

Cardiotoxicity and Capecitabine: A Case Report

Marybeth Singer, MS, ARNP, BC, AOCN®

As early as 1975, case reports of rare cardiotoxicity associated with IV administration of 5-fluorouracil (5-FU) began to appear in the literature (Roth, Kolaric, & Popovic, 1975). With the development of oral fluoropyrimidines and the continued use of IV fluoropyrimidines to treat a variety of solid tumors in adults, clinicians need to become aware of this toxicity.

The following is a case report of cardiotoxicity related to first-cycle administration of oral capecitabine (Xeloda®, Roche Laboratories, Nutley, NJ), a thymidine phosphorylase-activated fluoropyrimidine, in the treatment of a woman with metastatic breast cancer. Following the case report, a discussion of the possible pathophysiology of fluoropyrimidine-induced cardiotoxicity, literature to date, and implications for practice are presented.

Case Report

Ms. S is a 52-year-old Caucasian woman who initially presented with stage IV breast cancer in September 1998. Computerized tomography (CT) scans at presentation revealed a right middle lobe pulmonary mass, internal mammary lymphadenopathy, and left axillary adenopathy. A bone scan was negative for osseous metastatic disease. She received four cycles of cyclophosphamide, doxorubicin, and 5-FU every 21 days, followed by a left simple mastectomy. Pathology at the time of mastectomy revealed a residual tumor measuring 11 cm x 9 cm x 4 cm. Ms. S subsequently received tamoxifen and locoregional radiotherapy for local control. She was disease free for five months

Oral fluoropyrimidines increasingly are being developed and studied as a novel treatment for breast, colorectal, and other cancers. Fluoropyrimidines are designed to generate 5-fluorouracil (5-FU) preferentially within tumors. Cardiotoxicity is a rare complication associated with 5-FU and oral fluoropyrimidine treatments. Chest pain is the most common presenting symptom, and, in many cases, the cardiotoxicity is partly or completely reversible. This article reviews fluoropyrimidine-induced cardiotoxicity and presents a case report of a woman who experienced this complication during capecitabine treatment.

Key Words: prodrugs, capecitabine, myocardial ischemia

and then presented with new left supraclavicular adenopathy outside her previous radiation treatment field. A biopsy revealed metastatic adenocarcinoma consistent with a primary breast cancer. Further evaluation revealed presence of new osseous metastatic disease and asymptomatic bilateral pulmonary nodules. Ms. S received six cycles of paclitaxel and had an initial partial response. When her disease progressed, she was switched to docetaxel, and a radiographic response was observed at all sites. In September 2000, she began letrozole 2.5 mg orally daily. In December 2000, she presented with a new onset of back pain, and CT scans revealed a new left paraspinal mass and progression of pulmonary nodules.

Ms. S's past medical history included a 60 pack year smoking history, and she now smokes one to two packs per day despite numerous attempts to quit. She has significant emphysema on a chest radiograph and CT scan but no history of cardiac disease, diabetes, or hyperlipidemia.

On January 18, 2001, Ms. S began oral capecitabine at a total of 1875 mg/m² per day

x 14 days in two equally divided doses. Each cycle was a 21-day cycle. On the morning of day four of treatment (after three full days of medication), she reported severe, crushing chest pain with increasing dyspnea and was seen in the emergency room. She was admitted to the cardiac care unit to rule out myocardial infarction after an electrocardiogram (ECG) showed ischemic changes (new ST segment elevation). Cardiac enzymes were reported within normal limits, and cardiac troponin I was 0.8 ng/ml on admission and returned to less than 0.5 ng/ml within 24 hours of admission.

A ventilation perfusion scan showed moderate perfusion defect and was read as intermediate probability for pulmonary embolus but likely represented perfusion defect from severe chronic obstructive pulmonary disease. An echocardiogram revealed a left ventricular ejection fraction (LVEF) of 40% with mildly reduced global systolic function, a hypokinetic anterior septum, normal valves, and no pericardial effusion. The ECG initially revealed normal sinus rhythm, with normal axis; ST elevations in leads II, III, AVF, V3, and V4; ST depressions in V1; and PR depressions in leads II, III, and AVF. A second ECG later that first day revealed ST elevations in leads II,

This article was originally published, in part, in the Boston Oncology Nursing Society Bulletin, Vol. 19, No. 1. Reprinted with permission. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society.)

Digital Object Identifier: 10.1188/03.CJON.72-75