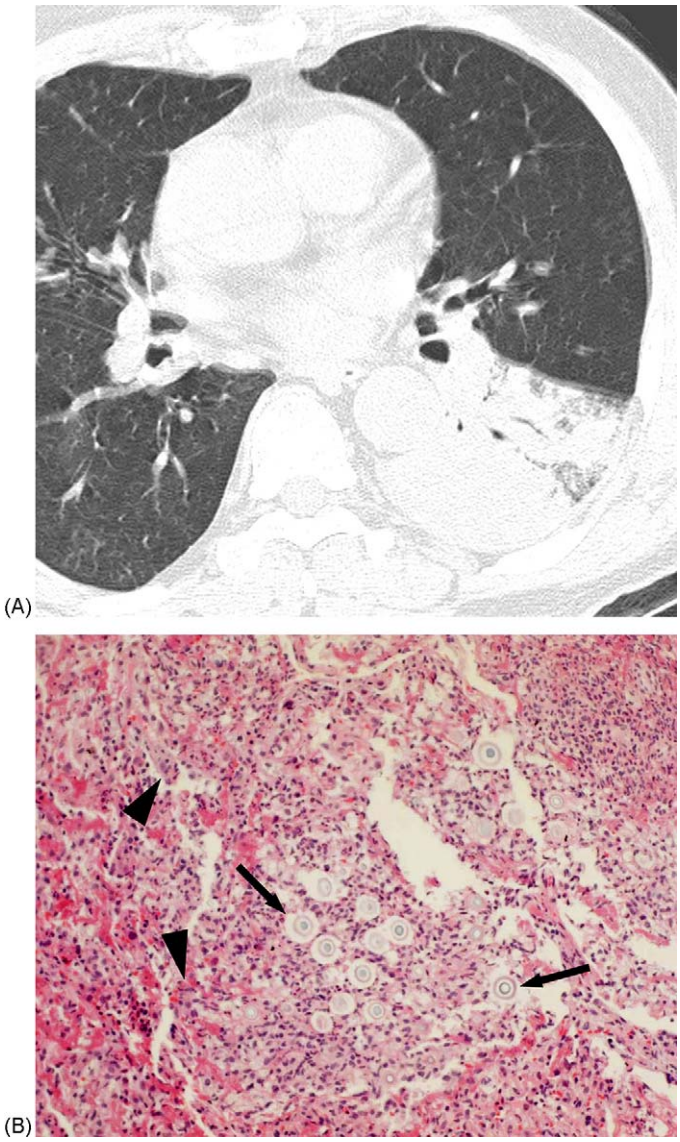

Fig. 11. Cryptococcosis in a 73-year-old heavy smoker. (A) Lung window transverse CT (1.0-mm section thickness) scan obtained at level of right middle lobar bronchus shows segmental consolidation in left lower lobe. (B) Photomicrograph of core biopsy specimen obtained from consolidative lesion shows acute suppurative inflammation with clusters of pale staining yeasts (arrows) in air spaces and surrounding histiocytes and multinucleated giant cells (arrowheads) (H and E, 100×).

Patients typically present with insidious symptoms of fever, non-productive cough, and dyspnea. A definitive diagnosis of PCP requires the demonstration of organisms in sputum or bronchioloalveolar lavage fluid. PCP is most common in patients with CD4 levels <100 cells/mm^3 [20–22].

Classically initial radiographs show a central and bilateral perihilar process that progressed over 3–5 days to a homogenous diffuse alveolar consolidation. Hilar adenopathy and pleural effusion are distinctly unusual. The most characteristic finding at HRCT is ground-glass opacity, which has often a mosaic or geographic pattern with relatively normal secondary pulmonary

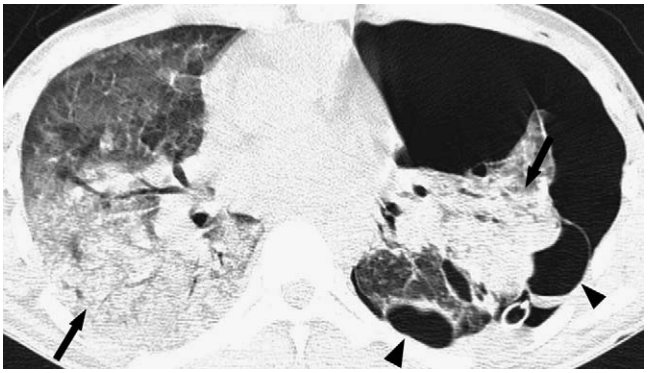

Fig. 12. *Pneumocystis* pneumonia in a 29-year-old man with AIDS. Lung window transverse CT (2.5-mm section thickness) obtained at the level of right basal truncal bronchus shows diffuse ground-glass opacity and consolidation (arrows) in both lungs, and multiple cystic lesions (arrowheads) in the left lung. Also note a thoracostomy tube for drainage of left pneumothorax.

lobules adjacent to diseased ones. The distribution may be diffuse, perihilar, or upper lobe. Other CT features include a miliary pattern, small nodules, focal masses, interstitial disease with reticulation, septal thickening, and small cystic lesions [20–23].

Thin-walled cystic lesions are recognized in about 10–34% of cases radiographically, but they are more commonly identified with CT (Fig. 12). The pneumatoceles are typically thin-walled with no intracystic material and no predilection for a particular area of the lung. They are present on the initial radiograph or developed during treatment of PCP. Cysts related to PCP are usually multiple, occur most often in the upper parts of the lungs, and tend to decrease in size or resolve after the acute stage of the infection. Cysts are responsible for spontaneous pneumothorax developments [24] (Fig. 12).

1.5. Histoplasmosis

Histoplasmosis is caused by the dimorphic fungus *Histoplasma capsulatum*. It is endemic in the Mississippi and Ohio-river valleys and in the St. Lawrence-river valley in Canada. The most common pathologic findings are focal granulomatous inflammation, necrosis, and fibrosis identical to that of tuberculosis.

The disease process is usually too limited in extent to be visible on chest radiograph and is not recognized clinically. Occasionally, enlargement or coalescence of several inflammatory foci results in single or multiple poorly-defined areas of airspace consolidation (Fig. 13). A much more common clinical presentation is that of a solitary nodule seen on chest radiographs or CT images. These nodules correspond histologically to an encapsulated focus of necrotizing granulomatous inflammation, and show central (target) or diffuse calcification radiologically, as a result of dystrophic calcification of necrotic material. Disseminated disease with a miliary or diffuse reticulonodular pattern occurs mainly in the immunocompromised patients. Enlarged hilar or mediastinal lymph nodes also may be seen. In some patients, the inflammatory process extends into the adjacent mediastinum, and results in fibrosing mediastinitis, which shows histologically as dense fibrous tissue containing

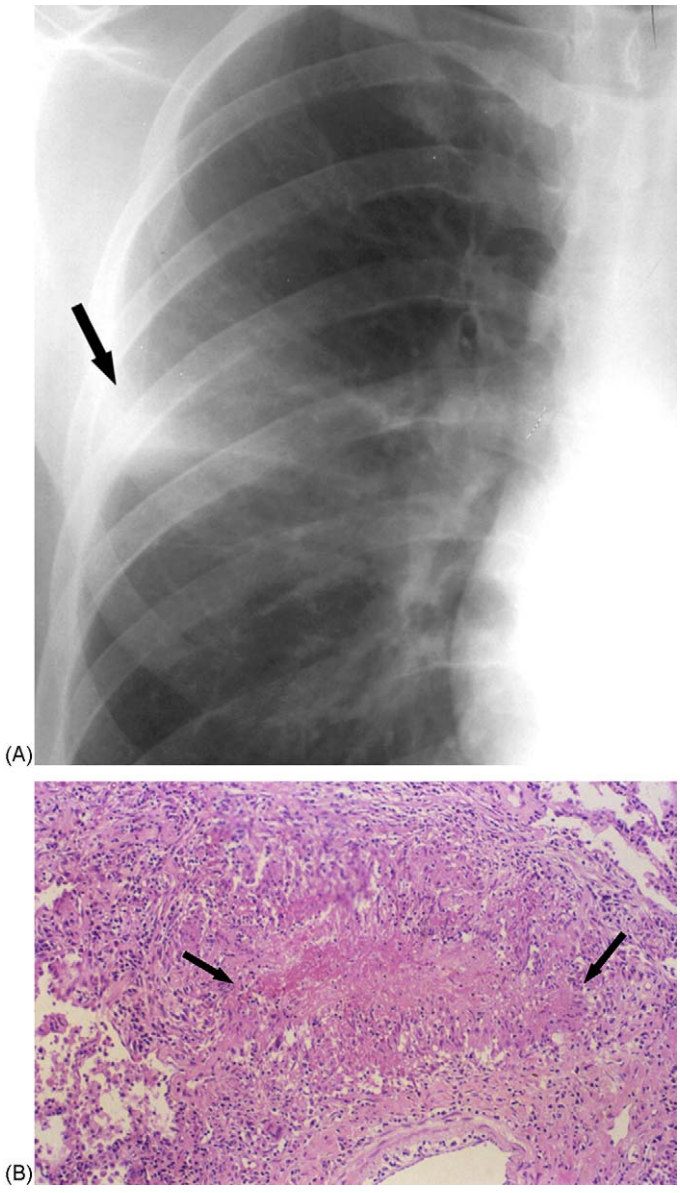

Fig. 13. Histoplasmosis in a 28-year-old man complaining of right chest pain. (A) Chest radiograph shows airspace consolidation (arrow) in right upper lobe. (B) Photomicrograph of pathologic specimen obtained from right upper lobe using video-assisted thoracoscopic surgery shows necrotizing granulomatous inflammation (arrows) with surrounding chronic inflammatory cell infiltration and fibrosis. (Courtesy of Dr. Sang Jin Kim, Department of Radiology, Yonsei University Yongdong Severance Hospital, Seoul, Korea).

variable numbers of mononuclear inflammatory cells and granulomas [25,26].

Chronic histoplasmosis is a rare disease manifestation that occurs in approximately 1 in 2000 exposures. The disease occurs almost exclusively in patients with chronic obstructive pulmonary disease and presents radiologically and pathologically as patchy areas of consolidation, sometimes with cavitation, involving mainly the apical and posterior segments of the upper lobes. Calcification of hilar and mediastinal nodes is commonly seen, and nodes may erode into the lumen of adjacent bronchi and result in broncholithiasis.

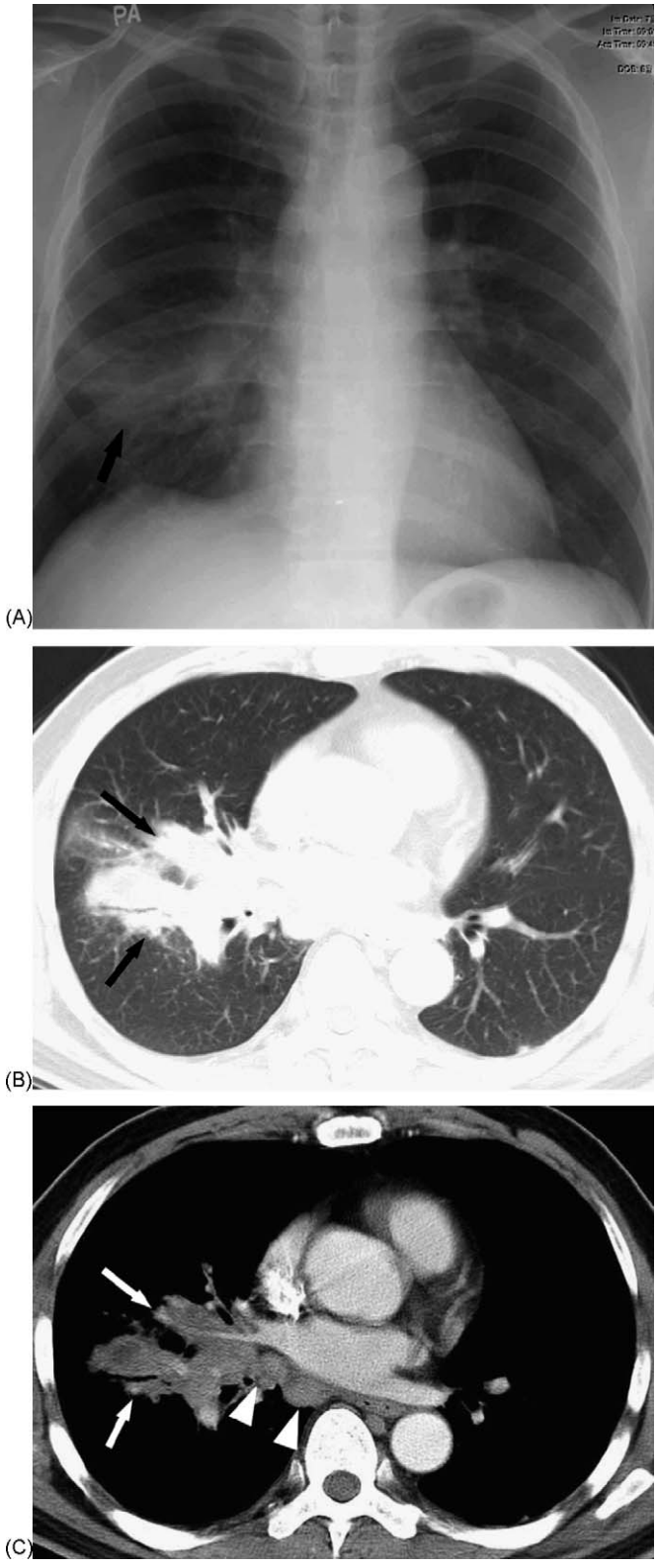

Fig. 14. Coccidioidomycosis in a 58-year-old man complaining of mild dyspnea. Patient had a travel history to south west part of the United States. (A) Chest radiograph shows parenchymal opacity (arrow) in right lower lung zone. (B) Lung window transverse CT (5.0-mm section thickness) scan obtained at left atrial level shows mass-like consolidation (arrows) in right middle and lower lobes. (C) Mediastinal window image obtained at same level to B shows enlarged ipsilateral hilar and subcarinal lymph nodes (arrowheads) as well as consolidation (arrows) in right middle and lower lobes.

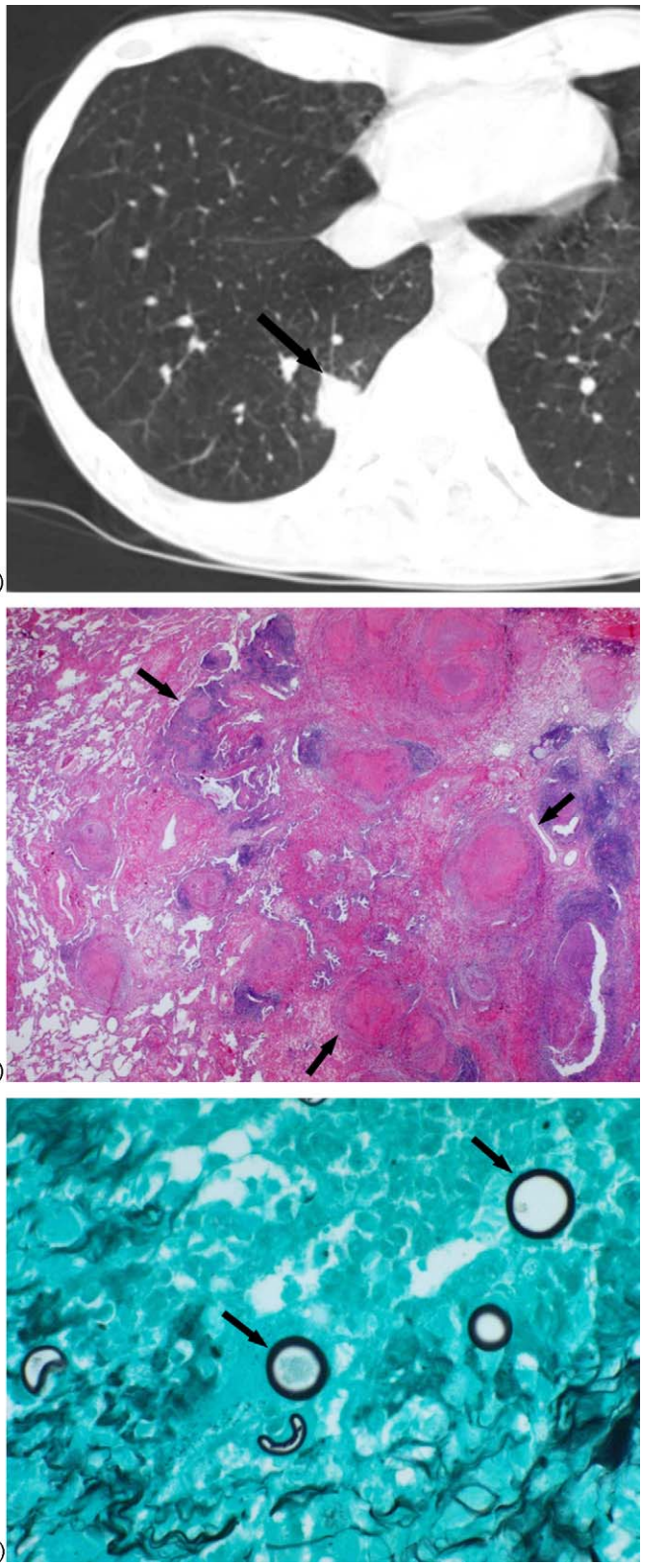

Fig. 15. Blastomycosis in a 69-year-old woman. (A) Lung window transverse CT (2.5-mm section thickness) scan obtained at level of suprahepatic inferior vena cava shows triangular nodule (arrow) in right lower lobe. (B, C) Photomicrographs of pathologic specimens obtained from nodule using video-assisted thoracoscopic surgery show multiples granulomas (arrows in B, H and E, 100×), and fungal organisms (arrows in C, Gomori-methenamine silver staining, 200×) of yeast or crescent form, morphologically consistent with blastomycosis.

1.6. Coccidioidomycosis

Coccidioidomycosis is caused by inhaling the spores of the dimorphic fungus *Coccidioides immitis*, which is endemic in the southwestern US and Mexico. Acute infection results in bronchopneumonia, initially associated with a neutrophilic exudate and subsequently with granulomatous inflammation.

In most patients, the chest radiographic findings are normal. However, about 40% of patients are symptomatic and have patchy areas of consolidation, which usually resolve over several weeks [27]. Hilar lymph node enlargement is also associated (20%) (Fig. 14). Radiologic findings of the chronic form show nodules or cavities, which may be the result of incomplete acute bronchopneumonia resolution (25%). Nodules or cavities are usually solitary, and may be thin-walled ("grape-skin") or thick-walled, usually with homogeneous attenuation on CT [28]. Disseminated disease occurs most commonly in immunocompromised patients with radiologic findings of a diffuse reticulonodular pattern or miliary nodules.

Histologically, lesions correspond to foci of necrotizing granulomatous inflammation. However, granulomas may occur without necrosis. Intact spherules induce fibrocaseous granulomas, whereas ruptured spherules may incite suppurative and BCG-like granulomatous reactions.

1.7. North American blastomycosis

North American blastomycosis is caused by the dimorphic fungus *Blastomyces dermatitidis*. The disease occurs most commonly in the Western Hemisphere, mainly in the central and southeastern US and southern Canada. Patients usually present with an abrupt onset fever, chill, a productive cough, and pleuritic chest pain. Histopathologically, necrotizing granulomas, especially the suppurative type are characteristic, but non-necrotizing granulomas can also be found as well (Fig. 15). Few to numerous, refractile, double-contoured wall, multinucleated yeast cells with broad-based budding are characteristic, but large forms can mimic small *Coccidioides* spherules, and smaller forms ("microforms") may mimic *Cryptococcus neoformans*.

The most common radiologic finding is acute airspace consolidation (25–75%), which is patchy or confluent and may be subsegmental, segmental, or non-segmental [29–31]. Cavitation may be seen and occurs in up to 48% of cases with airspace consolidation. A nodule or mass (30% of patients) is the next most common radiologic abnormality, and these are either soli-

Table 1
Synopsis of pulmonary fungal infection

Microbiology	Predisposing situations	Pathologic findings	Radiologic findings	Prognosis
Aspergillosis: Aspergillus spp.				
Aspergilloma	Within a cavity or ectatic bronchus (Tb or sarcoidosis)	Interwined fungal hyphae admixed with mucus and cellular debris	Ovoid or round soft-tissue intracavitary mass	Spontaneous lysis in 5–10%
Semi-IPA	Alcoholism, DM, connective tissue disorders	Necrotizing granulomatous inflammation containing fungal hyphae in parenchyma or airways	Consolidation/nodule	Depend on immune status, generally poor
IPA	Prolonged neutropenia (>3 weeks), steroid therapy, leukemia, AIDS	Angioinvasive; thrombosis, hemorrhage, lung necrosis, and systemic dissemination	Rim of GGO surrounding nodule or consolidation (halo sign)	
		Airway invasive; necrotizing bronchitis and bronchiolitis	Tree-in-bud pattern, and peribronchial consolidation	
ABPA	Asthma, cystic fibrosis, Kartagener's syndrome, after lung transplant	Distended proximal bronchi with mucus containing eosinophils and fungal hyphae	Mucous plugging, central bronchiectasis	Good long-term prognosis
Candida: *Candia albicans*	Antibiotic or steroid therapy, DM, AIDS	Necrotizing bronchopneumonia, with abundant neutrophils	Consolidation/diffuse nodular or miliary pattern	Depend on immune status
Mucormycosis: *Zygomycetes*	DM, transplantation, lymphoma or leukemia	Confluent pneumonia, infarction and hemorrhage, cavitation or abscess formation	Consolidation or nodule with halo sign	Grave
Cryptococcosis: *Cryptococcus neoformans*	Normal host, AIDS, chemotherapy	Granulomatous response or intact alveolar spaces filled with yeast	Single or multiple nodules or consolidation	Depend on immune status, dissemination of CNS
Histoplasmosis: *Histoplasma Capsulatum*	Acute or chronic	Focal granulomatous inflammation, necrosis, and fibrosis	Normal in acute, fibrosing mediastinitis in chronic	Variable, uncommon dissemination
Coccidioidomycosis: *Coccidioides immitis*	Southwestern US and Mexico	Initially a neutrophilic exudate and subsequently granulomatous inflammation	Consolidation/cavity	Usually confined to lung
Blastomycosis: *Blastomyces dermatitidis*	Central and southeastern US and southern Canada	Necrotizing granulomas, especially the suppurative type	Consolidation/nodule	30% of mortality rate in immunocompromised patient

IPA: invasive pulmonary aspergillosis, ABPA: allergic bronchopulmonary aspergillosis, DM: diabetes mellitus, AIDS: acquired immune deficiency syndrome, TB: tuberculosis, GGO: ground-glass opacity, CNS: central nervous system.

tary (Fig. 15) or multiple. Miliary dissemination accompanies clinically overwhelming infection. Pleural effusion occurs in 10–15% of patients, whereas hilar or mediastinal lymph node enlargement is occasional.

1.8. Timeline of pulmonary fungal infection after specific organ transplantation

In bone marrow or hematopoietic stem cell transplantation, Candida and disseminated Aspergillus infections occur 1–4 months after the transplantation, whereas histoplasmosis, coccidioidomycosis, blastomycosis may occur in areas where endemic fungi reside, usually more than 6 months after the transplantation [20,22]. In lung transplantation, Candida, Aspergillus, *Pneumocystis* pneumonia, or Cryptococcus infections occur within 1 month of the transplantation, and in liver transplantation, Candida infections occur also within 1 month of the transplantation [32]. In the case of kidney transplantation, Aspergillus infection usually occurs 1–4 months and Aspergillus or Mucoral infection 6 months after the transplantation [33].

1.9. AIDS and pulmonary fungal infection

Fungal infection in AIDS patients occurs within various CD4 lymphocyte count ranges. In patients with CD4 lymphocyte counts >200 cells/mm^3, bacterial pneumonia and *Mycobacterium tuberculosis* are the major diagnostic considerations. In patients with counts <200 cells/mm^3, *Pneumocystis jiroveci* pneumonia is the most common infection. At CD4 lymphocyte counts of 50-200 cells/mm^3, disseminated fungal infection becomes prevalent [34].

2. Summary

Imaging findings of pulmonary fungal infection are nonspecific and overlapping from each other. However, certain infections occur in specific conditions (Table 1). Integration of predisposing situations, clinical findings including immune status of patients, and imaging findings of various fungal infection is mandatory for making a specific diagnosis of pulmonary fungal infection.

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