CARDIOLOGY ASSOCIATES, LLC

Wednesday, December 21

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A Message from Cardiology Associates, LLC

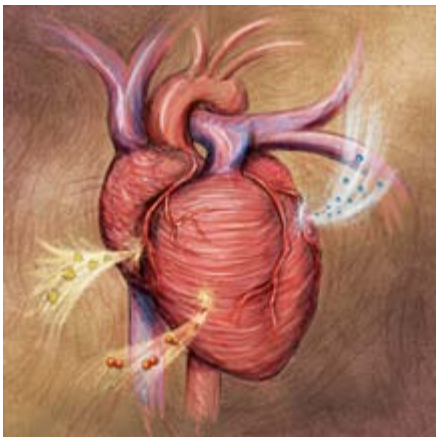
Dear Colleagues,

Happy Holidays! The December newsletter addresses the cardiac complications that can occur with chemotherapy. Understanding the adverse effects of chemotherapy is important for physicians who take care of cancer survivors. The ability for doctors to assess risk factors, appropriately monitor for heart disease, and initiate therapy early can make a big difference in the outcome of patients' lives.

About the author

Dr. Stuart Gould sees patients in our Olney office and at Montgomery General Hospital. Dr Gould completed his post-graduate training at Thomas Jefferson Hospital in Philadelphia, PA, including an additional year as chief medical resident. He practices consultative cardiology and has special interests in cardiovascular imaging.

Chemotherapy Cardiotoxicity



CASE PRESENTATION

• WB is a 68-year-old female with a history of breast cancer who underwent TAC (Taxotere, Adriamycin, and Cyclophosphamide) chemotherapy regimen. An echocardiogram immediately after chemotherapy showed normal left ventricular function and an ejection fraction of 55-60%.
• She then completed localized radiation therapy and started on Arimidex. Eighteen months after completion of her chemotherapy, she presented to the cardiology office with two weeks of dyspnea, orthopnea, and weight gain.
• Echocardiogram showed severely depressed left ventricular function with an ejection fraction of 15-20%. She was admitted to the hospital for diuresis and started on a heart failure regimen.

DISCUSSION

The development of effective therapeutic options for cancer patients has come so far over the past several decades. Like any treatment, physicians need to be mindful of the harmful side effects of drugs. Certain chemotherapeutic agents are known to cause cardiac toxicity, but fortunately cardiac complications are rare. Since the myocardium has limited regenerative capability, it is susceptible to damage from chemotherapy. Once myocyte injury has occurred, the heart is less likely to adapt to other stressors such as hypertension and ischemia. The multi-target theory of heart damage explains why the onset of heart failure may be delayed for some time after the completion of chemotherapy. Anthracycline agents (i.e. doxorubicin) and non-anthracycline agents (i.e. trastuzumab) are effective agents used to treat breast cancer, among other cancers, but also can lead to cardiac complications. The cardiac adverse effects include arrhythmias, heart failure, ischemia, and pericardial disease. Trastuzumab toxicity appears to be reversible with cessation of therapy, whereas doxorubicin appears to lead to more permanent myocardial damage. Many of these cardiac complications can be exacerbated by concomitant

radiation therapy. Physicians adjust timing of drugs, combinations of agents, and cumulative dosages to minimize cardiac risks. The challenge for doctors is to determine who is at risk for developing chemotherapy induced cardiotoxicity and how to best monitor these patients.

Heart failure thought to be from anthracycline toxicity can present sub-acutely up to one year post-termination of chemotherapy. The peak onset of symptoms usually occurs at three months, but symptomatic heart failure can present as late as one decade after treatment. Risk factors associated with chemotherapy cardiotoxicity include high cumulative dose, age older than 70, age less than 18 at initiation of treatment, hypertension, pre-existing coronary artery disease, female sex, and mediastinal irradiation (TABLE 1). Assessment of cardiac risks factors should be part of the pre-treatment assessment to limit the chances of cardiac toxicity. Cardiac function needs to be evaluated before, during, and for some time after treatment. Traditionally, radionuclide tests with multi- gated acquisition scans (MUGA) have been performed with high reproducibility. It still may be the preferred method in patients with large body habitus where echocardiographic images may be limited. Nonetheless, echocardiography overall is the better test in most patients given its widespread availability and no radiation exposure. It is important to note that the same noninvasive modality must be used pre- and post- treatment for direct comparisons.

Table 1. Risk Factors for Anthracycline Cardiomyopathy

Patient Characteristic
Young age (< 18 years) at treatment initiation
Age > 65 years at treatment initiation
Associated hypertension, pre-existing cardiac disease (coronary artery disease, left ventricular dysfunction)
Pregnant or contemplating pregnancy
Engaging in extreme/competitive athletics
Treatment Characteristic
Higher cumulative dose equal to ≥ 300 mg/m^2 of doxorubicin or ≥ 600 mg/m^2 of epirubicin
Associated mediastinal radiation therapy
Combination chemotherapy (trastuzumab, cyclophosphamide, etoposide, melphalan, paclitaxel, mitoxantrone, idarubicin)
Longer duration of survival

No official guidelines have been established to help physicians detect early signs of cardiotoxicity in adults. Some studies have suggested diastolic dysfunction evaluated by echocardiography may provide an early sign of toxicity. Exercise or dobutamine stress echocardiography has also shown to be a potential alternative to find subclinical heart failure. Few studies have shown that measuring troponin or BNP levels may help in early detection of cardiomyopathy, especially in patients receiving high dose chemotherapy. Without guidelines, surveillance is left to the physician's discretion. For cancer survivors, subclinical cardiac dysfunction can be detected with noninvasive imaging (i.e. echocardiography) if mindful surveillance is performed even months to years after cessation of treatment. This is especially important for pediatric patients who received cardiotoxic chemotherapy, since the incidence of cardiac complications increases over time with childhood cancer therapy.

Treatment options to prevent toxicity are limited. Dexrazoxane can reduce the free radicals that are thought to injure myocardial cells. Its use is considered in patients receiving high doses of anthracyclines, however, it has also been shown to reduce the anticancer effects of chemotherapeutic agents. A few small trials have shown some promise in administering beta-blockers or ACE inhibitors prophylactically for their cardio-protective effects. However, more studies need to be done before it is adopted into routine practice. Once heart failure develops or there are early signs of left ventricular dysfunction, then the classic heart failure regimen should commence with early administration of beta-blockers and ACE inhibitors. An ischemic evaluation should also be done either with stress testing or cardiac catheterization to ensure that the cardiomyopathy is non-ischemic and truly related to chemotoxicity. Stopping the assumed offending agent should be weighed against the benefits of continuing medication to treat the cancer. Patients who are receiving chemotherapy and/or mediastinal radiation therapy may want to seek the assistance of a cardiologist to help identify cardiac risk factors prior to treatment and surveillance for cardiotoxicity after treatment. Early detection is paramount with cancer and cardiac disease in order to be able to provide effective treatments.

Back to our case...

Nine months after diagnosis of chemotherapy-induced cardiomyopathy, repeat echocardiogram showed improvement of left ventricular function with an ejection fraction of 50-55%. Patient is feeling great, attending cardiac rehabilitation, and volunteering at the hospital. Her current medical regimen includes Toprol XL 100mg daily, Lisinopril 40mg daily, and Arimidex.

Healy, BR and Swain SM. Clin Cancer Res 2008;14:14-24.
Yeh, ETH, et al. Circ 2004; 109: 3122-3131.
Carver, JR et al. J Clin Oncol 25:3991-4008.

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Our focus will be on real questions and issues that we encounter in our day-to-day medical practice. In fact, if there is a topic that is of particular interest to you (or a question that is related to any of our articles) please e-mail your inquiries to our Project Manager, Nazar Snihur at nsnihur@heartcapc.com. (Of course, we will not share your e-mail address outside of our offices.)

Our Locations

Annapolis Cardiology Office
2002 Medical Parkway, Suite 500
Annapolis, MD 21401
Phone: 410-573-6480
Fax: 410-573-9413

Annapolis Vascular Office
2002 Medical Parkway, Suite 520
Annapolis, MD 21401
Phone: 410-571-8430
Fax: 410-573-5981

Bowie Office
4175 N. Hanson Court
Suite 100
Bowie, MD 20716
Phone: 301-809-6880
Fax: 301-805-4233

Irving Street 4800N
106 Irving Street, NW
Suite 4800N
Washington, DC 20010
Phone: 202-726-5484
Fax: 202-726-4587

Kent Island Office
1630 Main Street
Suite 208
Chester, MD 21619
Phone: 410-643-3186
Fax: 410-643-4098

K Street Office
2131 K Street, NW
Suite 800
Washington, DC 20037
Phone: 202-822-9356
Fax: 202-331-0451

Olney Office
18109 Prince Philip Drive
Suite 225
Olney, MD 20832
Phone: 301-774-5810
Fax: 301-774-0188