Infection is among the leading causes of morbidity and mortality in patients undergoing bone marrow transplantation. Although all infections create difficulties, the most troublesome to those patients are fungal infections. Therapies used to prevent rejection and graft-versus-host disease, as well as an increase in poorly matched or unrelated donors, are believed to contribute to the increase of fungal infections. Mucormycosis, also known as zygomycosis, is an opportunistic fungal infection that is seen rarely in the clinical setting but can be found in patients who are severely neutropenic or immunosuppressed. Oncology nurses caring for bone marrow and peripheral blood stem cell transplantation recipients must know the warning signs of this deadly infection. Early detection and aggressive treatment are patients’ best chances of survival.

At a Glance

- Mucormycosis, although relatively uncommon in the clinical setting, can spread rapidly in severely immunocompromised patients.
- Mucormycosis rarely is reported in transplantation recipients prior to reinfusion of donor stem cells.
- Nurses should recognize the warning signs of mucormycosis because early detection and aggressive treatment are patients’ best chances of survival.

must be vigilant about exposure to and reactivation of bacteria, viruses, and fungi.

Fungal infections can be troublesome for stem cell transplantation recipients. Studies show that, although Candida and Aspergillus species pose a more common risk of infection, other fungi have been identified as life-threatening to transplantation recipients.
Mucormycosis is an opportunistic invasive fungal infection commonly found in soil and decaying vegetation and is usually harmless. It remains quiescent until an opportunity presents itself, usually in a severe immunosuppression setting. Common sites of mucormycosis infection are the sinuses, lungs, skin, brain, and gastrointestinal tract. Although rare, mucormycosis also may appear in the form of disseminated disease (Bouza, Munoz, & Guinea, 2006; Lee et al., 2002). Mucormycosis has been described as the most invasive and progressive fungal infection in humans. Early detection and immediate treatment are key elements to patient survival (Hosseini & Borghei, 2004). Among patients with hematologic disorders, mucormycosis commonly occurs in those with leukemia or lymphoma who have neutropenia from chemotherapy and in transplantation recipients receiving immunosuppression (Pagano et al., 2004).

In transplantation recipients, researchers have found that mucormycosis can occur in the post-engraftment period and up to one year after transplantation (Darrisaw, Hanson, Vesole, & Kehl, 2000). Mucormycosis can rapidly spread in severely immunocompromised patients and usually is fatal (Tollemar, 2004). Amphotericin B, an antifungal agent, is coupled with rapid and aggressive surgical debridement to form the most effective treatment combination for patients (Bethge et al., 2005; Kara, Tasova, Uguz, & Sahin, 2007). However, in neutropenic and immunosuppressed patients, surgical debridement is risky given their lack of effective immune and clotting systems.

Nurses caring for allogeneic transplantation recipients must recognize the early warning signs of mucormycosis so that treatment can commence quickly (see Figure 1). Nurses also must advocate for their patients and provide the therapeutic medications and treatments to prevent, minimize, and treat infections. Educating patients on self-monitoring techniques to identify potential infections also is important.

Case Study

H.K., a 56-year-old businessman of Afghani origin, had lived in the United States for 25 years and was married with three grown children. H.K. had three brothers; one brother, a pharmacist, was very involved in all of the transplantation-related discussions that were held with the patient and his family. This brother eventually became the primary decision maker for the patient’s care, which was agreeable to H.K.’s wife in accordance with the family’s culture and the brother’s profession. H.K. was diagnosed with myelodysplastic syndrome (MDS) one year prior to presenting to the transplantation practice, which is part of an academic, level I trauma medical center. MDS, a preleukemic disease that is treated with blood product support, often converts to AML over time. As time went on, H.K. required more red blood cell support and was considered for an allogeneic stem cell transplantation. H.K. was told of the risks with continued blood support as well as the likelihood of his disease converting from MDS to AML. H.K. and two of his brothers were human leukocyte antigen typed to determine whether either brother was a potential match for a related allogeneic transplantation. The third brother was not a candidate because of a preexisting medical issue.

A bone marrow biopsy shortly after the meeting revealed that H.K.’s MDS had converted to AML. He was hospitalized and treated with chemotherapy. H.K. achieved a complete remission, and the decision was made to proceed with transplantation. Unfortunately, neither of the patient’s brothers was a match, so a search for a matched unrelated donor was initiated through the National Marrow Donor Program. A suitable match was found in Europe; the donor agreed to donate, and the workup of the patient and donor began. H.K. and the donor were fit to undergo their respective procedures.

The pretransplantation workup includes a bone marrow biopsy to restage the disease prior to transplantation. H.K.’s bone marrow biopsy, done four weeks prior to his planned hospital admission for transplantation, indicated that his AML had relapsed. H.K. received a low-dose course of consolidation chemotherapy consisting of fludarabine and mitoxantrone. He spiked a fever one week after the outpatient chemotherapy. The source of infection was not identified, but because the patient was still neutropenic, he was started on daily ceftriaxone and vancomycin.

H.K. was admitted to the hospital on a Friday. His conditioning regimen consisted of cyclophosphamide and mesna, 60 mg/kg daily for two days and total body irradiation twice a day for four days. H.K. would have three days of rest between his last total body irradiation and the reinfusion of stem cells.

Symptoms

On Tuesday, the second day of total body irradiation, H.K. complained of a vague headache starting above his right eye and on the right side of his head. He rated the pain at a 3 or 4 on a 10-point scale. His eyelid appeared puffy, and he complained of minimal photophobia. He was given acetaminophen followed by Percocet® (Endo Pharmaceuticals) with no relief. The nurse reported the headache to the oncologist. A computed tomography scan of the head proved negative for any pathology. A sinus infection was suspected and prophylactic caspofungin IV was started to treat fungal infections.

H.K.’s mental status deteriorated the next day. His headache had progressed from vague and annoying to severe, rated as a 10 on a 10-point scale. He became extremely agitated and combative. He fought his medication administration and pulled at his IV lines. Because Percocet was not providing relief, IV Dilaudid®

Figure 1. Early Mucormycosis Warning Signs

Note. Based on information from Pagano et al., 2004; Smith, 2006.
Mucormycosis is a rapidly growing fungus that invades and erodes the blood vessels, leading to necrosis and hemorrhaging.

This regimen seemed to alleviate H.K.’s headache, and he was able to rest comfortably with no complaints of pain. Amphotericin B was empirically added to the antifungal regimen. At that time, the nurse noticed a small, pinhead-sized dark spot on the right side of H.K.’s nose. It appeared to be small acne, but the nurse had not seen the spot on previous assessments. She mentioned the spot in her written assessment with a note to monitor the site for any changes.

The nurse found the patient to be very sedated during Friday morning rounds. She noticed that his right eye was edematous and closed shut, and H.K. was unable to open the eye when asked to do so. In addition, the skin above the eye was starting to look necrotic, his weight was 5 kg higher than his admission weight, and he had 2–3 plus peripheral edema on a scale of 1–4.

The change in H.K.’s condition was reported to the oncologist. Ophthalmology and ear, nose, and throat consultations determined that the fluid overload was contributing to the bulging eye, and aggressive diuresis as well as prophylactic steroid eye drops were ordered. The patient’s Dilaudid treatment also was stopped to better assess his mental status.

The ophthalmologist reassessed H.K. that afternoon. The pressure in the right eye had decreased significantly with the diuresis, but the necrosis had increased above the orbit and was spreading to the bridge of the nose. By Friday evening, the eye again was bulging. The patient remained confused and disoriented.

By Saturday morning, H.K.’s clinical symptoms had progressed, indicating that the patient had developed a virulent fungal infection. The oncologist suspected mucormycosis because of the necrosis and rapidity of the appearance of the symptoms. H.K. had purulent drainage coming from his right eye. A second computed tomography scan of the head showed progression of the mucormycosis infection into H.K.’s frontal lobe, a change from the previous scan. Because of H.K.’s precarious respiratory status, the decision was made to forgo the bone marrow reinfusion and observe the patient overnight. The healthcare providers were concerned that the reinfusion would only add to the respiratory difficulties.

H.K.’s family was frantic. They could not grasp the fact that he had deteriorated in such a short period of time. They wanted the reinfusion of stem cells to proceed as planned, believing that, once the new stem cells were in his system, they would start to combat the fungal infection. The family was told that it would take weeks for the stem cells to become functional and, therefore, the reinfusion would not combat the infection. They were told of H.K.’s grave situation but were unable and unwilling to make decisions regarding code or resuscitation status.

H.K.’s respiratory and mental status continued to deteriorate overnight. He became flaccid on his right side and had weakness on the left. At the request of the family, H.K. was sent to the neurosurgical intensive care unit where he was intubated and closely monitored. His vital signs began to deteriorate, and he was started on vasopressors to support his blood pressure. He was totally unresponsive. A computed tomography scan of the head showed massive cerebral hemorrhage and impending brain stem herniation.

Figure 2. Mucormycosis Infection in Lung Tissue

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Meetings were held with the family to explain the opportunistic nature of the infection as well as H.K.’s inability to fight it. The family began to realize that H.K. was not going to live. When the implication of brain stem herniation was discussed with the family, H.K.’s brother and wife instructed the healthcare team to keep him comfortable until all family members could come to the hospital to say goodbye. H.K. died late Monday night with his family members at his bedside, 10 days after he was hospitalized.

**Implications for Nursing Practice**

Infections prior to transplantation typically are bacterial in nature (Rupesh & Davies, 2006). Fungal infections are among the leading causes of mortality after conditioning but before engraftment. Mucormycosis is an opportunistic infection that is seen in patients with diabetes, kidney failure, organ transplantations, and neutropenic cancer (Leather & Wingard, 2001) (see Figure 2). It is a rapidly growing fungus that invades and erodes the blood vessels in the area, leading to necrosis and hemorrhaging. In the rhinocerebral form, early symptoms include fever, sinus pain, headache, and local cellulitis. Other symptoms include drooping eyelids, tearing eyes, dilated pupils, and bulging eyeballs. Unfortunately, even with early detection and treatment, the overall prognosis is very poor, with mortality ranging from 30%–70% (Sastry, Parikh, Kulkarni, Bhagwat, & Gadade, 2005; Ven, 2006).

In a patient undergoing stem cell transplantation from an unrelated donor, as H.K. was, the stem cells often do not engraft for 21–28 days, and mortality rates become even higher.

One of the long-term sequelae of a bone marrow or peripheral blood stem cell transplantation is graft-versus-host disease. The graft (donated stem cells) attack or reject certain organs of the host (patient). This results from the donor T cells mounting an immunologic response to the foreign environment of the patient’s body. To avoid this, patients are started on immunosuppressive therapy prior to transplantation and are continued on the therapy for 6-12 months after transplantation, leaving them extremely susceptible to all types of infection.

Patients who develop mucormycosis after transplantation have a better chance of success at treatment despite the immunosuppressive medications because the donor stem cells have engrafted and are providing some degree of defense against the infection. H.K. had relatively little chance of survival because of the timing of the infection. The fact that he developed the infection prior to reinfusion probably is related to his recent chemotherapy and treatment with IV antibiotics at the time of his preparatory regimen (chemotherapy and total body irradiation). When relying on an unrelated donor to provide stem cells, control over the timing of the actual transplantation is minimal, so the course of events for H.K. could not have changed too much.

Mucormycosis infection had only been observed in one patient at the clinic prior to H.K.’s case, and that infection occurred after engraftment of the transplanted cells. Because the infection rarely is seen in the clinical setting, nurses may not be attuned to early warning signs. Oncology nurses are aware of more common fungal infections that typically occur in the lungs, particularly *Aspergillus*. The patient is monitored and treated for fungus after the first onset of pulmonary symptoms. Mucormycosis has a classic presentation; the primary site of infection is the face and sinuses. The erosion of blood vessels causes early necrosis that must be assessed, reported, and monitored.

The bone marrow transplantation process is extremely complex, and nurses must be aware of the many parameters to provide quality care to patients. The balance between adequate immunosuppression to control graft-versus-host disease and too much immunosuppression that allows opportunistic infections to manifest is difficult to gauge. Nurses who care for transplantation recipients must be vigilant to the subtle signs of mucormycosis. Nurses must keep in mind that patients do not have an immune system until engraftment occurs, which could take as many as 28 days, particularly in matched unrelated transplantations. The best chance patients have of surviving this deadly infection is early detection and aggressive treatment.

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