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Editorial

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Trastuzumab and ECG Changes Dilemma

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Trastuzumab and ECG changes dilemma

Trastuzumab (Herceptin) is a humanized monoclonal antibody that targets the human epidermal growth factor receptor 2 (HER2)[1]. Trastuzumab is important in the treatment of HER2+ breast cancer, gastric, and colorectal carcinoma [2].

One of the known side effects of Trastuzumab is cardiotoxicity. The most important cardiac complications of Trastuzumab in previous studies included asymptomatic left ventricle dysfunction or symptomatic heart failure [3].

Periodic electrocardiographic assessment is recommended in patients receiving Trastuzumab. The ECG changes that have been reported in patients treated with Trastuzumab in studies so far include new negative T-waves in ECG, ventricular bigeminal rhythm, changes in the T-wave or ST-segment (depression or elevation), unspecified arrhythmias, sinus bradycardia, asymptomatic left bundle branch block (LBBB), asymptomatic right bundle branch block (RBBB), atrial fibrillation (AF), and non-sustained ventricular tachycardia (VT)[4-6].

Patients, who are candidates for Trastuzumab, range from those having no risk factor for cardiac diseases to patients with cardiac risk factors or previous heart diseases. Cardiac examinations, including ECG and transthoracic echocardiography, are performed in patients receiving Trastuzumab before starting treatment and are repeated at least every three cycles according to the Cardio-Oncology Guidelines[7]. Patients, especially those at high risk, are candidates for treatment with HER2 inhibitors and may benefit from cardioprotective therapies with angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) and beta-blocker (BB). High-risk factors include exposure to multiple cardiotoxic agents, *previous* exposure to *cardiotoxic drugs*, a history of mediastinal radiotherapy, previous heart diseases, old age, smoking, diabetes, hypertension, dyslipidemia, chronic renal failure, and obesity[7-9].

For these patients, we started with low-dose beta-blocker and ACEi/ARB and gradually titrated the dose according to the patient's tolerance based on heart rate, blood pressure, and renal function.

Due to the positive cardiac protective effects of statins in patients with HER2-Positive breast cancer receiving Trastuzumab therapy in clinical trial [10], we started high-dose statin (the patient tolerated it well and had no contraindication) in patients with diabetes and hyperlipidemia and patients with a history of previous heart diseases. Meanwhile, we started low-dose statin in patients with other cardiac risk factors.

Some of our patients being treated with Trastuzumab and had normal ventricular function in echocardiography showed nonspecific changes in the ECG in the form of nonspecific ST-T wave changes

in the precordial leads. But, sometimes, the ECG changes showed a deep T invert and significant ST depression in precordial leads, which can mimic ischemia. These ECG changes usually happen after the fifth or sixth cycles.

We evaluated these patients in terms of ischemia with Gated Technetium-99m-Sestamibi SPECT or Stress echocardiography. No evidence in favor of ischemia was found in these modalities among patients. These patients had no other evidence of ischemia, including chest pain, shortness of breath, or regional wall motion abnormalities, and LVEF was normal.

These findings show that patients treated with Trastuzumab may undergo these important ECG changes, and paying attention to this issue with careful notice of clinical and echocardiographic data can eliminate many unnecessary diagnostic assessments in these patients.

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