Anthracycline-induced cardiomyopathy in siblings with early breast cancer

A 41-year-old woman with no significant previous medical or family history underwent a left wide local excision (WLE) and axillary node clearance for a 9-mm grade 3 IDC, node-negative breast cancer. The tumour was estrogen receptor (ER), progesterone receptor (PgR) and HER-2 negative. She received six cycles of adjuvant chemotherapy with 5-fluorouracil, epirubicin and cyclophosphamide (FEC 75, total dose of epirubicin 450 mg/m$^2$) and adjuvant radiotherapy (40 Gy in 15 fractions) with a boost to the tumour bed (10 Gy in 5 fractions), completing treatment in February 2005.

She remained well in routine follow-up with no evidence to suggest recurrence of her breast cancer but in 2008 developed symptoms suggestive of cardiac failure and was found to have a cardiomyopathy. Subsequently, she has required insertion of a defibrillation device because of the risk of a life-threatening tachyarrhythmia. She remains well in relation to her cardiomyopathy but since insertion has utilised the defibrillation device on two occasions. To date, she remains recurrence free. The patient’s mother subsequently developed breast cancer.

The patient’s sister, aged 43 years, presented in October 2009 with a left breast cancer. Her medical history was uneventful. She underwent a left WLE and sentinel lymph node biopsy. Histology confirmed an 18-mm grade 3 IDC, which was node negative (zero of two sentinel lymph nodes). The tumour was ER positive, PgR negative and HER-2 negative. Her echocardiogram was normal with a normal left ventricular ejection fraction (LVEF). She received six cycles of adjuvant chemotherapy with epirubicin and cyclophosphamide (EC 90, total dose of epirubicin 540 mg/m$^2$) and adjuvant radiotherapy, completing treatment in April 2010. On completion of her chemotherapy, she was commenced on adjuvant tamoxifen. BRACA1 and BRACA2 genetic testings were negative.

In August 2010, she attended for routine review and was unwell with ankle oedema, a 5-week history of increasing breathlessness, orthopnoea and paroxysmal nocturnal dyspnoea. She had a sinus tachycardia with a gallop rhythm and an electrocardiogram showed the presence of Q-waves in leads V1–V3. An echocardiogram showed severely reduced contractility of the left ventricle and a large apical intraventricular thrombus consistent with severe cardiac failure. She was anticoagulated and treated with diuretics, a beta-blocker and an angiotensin-converting enzyme-inhibitor. A 4D cardiac scan estimated her LVEF to be 16%.

This is the first reported case in the literature of siblings both developing presumed anthracycline cardiotoxicity [1, 2] following treatment of early breast cancer, with no evidence of preexisting cardiac dysfunction. There is no established link between increased risk of anthracycline cardiotoxicity and breast cancer associated with a strong family history or any of the known high penetrance breast cancer predisposition genes [3].

The use of anthracycline-based chemotherapy in early breast cancer is in routine practice worldwide. Long-term survival of patients with breast cancer is increasing and thus side-effects of adjuvant treatment including cardiotoxicity are of increasing importance [4, 5].

The case described suggests that anthracycline cardiotoxicity may be related to genetic predisposition and supports ongoing research in this area. A family history of anthracycline-induced cardiomyopathy should alert clinicians to the possibility of enhanced susceptibility to cardiotoxicity from anthracyclines and may represent a rationale for the use of non-anthracycline adjuvant therapy.

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Disclosure

All authors declare conflict of interest.

References


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