

IMAGING VIGNETTE

INTERMEDIATE

CLINICAL VIGNETTE

Heart Transplantation for Early-Onset Anthracycline-Induced Cardiomyopathy Within 5 Months of Chemotherapy Completion



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ABSTRACT

A 9-year-old boy developed progressive anthracycline-induced cardiomyopathy three months after completion of chemotherapy for osteosarcoma. Five months after completion of chemotherapy, at the age of 10 years, heart transplantation was performed. At 29 months since transplantation, the patient remains free of rejection and recurrence of osteosarcoma. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1677-1679)

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A 9-year-old boy with high-grade osteosarcoma in the left humerus without metastases received treatment according to a 9-month-long EURAMOS-1 (European and American Osteosarcoma Study) protocol with good response (1). Radical surgery was performed, and no recurrence was detected. Anthracycline-induced mild left ventricular (LV) dysfunction (ejection fraction [EF] 55%, fractional shortening [FS] 28%) was observed in cardiac screening performed according to the EURAMOS-1 protocol after 300 mg/m² cumulative dose of doxorubicin (Figure 1A) and at completion of treatment (LV EF/FS 52%/28%, cumulative doxorubicin dose of 450 mg/m²) (1). Three months after completing chemotherapy, the patient presented to the emergency department with acute heart failure (HF). Echocardiography showed biventricular dysfunction: LV 3D-EF 20%, LV FS 10%, LV global longitudinal strain -3%, tricuspid annular plane systolic excursion 13 mm, right ventricular fractional area change 22%, and pericardial effusion (Figures 1A to 1C).

Based on the clinical evaluation, early-onset anthracycline-induced cardiomyopathy (ACM) was diagnosed. Despite intensive care, HF progressed, and a CentriMag LV assist device with Berlin Heart cannulas was implemented. During this operation, an endomyocardial biopsy (EMB) was taken to confirm the diagnosis. RV function was supported pharmacologically.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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**ABBREVIATIONS
AND ACRONYMS**

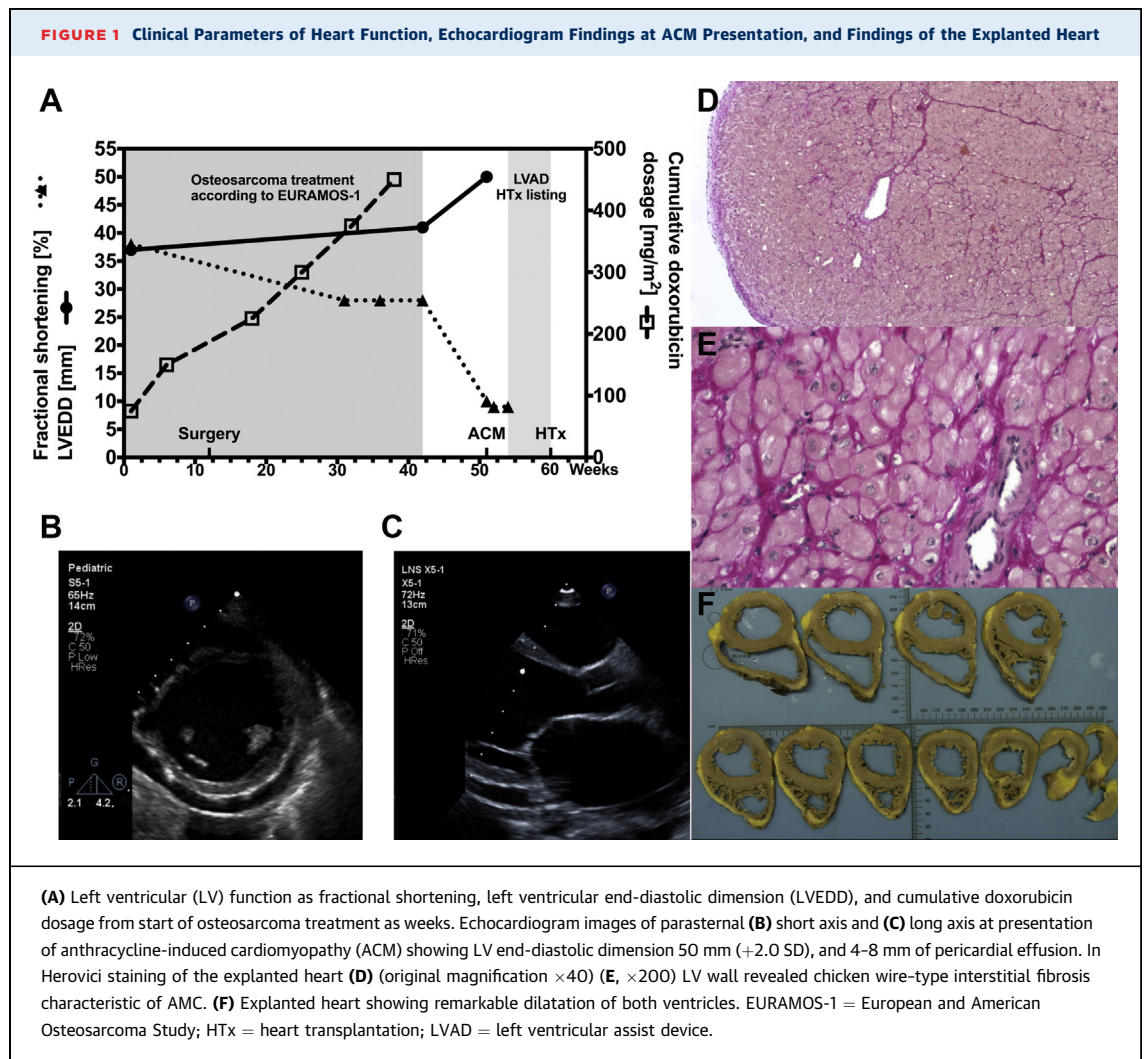
- ACM** = anthracycline-induced cardiomyopathy
- EF** = ejection fraction
- EMB** = endomyocardial biopsy
- FS** = fractional shortening
- HF** = heart failure
- HTx** = heart transplantation
- LV** = left ventricle/ventricular

The risk for osteosarcoma tumor recurrence, secondary malignancy, or death was estimated at 5% to 10% (1). On the basis of an international transplantation network consultation and multidisciplinary team evaluation, the patient was listed for urgent heart transplantation (HTx) after 2 weeks of intensive care.

Six weeks after listing, a HTx was successfully performed (see **Figures 1D to 1F** for explanted heart findings). The immunosuppressive therapy comprised tacrolimus, azathioprine, and steroids, with tacrolimus later replaced by cyclosporine because of septal hypertrophy. EMBs at 17 days and 1, 3, 6, 9, 12, and 24 months after HTx have revealed no rejection. At 29 months since HTx, the patient continues to thrive with no oncologic recurrence.

DISCUSSION

Approximately 2% of patients receiving anthracyclines present with congestive HF (2). The cardiotoxicity risk is dose dependent and is higher in younger patients (2). According to the International Society of Heart and Lung Transplantation guidelines from 2006, no arbitrary time for observation before HTx is necessary; instead, HTx can be considered based on individual assessment. This is supported by findings of cancer recurrence not increasing after pediatric HTx (3). The Pediatric Heart Transplant Study group, capturing data on approximately 80% of pediatric transplantation candidates worldwide, does not report time from completion of malignancy treatment to HTx in ACM (3). Notably, before this case, only two cases of early HTx <1 year after treatment of malignancy have been reported (3).



The osteosarcoma was initially treated according to the EURAMOS-1 protocol, wherein anthracyclines may be continued if FS is $\geq 28\%$ and EF is $\geq 50\%$ (1). It remains unknown whether the patient's outcome would have been improved by increasing echocardiographic sensitivity with strain imaging to detect ACM and by early initiation of cardioprotective treatment.

This case demonstrates HTx as a successful treatment option just 5 months after completion of chemotherapy in severe ACM with end-stage heart failure. When HTx is considered shortly after chemotherapy completion, individual assessment of life expectancy and recurrence risk remains essential.

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