



HER2 + Breast cancer – Case cardiotoxicity of trastuzumab therapy

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In recent decades, malignant diseases, represent a bigger and bigger problem of human population, and thus the challenge for scientists, researchers and clinicians worldwide. A special place occupies breast cancer, by far the leader in terms of number of cancer patients, and after death in the female population. 20-25% of all breast cancers characterized by HER2 positivity.

HER2 receptor belongs to a family of receptors for growth factors, which has a total of 4 (four) and are marked by HER 1-4. HER2 receptor by its structure is a glycoprotein, which is located in the normal epithelial cells. Encoded by a gene localized on chromosome 17. HER2 positive breast cancers are characterized by amplification of the HER2 gene or overexpression of the HER2 protein (receptor) on the cell surface. In most cases, both of these phenomena are simultaneous. In the modern therapeutic approach, HER2 positive breast cancer, the use of biological (immune) therapy based on humanized monoclonal antibody trastuzumab, occupies a central place. The mechanism of action of trastuzumab is based on a blockade of the HER2 receptor and there by prevention of the action of human epidermal growth factors on the growth and proliferation of tumor cells. It is applied after the anthracycline chemotherapy, in combination with taxanes, and also as mono agents. Proven is the most important side effect of trastuzumab cardiotoxicity. It manifests itself mainly as a reversible decrease contractile ability of the left ventricle. In rare cases takes irreversible character and manifested the symptoms and signs of dilated cardiomyopathy. In order to achieve the main objective of striking a balance between achieving the established therapeutic target and spotting the cardiotoxic effects, it is necessary to constantly bear in mind the contemporary guides and recommendations leading European cardiology and oncology associations (ESC ESMO), the algorithm monitoring, primarily based on echocardiography parameters. This approach allows the therapist, timely and appropriate response, including the use of cardioprotective therapy based on angiotensin converting enzyme inhibitors or angiotensin receptor blockers and beta blockers application.

In March 2004, patient aged 48 years, made a self-examinations due to observed changes in the left breast. Less than two months earlier the patient noticed the

change, but wasn't immediately reported to the doctor after she noticed an increase in the change of node. Then, she asked for help in the Institute for Oncology and Radiology of Serbia in Belgrade. From anamnesis we get the information that patient has premenopausal irregular menstrual cycles, with the denial of the personal history of cardiovascular disease and does not use any cardiac medications or other therapies.

Once fully implemented diagnostic diagnosis is cancer of the left breast with the HP findings: CDI gl. mammae GR II II NG hormone positive and HER2-positive tumor. Based on the consultative decisions therapy course was as follows: radical mastectomy left, after that, in the context of adjuvant treatment was carried out 6 cycles of FAC HT, postoperative RT left hemothorax, and less than 5 years of adjuvant hormone therapy Nolvadex. After completion of adjuvant treatment, the patient is converted to the regime of regular check-ups. In May 2009, as part of routine monitoring was performed MSCT thorax in which disease progression was measured by type of meta changes in the lung with mediastinal lymphadenopathy. The patient was shown to a specialist consultant to implement systemic chemotherapy Taxol + W-s.Herceptin. Initial echo of the heart, which was conducted before starting the application herceptin, left ventricular ejection fraction (LVEF) was identified as 65%. After three months of application of this therapy, the control was done. Echocardiogram showed LVEF 54%, which meant a drop in the value of an LVEF > 15% compared to baseline. The therapist decided to carry out a break of 4 weeks without the use of Herceptin and s. W-taxol times. After that, a new control was made; echocardiogram showed an insignificant increase in LVEF, which now stands at 55%, but with the subjective symptoms by an unusual type of fatigue and shortness of breath. Introduced cardioprotective therapy ACE inhibitors and beta blockers with strict monitoring of blood pressure values, potential contraindications for the use of cardioprotective therapy. HT System with Herceptin has been suspended until further notice for new 4 weeks. At the next control echocardiogram showed a marked increase in the LVEF, i.d. it was 60%. Continue the implementation of systemic HT W-Taxol with Herceptin. Achieved therapeutic response with

oncologic aspect was complete regression of lesions in the lungs and in the meantime the patient HT taxane ended with 20 cycles, while still ongoing system maintenance therapy with Herceptin (so far received 100 cycles). The aforementioned therapeutic response is maintained with good subjective submission and with regular echocardiographic controls. Until now no note of significant changes in LV voliens or LVEF were found.

Discussion

In recent decades, the use of biological therapies in the treatment of HER2 positive breast cancer has a leading role.

It is based primarily on the use of monoclonal antibody, trastuzumab, as in adjuvant approach, and in the treatment of metastatic HER2 + breast cancer. The most important side effect of trastuzumab is cardiotoxicity. In most cases it is manifested by a reversible decrease in contractile function of the left ventricle. Much less cardiotoxicity of trastuzumab takes irreversible character and manifests as dilate cardiomyopathy. This applies primarily to high-risk patients: older than 65 years, positive family and personal history of cardiovascular diseases, previously receiving anthracycline HT.

The main task of the therapist, is to detect signs of potential cardiotoxicity of trastuzumab and adequate response. That's the most important echocardiographic monitoring that is carried out according to a specific algorithm, in accordance with the guides and recommendations of European cardiology and oncology associations. Trastuzumab therapy is carried out in three-week intervals at which it is monitoring echocardiography initially, and then every three months after receiving the therapy. Upon completion of the same, echocardiographic controls could be done on 6 months and yearly. It is especially important for LVEF. Decrease value of LVEF of 15% or more compared to baseline, and 10% or more between the two measurements, implies the need for break in the application of trastuzumab 3-4 weeks and then re-check. If there is a recovery, the treatment could

be continued according to the protocol. If there is no recovery, or possibly on the eve of an LVEF value decrease or signs and symptoms of heart failure, introduced cardioprotective therapy, ACE inhibitors or beta blockers along with continued break in the application of trastuzumab and a new echo checking. Respect for algorithm monitoring in accordance with tiered guides and recommendations, but also with appropriate modifications, the best way to ensure a balance between therapeutic efficacy and potential toxicity of treatment.

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