Is anthracycline-induced heart failure reversible?

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A 38-year-old woman was referred to an oncologist due to multifocal left breast cancer as well as overexpression of estrogen receptor and human epidermal growth factor receptor 2 (HER2). Metastases to the axillary nodes were confirmed. Prior to oncological treatment, left ventricular ejection fraction (LVEF) was 71%. The patient received 4 cycles of anthracycline with a total dose of 240 mg/m². The control LVEF was 60% before the administration of paclitaxel and trastuzumab. After the second trastuzumab cycle, the patient reported shortness of breath. LVEF decreased to 35%. The patient was hospitalized due to resting shortness of breath and peripheral edema. Laboratory tests showed N-terminal pro-B-type natriuretic peptide level of 15,324 pg/ml (reference value, <125 pg/ml). On echocardiography at that time, LVEF was 15% and left global ventricular longitudinal strain was 5.1% (Figure 1A and B).

Due to no improvement after a dobutamine and furosemide infusion, levosimendan was added. An improvement in the patient’s condition was observed. On the third day after the end of the infusion, a significant increase in LVEF from 15% to 35% and global ventricular longitudinal strain of 14% were noted. A follow-up study showed a gradual decrease in LVEF from day 7 up to a baseline of 15% by day 10. A second infusion of levosimendan was given. On the third day after the end of the second infusion, a mastectomy was performed. The patient was discharged home after a week. After 2 months, she was hospitalized again because of heart failure (HF) exacerbation. LVEF dropped to 15%. She received a third infusion of levosimendan. The patient qualified for an implantation of a left ventricular assist device (LVAD) using the Heart Mate III system.

FIGURE 1 A – echocardiography, the parasternal view showing fluid in the pericardial sac (arrow); B – tissue Doppler echocardiography showing a reduced global longitudinal strain of the left ventricle; C – chest x-ray showing a left ventricular assist device (arrow)
The procedure was completed without complications. The 12-month follow-up visit showed an increase in LVEF to 50%. Currently, it is planned that the patient will discontinue the use of the device.

The prognosis of young patients with HER2-positive breast cancer with axillary lymph node metastases is usually poor, but the use of trastuzumab in combination with chemotherapy reduces the risk of recurrence by around 40%.

 Anthracyclines lead to symptomatic HF in up to 10% of patients. The incidence of cardiotoxicity after the use of anthracyclines reaches 9%, and 98% of cases occur within the first year.\(^1,2\) The total dose of anthracyclines taken accumulates. At a dose of 400 mg/m\(^2\), the risk of HF is about 5%; with a dose of 700 mg/m\(^2\), it can reach up to 48%.\(^1,3\) Anthracycline metabolites accumulate in the myocardial cells and disturb calcium hemostasis. Levosimendan increases the contractility of the heart by rising the sensitivity of troponin C to calcium. In our case, we observed an increase in LVEF from 15% to 35%, which reduced the risk of mastectomy. There are 2 reports in the literature of a lasting improvement in left ventricular systolic function after the administration of levosimendan in patients with anthracycline-induced heart failure (ACT). This suggests that levosimendan may be an effective drug in patients with anthracycline-related HF. The question remains regarding when to administer levosimendan for ACT and how many drug doses are needed for improvement.

For the first 5 years after cancer diagnosis, a patient with HF cannot be a candidate for a heart transplant. LVAD may be a bridge for heart transplantation in patients with a good oncological prognosis.\(^5\) ACT is considered irreversible. Perhaps the support of the left ventricle in a short time from the introduction of a HF LVAD implantation allows myocardial regeneration.

**ARTICLE INFORMATION**

**CONFLICT OF INTEREST** None declared.

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**REFERENCES**
