Multiple Chest Nodules on Computed Tomography Scan

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Mr. M is a 75-year-old man recently diagnosed with chronic lymphocytic leukemia. The first two courses of chemotherapy were administered without problems, and Mr. M said he was feeling well enough to continue the remodeling of his home. While undergoing his third course of chemotherapy, he returned to the outpatient clinic with neutropenia, fever, chest pain, and shortness of breath. A chest x-ray revealed a left peripheral infiltrate, initially thought to be a slow-healing left lower lobe pneumonia. Mr. M was started on antibiotics and returned home. During a follow-up visit one week later, his chest x-ray findings had improved but were not resolved. Mr. M was admitted to the hospital for IV antibiotics. He continued to be neutropenic and progressively developed a low-grade fever that reached 101°F with chills, headache, posterior nasal drainage, intermit-tent nosebleeds, and hemoptysis. During the course of several weeks, a macular pruritic rash also developed on his chest.

Differential diagnoses included bacterial or fungal infection and allergic pulmonary diseases of the lung. Patients with hematologic malignancies and those undergoing hematopoietic stem cell transplantation are at high risk for invasive fungal infections. In this population, these infections cause morbidity and mortality with an overall fatality rate exceeding 50% (Groll & Walsh, 2002). Aspergillus and Candida species account for a majority of documented infections, although recent trends indicate a shift toward infections of the Aspergillus species and nonalbicans Candida species.

Based on the persistence of Mr. M’s symptoms, he was sent to a pulmonologist for bronchial alveolar lavage and biopsy. Cultures were negative for bacterial and fungal infections. No indication of allergic pathology was noted. A computed tomography (CT) scan of the chest was performed, and it showed a 2.8 cm rounded mass with somewhat indistinct margins involving the left lower lobe immediately posterior to the left hilum. This mass was surrounded by a “halo” or “crescent sign” of low attenuation (see Figure 1). Given the history and rapid onset of the condition, the radiologist concluded that the mass most likely represented an aspergilloma in an inflammatory cavity.

The classic “halo sign,” characterized by a ground-glass opacity surrounding a nodule, results from hemorrhage and edema around the focus of a fungal infection. This is a valuable early sign of invasive aspergillosis in high-risk patients with neutropenia, although the sign is not as specific in patients at lower risk and may be found in other types of fungal infections (Soubani & Chandrasekar, 2002).

Pathophysiology

The common species of Aspergillus causing disease in humans is ubiquitous in the environment. Aspergillus fumigatus is the most common strain of the organism. However, A. flavus, A. niger, and several other species also can cause the disease. Aspergillus spores are found growing on dead leaves, stored grain, compost piles, hay, decaying vegetation, household dust, and building materials. Processed foods, such as cereals, powdered milk, nuts, and spices, can culture the organism as well (Soubani & Chandrasekar, 2002). Nosocomial infections may be associated with dust exposure during building renovation or construction. Occasional nosocomial outbreaks of cutaneous infections have been traced to contaminated biomedical devices, an important consideration for nurses.

Invasive pulmonary aspergillosis (IPA) is a commonly fatal disease seen in immunocompromised patients and has increased in incidence since it first was described in 1953 (Bartlett, 2000). Researchers believe that inhalation of the spores is quite common but disease with invasion of lung tissue is rare and confined almost entirely to patients with immunosuppression. Major immunosuppressive risk factors for IPA include prolonged neutropenia, the diagnoses of hematologic malignancies or AIDS, corticosteroid therapy, transplantation, and cytotoxic therapy (Stevens et al., 2000).

Clinical Presentation

In the immunosuppressed host, the lower respiratory tract is usually the focus of infection; however, the infection may disseminate to the upper respiratory tract and other organs, including the brain, skin, gastrointestinal tract, and bone. If severe neutropenia persists, mortality can reach 100%, particularly in patients with cerebral abscesses. Presenting symptoms include fever, chills, and pleuritic chest pain (Soubani & Chandrasekar, 2002).

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Aspergillus species have a propensity to invade blood vessels and produce hyphae (branching filaments) that can branch at acute angles. The resulting infectious mass can cause venous and arterial thrombosis and infarction distal to the obstruction. Erosion of a large central vessel wall can lead to massive pulmonary hemorrhage and exsanguination secondary to vascular invasion, resulting in hemoptysis. Severe tracheobronchitis with inflammation of the airways associated with ulcerations can occur but is less frequent (Stevens et al., 2000).

Diagnosis

Diagnosis of IPA can be difficult. Prompt and aggressive workup with treatment initiated after suspicion of the diagnosis is recommended even without definitive proof of the infectious agent. Diagnosis often is made after the disease has advanced and is difficult to cure (Denning, 1996). Laboratory diagnosis includes direct microscopic examination and culture of the organism and DNA probe and serologic testing. Direct microscopic examination of biopsy tissue or secretions has the most definitive diagnostic value. Biopsy specimens typically will show branched hyphae invading the tissue.

Bronchoalveolar lavage, sputum culture, and blood cultures have a low diagnostic yield in IPA. Advances in DNA probes, such as the polymerase chain reaction, may be used more commonly in the future. High titer of serum immunoglobulin G glactomannan antigens may exist. Glactomannan is a fungal cell wall constituent and is sensitive to an enzyme-linked immunosorbent assay for detection (Groll & Walsh, 2002).

The chest radiograph often shows nonspecific changes. Chest CT scans with high resolution are much more helpful in diagnosis of IPA. Better clinical outcomes have been associated with the use of chest CT scans, probably because of earlier diagnosis. Multiple nodules are seen frequently on CT scans. As lesions advance, a surrounding halo of low attenuation, termed the halo sign and characterized by a ground-glass opacity surrounding a nodule, can be seen on CT scans. An air-crescent sign is a positive sign for an aspergilloma but is a relatively late finding and occurs following recovery from neutropenia and secondary to necrosis of the original lesion (Soubani & Chandrasekar, 2002).

Prophylaxis and Treatment

Prophylactic treatment of patients undergoing marrow transplantation for invasive opportunistic fungal infections has been effective for Candida species (Slavin et al., 1995). However, effective prophylaxis against infections by Aspergillus species has not been determined (Lortholary & Dupont, 1997).

Positive patient outcomes depend on resolution of granulocytopenia and early initiation of effective antifungal drug therapy. Medical treatment includes the need to reduce the duration of neutropenia. Administering cytokines to increase the production of neutrophils and macrophages can be an effective strategy. Pharmacologic treatment traditionally has been with amphotericin B. Three lipid forms of the drug amphotericin B have been developed to decrease nephrotoxicity. High cost is their major disadvantage. Amphotericin B lipid complex, amphotericin B cholesteryl sulfate complex, and liposomal amphotericin B are the three lipid forms.

The azoles are another category of agents that have been used in the treatment of aspergillosis. Itraconazole is as effective as amphotericin B for treatment of less severe infections. The U.S. Food and Drug Administration (FDA) cautions about the increased risk of congestive heart failure and liver problems in patients takingitraconazole. Voriconazole (Vfend®, Pfizer Inc., New York, NY) was FDA approved in May 2002 for treatment of aspergillosis.

Caspofungin acetate (Cancidas®, Merck & Co., Inc., Whitehouse Station, NJ) is a new echinocandin agent administered via IV that interferes with fungal cell wall synthesis. This agent typically is used in patients with invasive aspergillosis who cannot tolerate other forms of treatment. Although fluconazole is effective in treatment of Candida infections, it has not been found to be effective against the filamentous fungi of Aspergillus (Groll & Walsh, 2002).

Nursing Management

Challenges for nurses include identifying modifiable risk factors for disease in patients who are immunocompromised. When neutrophil counts decline to less than or equal to 500 cells/mm³, fungal infections present greater risk. Adhering to infection-control protocols and improving the understanding of sources and routes of transmission from the environment is important. Nurses need to be aware that IPA can result from the insertion of IV catheters, prolonged skin contact with adhesive tapes, or burns (Soubani & Chandrasekar, 2002).

Research has associated hospital construction and remodeling in or around hospitals with increased incidence of nosocomial aspergillosis outbreaks. High-efficiency particle air filtration is the most effective way to reduce cases of nosocomial aspergillosis among patients who are immunocompromised in the hospital setting.

Patients receiving amphotericin-containing drugs in the treatment of aspergillosis require close monitoring and prompt management of side effects. Nurses need to be aware that toxicities may include decreased glomerular filtration, renal tubular acidosis, hypokalemia, hypomagnesemia, thrombophlebitis, chills, nausea, vomiting, fever, and hypotension. Pretreatment with acetaminophen and diphenhydramine may help minimize fever and other allergic symptoms. Chills or rigors, which may be severe, are treated commonly with meperidine 12.5–25 mg IV push.

Patient and family education about the side effects of amphotericin drug infusion is important. Skin and mucous membrane integrity should be assessed diligently. Safety practices must be followed at home for severely immunosuppressed patients. Air conditioning and air filtering systems should be kept meticulously clean. Home renovation also should be postponed. Patients and families may need to be taught to inject white blood cell growth factors when needed. Patients with invasive pulmonary aspergillosis have many aspects of the disease to manage. Nurses play a pivotal role in the prevention, assessment, and interventions needed for patients faced with this serious disease process.

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References