Prechemotherapy Cardiac Assessment

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The topic for this article arose from a question submitted by Doris Cowell, RN, BSN, OCN®, from the University Medical Center of Southern Nevada in Las Vegas, asking about a nurse's liability if the physician does not want to have a standard prechemotherapy test completed (e.g., multigated radionuclide acquisition [MUGA]) for doxorubicin in a patient diagnosed with early-stage breast cancer. This column will discuss clinical and legal issues related to pretreatment cardiac assessment.

Case Study

M.G. was a 39-year-old woman diagnosed with stage I, 1.5 cm, grade 3, hormone receptor-positive, HER2-negative invasive ductal carcinoma in the upper inner quadrant of her left breast. She underwent a lumpectomy and sentinel node biopsy that confirmed no spread to the lymph nodes. M.G. consulted a medical oncologist who recommended systemic chemotherapy consisting of four cycles of doxorubicin and cyclophosphamide (AC) followed by radiation therapy and hormonal therapy. M.G. was in excellent health, took no prescription medications, and had no personal or family history of heart disease. She was physically active and worked out daily. Her blood pressure was normal at 110/62 during her examination. A note in M.G.'s medical record stated that, "Patient is in excellent health without history or signs of cardiac dysfunction. Okay to give AC without MUGA." The nurse clinician in the ambulatory infusion center noted the physician's comment and was concerned about not having pretreatment MUGA results before M.G.'s chemotherapy.

Definition of Cardiac Failure

Cardiac failure is defined as inadequate contractile force of the left ventricle to eject the required amount of blood for perfusion (Hunt et al., 2005), and an absolute decrease in left ventricular ejection fraction (LVEF) greater than 10% from baseline and is associated with a decline below the institutional lower limit of normal, generally accepted to be 50% (Rosenthal & Braunwald, 2001). Anthracycline-induced cardiotoxicity (AIC) may include cardiomyopathy (enlargement of the cardiac muscle).

Risk Factors

The most obvious risk factor for AIC is exposure to anthracycline chemotherapeutic agents. M.G. had a left-sided breast cancer, raising the question about increased risk if radiation therapy involves the left mediastinum region. Giordano et al. (2005) examined cancer registry datasets (N = 27,283) to evaluate the risk of cardiac-related mortality in patients with breast cancer following adjuvant radiation therapy, specifically evaluating differences in mortality for left- versus right-sided radiation therapy. For women diagnosed from 1973–1979, a statistically significant difference exists in 15-year cardiac-related mortality between patients with left-sided (13.1%) and those with right-sided (10.2%) breast cancer. No difference was found for women diagnosed from 1980–1984 (9.4% versus 8.7%, respectively) or from 1985–1989 (5.8% versus 5.2%, respectively). The investigators concluded that risk of cardiac-related mortality associated with left-sided radiation therapy has decreased substantially over time (Giordano et al.). Additional risk factors are found in Figure 1.

Pathophysiology

Injury to the myocardium can be caused by a number of chemotherapy and biologic agents. For the purposes of this article, the focus is on AIC (see Table 1). Anthracycline antitumor antibiotics include doxorubicin, epirubicin, daunorubicin, and idarubicin. Cardiac muscle is composed of cells called myocytes that contain myofibrils (cells that cause the cardiac muscle to contract). The mechanism for AIC remains poorly understood but is thought to be caused by free radical-induced oxidative stress and elevated levels of intracellular calcium (Safra, 2007; Shan, Lincoff, & Young, 1996).

Incidence

The incidence of AIC is about 3% in patients receiving a lifetime cumulative dose of 400 mg/m^2 of doxorubicin, rising to 7% at 550 mg/m^2, and 18% at 700 mg/m^2 (Youssef & Links, 2005). When combined with taxanes, the incidence of AIC is reported to be 11% (Gianni, Salvatorelli, & Minotti, 2007). Taxanes were not found to increase AIC in a European Cooperative Trial in operable breast cancer study when lower cumulative doses of doxorubicin (240 mg/m^2) were given (Gianni et al., 2005).

Prechemotherapy Cardiac Evaluation

MUGA or echocardiography assess systolic cardiac function through measurement of LVEF and are the most common methods of monitoring cardiac function during cancer treatment. However,

- Cumulative dose more than 450 mg/m^2
- Concurrent administration of paclitaxel or docetaxel
- Concurrent administration of trastuzumab
- Administration schedule (shorter infusion equals higher risk of toxicity)
- Radiation therapy to mediastinum
- Preexisting cardiac disease including poorly controlled hypertension
- Increased age
- Smoking

Figure 1. Risk Factors for Anthracycline-Associated Cardiotoxicity in Early Breast Cancer Treatment

Note. Based on information from Gianni et al., 2007; Giordano et al., 2005; Kaszyk, 1986; Loerzel & Dow, 2003; Von Hoff et al., 1979.