ABSTRACT
The use of neoadjuvant chemotherapy in older patients is increasing. However, chemotherapy should be administered considering the medical comorbidities of the patients and the toxicity of chemotherapeutic agents. Here, we present a case of abdominal wall hematoma with spontaneous inferior epigastric artery injury caused by coughing in a 70-year-old woman who was treated with neoadjuvant chemotherapy. Abdominal computed tomography demonstrated an abdominal wall hematoma with active bleeding. However, angiography with selective embolization of the right inferior epigastric artery and the right internal mammary artery was performed successfully. Scheduled chemotherapy was discontinued over concerns of rebleeding and breast-conserving surgery was performed. When deciding on chemotherapy for older patients, attention should be paid to the various complications.

Keywords: Aged; Breast Neoplasms; Hematoma; Neoadjuvant Therapy; Rectus Abdominis

INTRODUCTION
Breast cancer incidence is increasing among older Korean women. In Korea between 1999 and 2018, the average annual percent change of breast cancer was highest for women ≥ 60 years (7.4%) [1]. Traditionally, the lack of sufficient randomized trials highlighting the benefit of cytotoxic chemotherapy in older breast cancer patients often led to the omission of chemotherapy especially in those above 70 years [2]. However, data from the Surveillance, Epidemiology, and End Results database between 1992 and 1999 and the National Cancer Database between 2004–2014 both suggested that older (> 65 years) patients with breast cancer can benefit from adjuvant cytotoxic chemotherapy [3,4]. Additionally, the benefit of cytotoxic chemotherapy is greater with standard chemotherapy regimens than with alternative, more tolerable regimens in older breast cancer patients [5]. The aforementioned observations have led to the more active adoption of cytotoxic chemotherapy for treating breast cancer in older patients [5,6]. In 2018, nearly half of breast cancer patients ≥ 55 years received cytotoxic chemotherapy [1].

Older patients are at an increased risk of developing severe toxicity during chemotherapy. In a multicenter study, 46% of older patients with breast cancer who underwent cytotoxic
Chemotherapy developed grade 3–5 toxicities [7], and the toxicities were more commonly observed in patients with reduced kidney function [8]. Therefore, the decision to administer cytotoxic chemotherapy in older patients with breast cancer should be a balanced one considering both survival benefits and potential toxicities [9].

In this report, we describe the case of a 70-year-old breast cancer patient who developed a life-threatening non-traumatic rupture of the right internal mammary artery and inferior epigastric artery during neoadjuvant chemotherapy.

CASE REPORT

A 70-year-old woman newly diagnosed with cancer in the right breast visited our outpatient clinic. Breast imaging, including magnetic resonance imaging and ultrasonography, revealed a 4.2 cm-sized irregular mass in her right breast and a 2.0 cm-sized enlarged lymph node in the right axillary area. A subsequent axillary node biopsy revealed metastatic cancer cells in the enlarged lymph nodes. Moreover, the tumor was 10% positive for estrogen receptors and negative for progesterone and human epidermal growth factor receptor type 2. The woman had no other medical history except dyslipidemia, and her Eastern Cooperative Oncology Group was 0 [10]. Initial imaging revealed no evidence of distant metastasis, and the clinical stage was cT2N2M0.

After discussing the treatment options, the patient decided to undergo neoadjuvant cytotoxic chemotherapy. The recommended chemotherapy regimen was four cycles of doxorubicin and cyclophosphamide followed by four cycles of docetaxel. Dyslipidemia medication (ezetimibe/rosuvastatin calcium) was continued during chemotherapy. During the initial four cycles of doxorubicin and cyclophosphamide, no dose-limiting adverse events were observed, and the tumor demonstrated a partial response, with a 60% size reduction.

Ten days after the first docetaxel administration, the patient visited our emergency room with severe right upper quadrant abdominal pain. She had experienced intermittent dry coughing for nearly one month. Moreover, pain in the right upper quadrant developed one week ago and abdominal bruising became visible two days after the onset of pain which grew gradually (Figure 1A). Severe abdominal pain and increased abdominal wall swelling were the main reasons for emergency department visits. The patient denied having experienced any trauma to the torso.

At the emergency room, her initial hemoglobin and platelet level was 8.8 mg/dL and 114 × 10^3/uL, respectively. Before the administration of docetaxel, the hemoglobin level was measured at 11.6 mg/dL, and the platelet count was 433 × 10^3/uL. The vital signs demonstrated a low systolic blood pressure (99 mmHg) and marginal tachycardia (102 beats/min). Emergency abdominal computed tomography revealed a large hematoma in the right chest and abdominal wall and suspicious contrast extravasation in the right internal mammary artery (Figure 1B and C). Subsequent angiography revealed active hemorrhages at the branches of the internal mammary and inferior epigastric arteries (Figure 2A, B, and C). Moreover, successful angiographic embolization of the bleeding arteries was performed (Figure 2D and E), and the patient fully recovered after a few days of close observation. Considering the life-threatening nature of the adverse event, the remaining three cycles of docetaxel were discontinued, and the patient underwent breast conservation surgery four weeks after embolization.
DISCUSSION

Multiple studies have demonstrated that the clinical benefits of adjuvant chemotherapy in older patients with breast cancer are comparable to those in younger patients [11-13]. In addition, some studies indicated that the benefits of chemotherapy are independent of age [12,14]. Furthermore, neoadjuvant cytotoxic chemotherapy can result in favorable clinical outcomes in older patients with breast cancer [4,15]. However, reducing or discontinuing the dosage of chemotherapy is a common practice in older patients because of the adverse events associated with cytotoxic chemotherapy. Commonly reported adverse events of cytotoxic chemotherapy include haematotoxicity, nephrotoxicity, cardiotoxicity, and peripheral neuropathy [16-18]), with older patients being more susceptible to the aforementioned adverse events [19,20]. Therefore, comorbidities and potential toxicities for each patient should be considered when deciding whether to recommend neoadjuvant cytotoxic chemotherapy for older patients. In this case, although chemotherapy was discontinued due to an unexpected hemorrhage, neoadjuvant therapy exhibited an excellent clinical response, with the tumor size decreasing from 4.2 cm to 1.5 cm. Although cough is a relatively common and modest side effect of chemotherapy, a case of life-threatening coughing-induced spontaneous hemorrhage has been previously reported [21].
Other potential less common causes could explain this rare adverse event. First, cytotoxic chemotherapy may cause damage to endothelial cells [22,23]. Second, chemotherapy-induced thrombocytopenia (CIT) might also have played a role. As CIT is a common complication of myelosuppressive chemotherapy [24,25], it can lead to a delay or dose reduction in chemotherapy due to major or minor bleeding [26]. The incidence and prevalence of CIT varies according to the type of cancer and chemotherapy regimen used. In one study, the prevalence of CIT was 21.9% in patients treated using taxane-based regimens [27]. The incidence of grade 3 or 4 CIT in patients with breast cancer treated with taxanes was 1.9% [28].

In conclusion, we report a case of life-threatening nontraumatic rectus sheath hematoma in an older patient with breast cancer who underwent taxane-containing cytotoxic chemotherapy. Our case demonstrates the complexity of the selective use of cytotoxic chemotherapy in older patients with breast cancer and the need for cautious monitoring of potentially rare adverse events.

REFERENCES


