

DRUG POINTS

Epirubicin for breast cancer may cause considerable venous sclerosis

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The use of the adjuvant epirubicin for breast cancer in the United Kingdom has increased since initial data from the national epirubicin adjuvant trial (NEAT) were presented in 2003.¹ Two women, aged 53 and 55 years, developed pain and restriction of movement of the arm due to venous sclerosis after having infusions of epirubicin. They both had grade 3 invasive ductal carcinoma and had had surgery and axillary node dissection followed by eight courses of adjuvant chemotherapy using the epirubicin, cyclophosphamide, methotrexate, and fluorouracil regimen. This includes four cycles of epirubicin 100 mg/m² given at 21 day intervals.

Neither woman experienced extravasation or pain at the sites of infusion. The first woman had the first two injections into a large antecubital vein. At the time of the second infusion, two other ipsilateral antecubital veins had thrombosed. The infused vein became hard, swollen, and tender 18 days after the second infusion. Subsequent doses were given into two different veins in the back of the hand. The vein used for the third infusion thrombosed together with associated nearby veins, leading to painful symptoms within a week or two in the network of veins further up the arm. The fourth infusion was given into the back of the hand and resulted in sclerosis of veins on the anterior surface of the arm proximal to the wrist, but not directly involving the infused vein.

The second woman described similar symptoms, with aching and pain in the arm days after the second infusion. Both patients experienced pain on extension of the elbow due to tightening of the affected veins and developed puckering of the skin over most of the venous networks in the arm (figure). Similar symptoms developed around the wrist; extension and flexion became painful, lasting more than three months. The second woman gave up driving her car.

This complication had not previously been reported to the Committee on Safety of Medicines or the drug company, although the serious effects of extravasation of the drug are known.^{2,3} The medical information for epirubicin contains a limited statement indicating venous sclerosis occurs if small veins are used or with

repeated use of the same vein. Irritant drugs are those defined as causing symptoms such as these, which are described as self limiting with no long term sequelae.² The experience of these women indicates that venous sclerosis may be more extensive and troublesome than has previously been recognised, and that extravasation injury is merely the tip of the iceberg.

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- 1 Poole C, Earl H, Dunn JA, Hiller L, Bathers S, Spooner D, et al. NEAT (National Epirubicin Adjuvant Trial) and SCTBG BR9601 (Scottish Cancer Trials Breast Group) phase III adjuvant breast trials show a significant relapse-free and overall survival advantage for sequential ECMF. *Proc Am Soc Clin Oncol* 2003;22:4(abstr 13).
- 2 Schrijvers DL. Extravasation: a dreaded complication of chemotherapy. *Ann Oncol* 2003;14(suppl 3):S26-30.
- 3 Bertelli G. Prevention and management of extravasation of cytotoxic drugs. *Drug Saf* 1995;12:245-55.

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Left arm of the first woman showing puckering of the skin due to a sclerosed network of forearm veins