

# Case 01

## Chronic Anthracycline-Induced Cardiotoxicity

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### 1.1. Case Presentation

A 44-year-old woman with a history of invasive ductal mammary carcinoma (pT1, cN1a, G2, RH + HER2-) was admitted to the emergency department because of heart failure. The patient had been in her usual state of health until two months ago, when she reported progressive dyspnea, fatigue, abdominal distension, and peripheral edema. A total of 15 months before admission she had received combination chemotherapy with doxorubicin, cyclophosphamide and paclitaxel, followed by radiation therapy.

At the moment of presentation in the emergency department the patient complained of unease. She was alert and oriented. Her blood pressure was 100/50 mmHg; her heart rate was 110 bpm and her oxygen saturation was 91%. Auscultation revealed attenuated heart sounds with a pansystolic murmur (punctum maximum at the apex) and late inspiratory crackles audible over both lung fields. The ECG confirmed sinus tachycardia (110 bpm) with no associated repolarization abnormalities and the chest X-ray confirmed mild cardiomegaly and interstitial edema. Laboratory testing showed normal serum creatinine, NT-proBNP 32.560 pg/mL (normal range < 125 pg/mL), and TnI 0,25 ng/mL (normal range < 0,027 ng/mL). Upon diagnosis of acute heart failure, standard medical therapy was initiated.

Echocardiographic examination showed mild left ventricular dilatation (end diastolic volume 82 mL/m<sup>2</sup>) and global left

ventricular hypokinesia with overall severely impaired systolic function (2D-ejection fraction 24% and 3D-ejection fraction 27%) (**Video 1.1, Video 1.2, and Video 1.3**). Left ventricle filling pressures were also increased (E/E' ratio at the lateral side of mitral annulus of 22).

A severe decrease in global longitudinal strain (GLS -5.6%) was documented (**Video 1.4**), as well as a severe mitral regurgitation (**Video 1.5, Video 1.6, and Figure 1.1**). Right ventricular function was normal (TAPSE 17 mm; S' 11.2 cm/s).

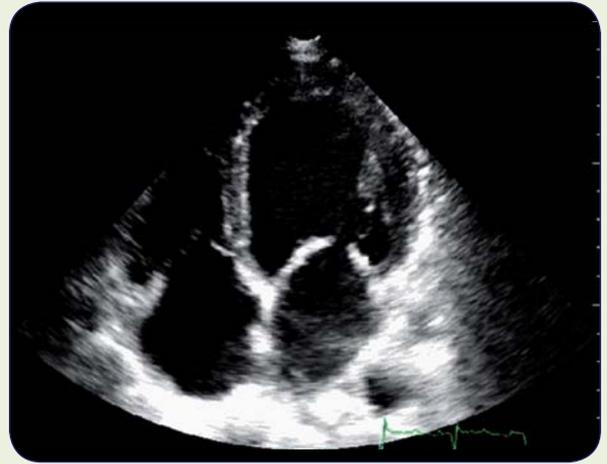
An echocardiogram performed eight months before, in order to rule out endocarditis, already revealed a mild reduction in left ventricular systolic function (end diastolic volume 75 mL/m<sup>2</sup>; 2D-Ejection Fraction 48%; E/E' 12; MAPSE 10 mm) and a mild mitral regurgitation.

Heart failure treatment was commenced, and at seven-months follow-up we found an initial recovery in echo parameters: 2D-ejection fraction of 45% (**Video 1.7**) with a GLS of -13% (**Figure 1.2**) and mild mitral regurgitation (**Video 1.8**). However, despite improvements in systolic function the patient continued to experience exercise intolerance and was finally referred to a cardiac rehabilitation heart failure program, which consisted of specific exercise training and congestive heart failure self-care counseling. At one-year follow-up she remained in NYHA class I and on beta-blocker, ACEI and eplerenone treatment.

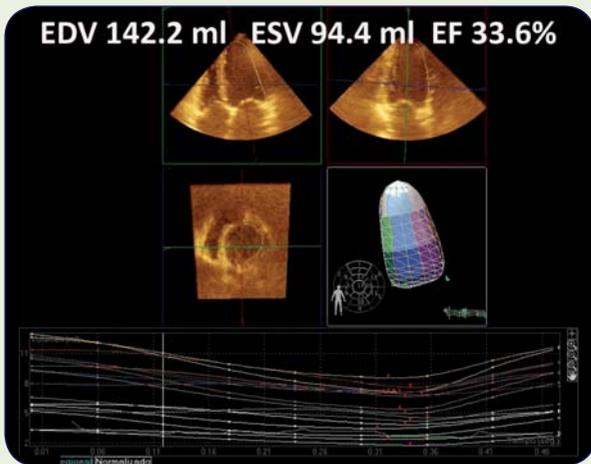
Videos



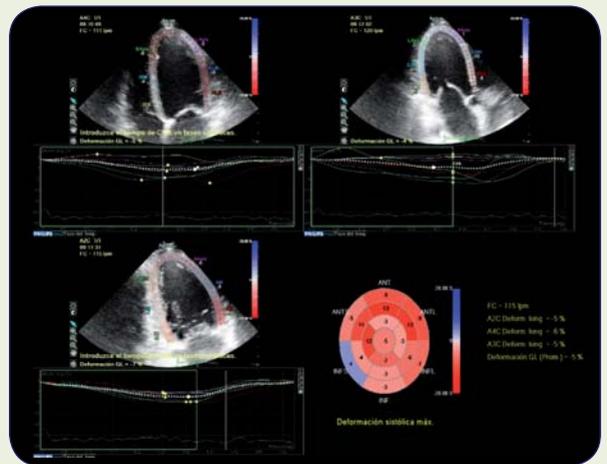
Video 1.1. 2D parasternal long-axis view of the left ventricle



Video 1.2. 2D four-chamber view



Video 1.3. 3D quantification of ejection fraction



Video 1.4. Global longitudinal strain measurement



Video 1.5. 2D color severe mitral regurgitation



Video 1.6. 3D evaluation of mitral regurgitation



## 1.2. Discussion

Cardiovascular complications due to cardiotoxicity of chemotherapy are a growing problem that limits survival in cancer patients. Retrospectively it seemed that we had missed the opportunity to properly treat our patient. According to heart failure guidelines the diagnosis of an asymptomatic decrease in ejection fraction below 53% in a patient receiving chemotherapy must be classified as stage B heart failure. Thus, treatment is recommended in order to prevent left ventricular remodeling and symptoms. Since a timely initiation of adequate treatment is critical to maintain a patient's chances of recovery and depends on early diagnosis, cancer patients need to be monitored systematically.

A delay on initiation of heart failure treatment significantly reduces the chances of recovery of ventricular function. However, in the real world, many cancer patients with asymptomatic decrease in ejection fraction are not referred for cardiac consultation and do not receive proper heart failure treatment. In a recent study performed at Stanford University the vast majority of cancer patients with asymptomatic decrease in the ejection fraction did not receive cardiology consultation (Yoon GJ, *et al.* Left

ventricular dysfunction in patients receiving cardiotoxic cancer therapies are clinicians responding optimally? *J Am Coll Cardiol* 2010; 56: 1.644-1.650). This suggests that closer collaboration between cardiologists and oncologists is needed to prevent and treat cardiovascular toxicity in cancer survivors.

Similar to other cardiac patients, cancer survivors are subject to the effects of deconditioning which eventually leads to a reduction in exercise tolerance. Cardiac rehabilitation programs through exercise training and heart failure self-care counseling confer significant clinical benefits on individuals with cardiotoxicity-related heart failure. Cardiac rehabilitation increases exercise capacity, improves clinical symptoms, enhances quality of life, and decreases future clinical events.

## 1.3. Conclusions

Cardiologists together with oncologists need to define criteria that help successfully identify high risk patients, introducing valuable and novel parameters (global longitudinal strain), so that therapeutic intervals are optimized.