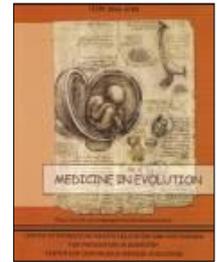


CARDIOTOXICITY OF ANTICANCER TREATMENTS



D. A. PURCARITA TRANDAFIR

ABSTRACT

Heart disease and cancer are the 2 leading causes of death in developed countries according to CDC 2010. Worldwide, more than 28 million people live with cancer. This number could triple by 2030. Heart disease or cardiopathy is an umbrella term for a variety of diseases affecting the heart. Worldwide, more than 28 million people live with cancer. This number could triple by 2030.

Cardiotoxicity is damage to the cardiac muscle inhibiting the normal function of the heart. The heart can be temporarily or permanently damaged by exposure to toxic substances. Radiation therapy to the chest and heart area damages coronary blood vessels. Patients receiving drug and radiation therapy are at an even greater combined risk for Cardiotoxicity. Damage to the heart from cancer chemotherapy can be so severe that the patient may require a heart transplant.

The physiological mechanisms of cardiotoxicity are not completely understood.

More research is definitely needed to define appropriate follow-up and screening of "at risk" patients, determine best treatment for those with established cardiac dysfunction and prevent such damage from occurring during chemotherapy treatment.

Keywords: *heart disease, cancer, cardiotoxicity.*

Correspondence to:

Purcarita Trandafir Dacian Amandos

Phone: +40742343439

E-mail: purcarita_dacian@yahoo.com

INTRODUCTION

Heart disease and cancer are the 2 leading causes of death in developed countries according to CDC 2010. Since the incidence of cancer increases with age and the number of older people is rising, there is a growing population of elderly patients with cancer. By the end of the next decade, it is estimated that in many countries, 70% of all newly diagnosed cancers will be in patients' older than 65 years. Heart disease or cardiopathy is an umbrella term for a variety of diseases affecting the heart. As of 2007, it is the leading cause of death in the United States, England, Canada and Wales, accounting for 25.4% of the total deaths in the United States. Anticancer treatments can have many cardiac complications so increasing the number of heart disease patients. Worldwide, more than 28 million people live with cancer. This number could triple by 2030. With the increasing number of patients with cancer and improvements in can-

cer management that continue to reduce cancer death rates, the number of cancer survivors is projected to increase rapidly, in particular, those afflicted during childhood. More than 70 percents of children who are treated for childhood cancer can be cured. For long-term survivors, possible late effects of treatment and their consequences for the quality of life are a major concern. The growing population of childhood survivors is notable for its vulnerability to adverse health outcomes, many of which may not become clinically apparent until years after the completion of therapy. Despite surviving their initial cancer, childhood cancer survivors continue to face considerable premature mortality as adults. The excess risk of dying from other causes that contributes most to loss of life expectancy is the increased incidence of chronic conditions among survivors of childhood cancer.

ABOUT CARDIOTOXICITY

Cardiotoxicity is damage to the cardiac muscle inhibiting the normal function of the heart. The heart can be temporarily or permanently damaged by exposure to toxic substances. Recreational drugs, such as alcohol and cocaine, are known to cause cardiac damage. Therapeutic agents, including that used for the treatment of cancer, can also result in cardiac disease. Radiation therapy to the chest and heart area damages coronary blood vessels. Patients receiving drug and radiation therapy are at an even greater combined risk for Cardiotoxicity.

Most of the cardiac complications associated with chemotherapy occur during or shortly after the completion of therapy. However, some of these problems can persist and become chronic.

In addition, some chemotherapy drugs can cause heart damage that is only apparent months to years after the completion of cancer treatment. Heart problems can be mild and only detectable by sophisticated tests, such as determining the left ventricular ejection fraction (LVEF), or they can be severe, resulting in congestive heart failure (CHF). Damage to the heart from cancer chemotherapy can be so severe that the patient may require a heart transplant.

The physiological mechanisms of cardio toxicity are not completely understood. What is known is that an overabundance of free radicals leads to oxidative stress causing the death of cardiac muscle cells so the heart can respond with a decrease in left ventri-

cular systolic function. This may be caused by myocyte loss, which is generally permanent, or it may be because of a functional loss of the contractile elements within the cell that results in a transient, reversible decrease in systolic function. Although left ventricular dysfunction is often considered the most important end effect of cardio toxic anticancer treatment, other sequel may also be encountered. Some treatments are associated with coronary vasospasm and can result in myocardial ischemia or, if sufficiently prolonged or severe, may progress to myocardial infarction. In addition, arrhythmias of various types, other abnormalities of cardiac structure such as pericardial inflammation or thickening, and valvular abnormalities are also possible.

Left ventricular systolic dysfunction affects the heart differently ranging from temporary impairment with few long-term implications to severe cardiomyopathy that can ultimately lead to death or need for cardiac transplantation. Agents that affect the heart can be classified as those that have the potential to cause permanent cell loss and those that may not destroy myocytes but modify the functionally of the contractile elements within the cell and impair contractility. From the first group the most used are anthracyclines, but they remain an important part in the treatment of cancer. Anthracyclines are used in a wide range of both hematologic and solid cancers such as lymphoma, leukemia, and breast cancer. Anthracyclines work by inhibiting DNA and RNA synthesis, blocking topoisomerase II to prevent DNA and RNA transcription and replication, and

creating iron-mediated free radicals that damage DNA. Free radical damage to cardiac myocytes is also thought to be the primary mechanism for anthracycline-induced cardiomyopathy. It has long been recognized that cardiomyopathy is the dose limiting toxicity associated with this class of drugs. Patients with anthracycline induced heart failure are generally treated the same as patients with heart failure from other causes. This usually means diuretics to control fluid accumulation and digitalis drugs to strengthen the heart. If progressive and severe, the only treatment may be a heart transplant.

Although a number of efforts have been directed towards prediction of risk, so far no consensus exists on the strategies to prevent and monitor chemotherapy-related Cardiotoxicity. Recently, a new dimension of the problem has emerged when drugs targeting the activity of certain tyrosine kinases or tumor receptors were recognized to carry an unwanted effect on the cardiovascular system.

Cancer survivorship is a growing field in oncology and the numbers of survivors are expected to continue to rise. Many of these individuals will have been exposed to anthracyclines. General internists should be aware of the increasing numbers of asymptomatic cancer survivors at risk for late onset cardiac dysfunction. A clinical history suggestive of risk include high cumulative doses of anthracycline treatment, mediastinal radiotherapy, or young age at the time of anthracycline treatment may help identify high-risk subgroups and prompt closer evaluation of ventricular function.

CONCLUSIONS

More research is definitely needed to define appropriate follow-up and screening of "at risk" patients, deter-

mine best treatment for those with established cardiac dysfunction and

| prevent such damage from occurring

| during chemotherapy treatment.

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