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Concurrent Therapies That Protect Against Doxorubicin-Induced Cardiomyopathy

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Nancy was diagnosed with low-grade follicular lymphoma in 1991 at the age of 44. Chemotherapy was initiated but did not result in a complete remission, so Nancy began a watch-and-wait plan of no treatment until the cancer became active. In December 2000, she developed rapidly increasing adenopathy and endometrial carcinoma. In January 2001, she began a course of the chemotherapeutic agents fludarabine, mitoxantrone, and dexamethasone (FMD). Upon completion of the FMD protocol, she underwent a computed tomography scan that revealed a necrotic mass in her retroperitoneum and was concurrently diagnosed with transformed large B-cell lymphoma. In August 2002, she began therapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) along with rituximab. A multiple-gated acquisition scan, a noninvasive diagnostic test used to determine left ventricular ejection fraction and velocity (Pagana & Pagana, 1999), showed a cardiac ejection fraction of 65% prior to her fifth cycle of CHOP. In November, she presented to her physician with shortness of breath and weakness. An S3 gallop had developed, and a chest x-ray showed cardiac enlargement. She was admitted to the hospital with a diagnosis of doxorubicin-induced cardiomyopathy. In late February 2003, Nancy died in the intensive care unit from complications of heart failure.

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Doxorubicin is a chemotherapeutic agent successfully used in the treatment of a wide range of cancers. However, with cumulative doses, doxorubicin also is known to have cardiotoxic effects, including cardiomyopathy and heart failure. Research is targeted at maximizing the antitumor effects of doxorubicin while attenuating the potential cardiotoxicity. Concurrent therapies under study are combinations of doxorubicin with drugs such as probucol, carvedilol (Coreg®, GlaxoSmithKline, Research Triangle Park, NC), dexrazoxane (Zinecard®, Pfizer, New York, NY), and antioxidant nutrients. As patient advocates, nurses must be aware of current research, treatment options, and evidence-based patient resources and be diligent in assessing and educating patients before, during, and after treatment with doxorubicin.

Key Words: doxorubicin, cardioprotective agents, antioxidants

omyopathy is a possible side effect (Danelisen, Palace, Lou, & Singal, 2002). This article reviews the current research in the pathophysiology of doxorubicin-induced cardiomyopathy, the concurrent therapies being explored to minimize toxic effects, and care implications for oncology nurses working with patients receiving chemotherapy with doxorubicin.

Doxorubicin and Cardiotoxicity

In the early 1960s, doxorubicin, an anthracycline antibiotic, was found to be a potent and effective chemotherapeutic drug (Danelisen et al., 2002; Sparano, Wolff, & Brown, 2000). Used in concurrent therapy, doxorubicin increased cure rates in early-

stage breast cancer (Sparano et al.) and was effective against ovarian cancers, leukemia, lymphoma, stomach cancers, multiple myeloma, sarcoma, and bone tumors (Danelisen et al.; Gahart & Nazareno, 2003; Li & Singal, 2000; Quiles, Huertas, Battino, Mataix, & Ramirez-Tortosa, 2002; Sparano et al.). Shortly after the beneficial antitumor properties were discovered, the drug was found to be cardiotoxic (Iliskovic et al., 1999).

The cardiotoxic effects caused by doxorubicin are believed to occur after a critical cumulative dose is administered (Danelisen et al., 2002). A cumulative dose limit of 500 mg/m² of body surface area has been suggested to reduce the potential for cardiotoxicity and resultant

heart failure (Quiles et al., 2002). However, Swain, Whaley, and Ewer (2003) determined that congestive heart failure (CHF) occurred with a total cumulative doxorubicin dose of 300 mg/m² or less. In a retrospective analysis of three phase III trials, "An estimated cumulative percentage of 5% of patients at a cumulative dose of 400 mg/m², 26% of patients at 550 mg/m², and 48% of patients at 700 mg/m²" (Swain et al., p.

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