Acute, Unilateral Breast Toxicity From Gemcitabine in the Setting of Thoracic Inlet Obstruction

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CASE PRESENTATION

A 63-year-old woman with metastatic lung adenocarcinoma presented with acute swelling and pain of her left breast. One year before admission, she was diagnosed with a 6.0-cm tumor in the left upper lobe and had undergone radiation, chemotherapy, and resection of metastases to treat her disease. Most recently, she was switched to single-agent gemcitabine. She was also taking warfarin for a history of lower extremity deep venous thrombosis.

The patient tolerated her first two infusions of gemcitabine without complication. However, 4 hours after the third infusion, she experienced acute onset of left breast swelling and pain, prompting her to present to the emergency department. She was found to have a diffusely enlarged, tender left breast without masses, induration, or fluctuance. Laboratory studies were only remarkable for a C-reactive protein (CRP) that was elevated to 6.6 mg/dL (normal, $<$ 0.9 mg/dL). The patient was started on broad-spectrum antibiotics for a presumed soft tissue infection, but her condition progressed over the next 2 days. Her left breast became twice the size of her right breast, with erythema, warmth, and severe tenderness to light palpation (Fig 1A). Dilated veins were prominent on her left anterior chest. There were no abnormalities of the ipsilateral antecubital fossa or forearm. Her CRP had increased to 19.7 mg/dL, yet she remained afebrile, with a normal white blood cell count and serum lactate level.

The patient had received the first two gemcitabine infusions in her right arm, whereas the most recent infusion was administered through a peripheral intravenous catheter in her left arm. Furthermore, a recent chest computed tomography scan demonstrated the tumor in her left upper lobe invaded into the first and second ribs, with compression of the left subclavian and brachiocephalic veins. It was therefore suspected that her breast toxicity was a result of the gemcitabine infusion. Antibiotics were discontinued, and the patient was treated with oral prednisone 40 mg per day for 5 days. The patient's CRP decreased to 5.6 mg/dL after 3 days of treatment, and her erythema and tenderness resolved. The patient underwent placement of a port in her right upper chest and received subsequent gemcitabine infusions through the port without complication. Breast swelling decreased by 50% over 1 month, and stenting was considered to improve central venous return. Left arm venography demonstrated complete occlusion of the left subclavian vein with reversed flow through paired lateral thoracic veins into the left breast (Fig 1B). Stenting was deferred given the diminutive size (3 mm) of the axillary vein.

DISCUSSION

Cutaneous toxicity from gemcitabine is common but typically mild, with an

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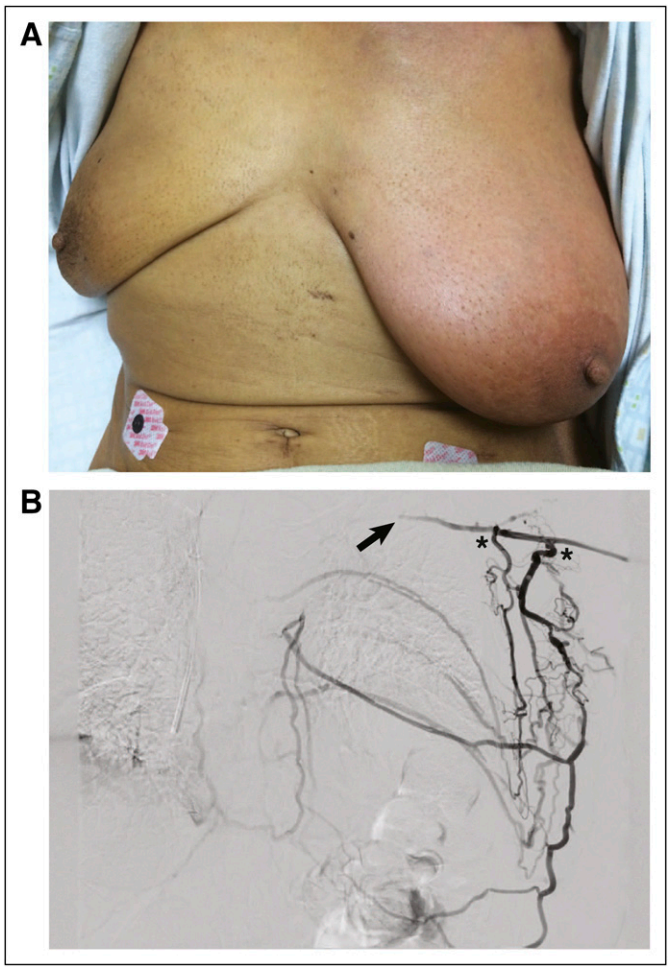

FIG 1. (A) Appearance of the breasts on the day of discharge, with persistent, diffuse left breast swelling and erythema. (B) Digital subtraction venogram of the left basilic vein demonstrating complete occlusion of the left subclavian vein (arrow) with enlargement of paired lateral thoracic veins (*) and reversed flow (caudally) into the left breast.

approximate 25% incidence but only 0.7% of infusions resulting in serious rash.[1] Gemcitabine is not considered a vesicant because extravasation injuries are rare, but this case demonstrates the potential of gemcitabine to act as an irritant, causing tissue inflammation and severe pain.

Central venous obstruction often leads to dilated chest vein collaterals,[2] and unilateral breast swelling has been described in other rare cases of altered or obstructed venous flow.[3-5] Subclavian vein occlusion typically leads to hypertrophy of the venous structures in multiple regions, including the costocervical and thyrocervical venous distributions. In this instance, these collateral pathways were ablated by tumor involvement and/or radiation damage, leading to reversal and primary flow through lateral thoracic veins. Consequently, the patient suffered from a supratherapeutic local concentration of gemcitabine in the left breast due to altered venous return. Tumors in the lung apices are among the most common causes of thoracic inlet obstruction. This case illustrates that special caution must be taken when administering cytotoxic therapies through peripheral lines in the setting of superior sulcus tumors or vascular compromise. JOP

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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