Sudden death during adjuvant trastuzumab therapy of breast cancer

Trastuzumab is a major treatment breakthrough for Her2-positive breast cancer (BC). Its only worrisome toxicity is cardiac, manifested as congestive heart failure (CHF) from left ventricle (LV) systolic dysfunction [1, 2]. In contrast to anthracycline-related CHF, trastuzumab-related LV dysfunction can be reversed by treatment discontinuation and supportive treatment. To our knowledge, there are no reports of non-CHF deaths related to trastuzumab. We report an asymptomatic patient who had sudden death (SD) while receiving adjuvant trastuzumab.

A 57-year-old woman underwent breast conservation surgery in March 2008 for a pT1cN1M0, grade 2, estrogen receptor-negative, progesterone receptor-negative, Her2-positive invasive ductal carcinoma of the left breast. Her past medical history was remarkable for a depressive syndrome treated with tianeptine, diazepam and estazolam, a prior episode of multiform erythema with skin and liver involvement attributed to lamotrigine and supraventricular extrasystoles documented on a Holter 6 months before surgery, medicated with atenolol. The prechemotherapy echocardiogram showed mild posterior leaflet mitral valve prolapse and normal LV systolic function (shortening fraction of 28%). She was treated with six cycles of TAC (docetaxel, doxorubicin and cyclophosphamide) followed by adjuvant radiotherapy (64 Gy, left breast) with minimal toxicity. An echocardiogram carried out 6 weeks after the last cycle of chemotherapy and before trastuzumab documented normal LV function (shortening fraction of 38%). She started tamoxifen in September and adjuvant trastuzumab in October. In January 2009, the patient had a short hospital admission for depression triggered by the death of a friend from BC. On 16 March, an echocardiogram showed mild posterior mitral valve prolapse and normal LV systolic function (shortening fraction of 23%), absence of wall motion abnormalities and left atrial enlargement (64 mm). Her cardiologist stopped atenolol and started perindopril (5 mg/day). Trastuzumab was withheld (last infusion on 9 March) and an echocardiogram was programmed for 1 month later. Fourteen days later, she was found dead at home, after having talked to her husband a few hours earlier; there was no evidence of suicidal intent. Autopsy showed LV hypertrophy, myocardial lymphocytic infiltrate, pulmonary congestion and no evidence of BC. Arrhythmia was assumed and reported as the cause of death.

Despite serial cardiac monitoring, symptomatic or asymptomatic LV dysfunction may develop with trastuzumab [1]. This patient had an asymptomatic decrease in LV systolic function, which led to trastuzumab withdrawal. However, SD did occur, presumably from cardiac arrhythmia. To our knowledge, there are only three reported cardiac events not related to pump failure, but none associated with SD. One patient experienced syncope with documented bradycardia from sinus node dysfunction [3], one palpitations and near-syncope with nonsustained ventricular tachycardia on Holter monitoring [4] and a third patient had chest pain with T-wave inversion in the anterior precordial leads without decrease in LV ejection fraction [3]. We believe that the patient now reported had sudden cardiac death from arrhythmia, which may have been triggered by the proarrhythmic effect on antidepressants, in the setting of subclinical LV dysfunction. We caution on the potential cardiac risk of concomitant use of potentially proarrhythmic drugs, such as antidepressants, in patients undergoing treatment with trastuzumab, at least if there is impairment of LV function.

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references


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