

Supraventricular Tachycardia in a Patient on Trastuzumab

Sir,

Trastuzumab is a recombinant DNA derived humanized monoclonal antibody that has significant antitumour activity in patients with human epidermal growth factor receptor – 2 (HER2) – overexpressing metastatic breast cancer. Treatment with trastuzumab results in many durable objective responses as a single agent. The drug is generally safe, however, decrease in left ventricle ejection fraction

(LVEF) was observed as the important cardiac toxicity in pivotal trials. Supraventricular tachycardia as a cardiac toxicity has not been reported. Here, we report one such patient who developed supraventricular tachycardia while on Trastuzumab.

CASE: Mrs. M.U., a 42-year-old perimenopausal lady presented in October 2003 with lump in

right breast. She had no other significant medical history. All other investigations, x-ray chest, ultrasound scan, ECG, and 2D Echo were within normal limits. She underwent right modified radical mastectomy in October 2003. Histopathology was suggestive of infiltrating duct carcinoma grade III, 8/9 nodes were positive. Cut margins were free. Immunohistochemistry stain for Estrogen and progesterone receptor – was negative and for C-erb-2 was positive.

She received 3 cycles of chemotherapy with 5-fluorouracil, epirubicin, and cyclophosphamide. While on chemotherapy, she complained of backache. Bone scan was suggestive of bony metastases. In view of metastatic disease, and she being cerb2 positive, she was started on Trastuzumab (Herceptin), IV, a monoclonal antibody against C-erb-2.

She received three doses of Trastuzumab. On February 3rd, 2004, when she was due for 4th dose, she complained of palpitation. On clinical examination, she had tachycardia, BP was 90/70mm Hg. 12 lead ECG was suggestive of paroxysmal supraventricular tachycardia. She was immediately shifted to ICCU and given carotid massage to which there was no response. She was then given inj. Adenosine 6mg IV. Patient immediately reverted to sinus rhythm. Patient was observed and discharged. Since this episode, she is in normal sinus rhythm.

COMMENTS

HER-2; a tyrosine kinase receptor protein is over-expressed in 25-30% of patients with breast cancer, usually as a result of gene amplification. This alteration is associated with an adverse prognosis. Laboratory evidence have suggested that the overexpression of HER-2 has a pathogenic role in malignant transformation, hence it makes the inhibition of this receptor a logical therapeutic strategy. Overexpression of HER-2 has been associated with potentially more aggressive tumours.

Trastuzumab is a humanized monoclonal antibody used for the treatment of metastatic breast cancer in women whose tumour overexpress the HER2 protein. Trastuzumab produces durable objective response as a single agent and produces statistically significant improvements in response rate, median overall survival when used in combination with chemotherapy as compared to chemotherapy alone. Responses rates to the antibody given as a single agent have ranged from 12% to 27%.

An unexpected adverse effect first observed during the pivotal trials of trastuzumab was cardiac dysfunction observed in 3% to 7% of women treated with this drug as a single agent. Most common adverse effect is - asymptomatic fall in left ventricular ejection fraction (LVEF) or symptomatic cardiac failure. In the combination chemotherapy trial, the incidence of any cardiac dysfunction (including all grade of dysfunction) was 27% for patients treated with trastuzumab plus an anthracycline and cyclophosphamide, 8% for those receiving trastuzumab plus paclitaxel alone. Thus, the risk of cardiac dysfunction was greatest in patients receiving trastuzumab in combination with anthracycline / cyclophosphamide. The majority of reported cardiac effects are mild to moderate, non-specific and medically manageable. The exact pathogenesis and histologic changes responsible for trastuzumab-associated cardiotoxicity are under investigation. There is some in vitro evidence that HER-2 may be involved in myocyte resistance to stress or repair. HER-2 receptors and ligands are expressed in the heart. HER-2 activates transcription factors such as activator protein 1, involved in regulation of cardiac hypertrophy and NF- κ B involved in cellular response to stress.

Our patients had no dyspnea. She had no other previous cardiac ailments and her baseline 2D echo was normal. She complained of palpitations after receiving 3 doses of trastuzumab. Her supraventricular tachycardia responded to adenosine. Repeat 2D Echo after

the episode is also normal. Supraventricular tachycardia as an isolated cardiac toxicity with trastuzumab has not been repeated so far.

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