patients developing cardiotoxicity. In 40 (17% of patients), enalapril was given. The remaining 186 patients received enalapril and carvedilol or bisoprolol. Intravenous diuretics were required only in patients hospitalized for acute heart failure. Oral diuretics were added to the therapy in 43 (20% of cases). One hundred eighty-five (82% of patients) recovered from cardiotoxicity, of those 25 (11% of patients) achieved full recovery, and 160 (71% of patients) achieved partial recovery (11).

Regarding cardiotoxicity, there is no safe cumulative dose of anthracycline. According to renowned experts in the field of cardio-oncology lifelong follow-up of childhood cancer survivors treated with anthracyclines is recommended. The most widely known are the recommendations of the Children's Oncology Group (drawing from evidence-based medicine) for the long-term follow-up of patients treated in childhood and under the age of 25 (5). According to these recommendations, the patient should be clinically examined annually after the completion of anthracycline treatment. At the same time, his blood pressure should be monitored annually and he should also be monitored by echocardiography (or using other imaging methods) regularly, according to the dose of doxorubicin (or equivalent dose of other anthracycline), age at time of diagnosis and chest radiotherapy as shown in Table 2. ECG also focusing on QTc interval should be performed after the completion of potential cardiotoxic treatment and later as needed. At the same time, the patient should be instructed on healthy lifestyle and aggressive management of cardiovascular risk factors. Any cancer patient under age of 5 years is considered to be at risk of cardiotoxicity when starting chemotherapy included anthracyclines. Our patient in the present article underwent cardiological examination in 2010, before the onset of cardiological symptoms, with the finding of diffuse hypokinesis and a slightly reduced LV ejection fraction of 50%. Twenty-seven years after the completion of chemotherapy, the patient develops manifestations of heart failure and is diagnosed with sinus tachycardia and numerous ventricular extrasystoles. There is no relevant evidence for acute viral myocarditis. This patient should have been monitored annually or every other year. With regard to the type of anticancer therapy and the development of dilated cardiomyopathy, late anthracycline toxicity is considered to be the aetiology of myocardial dysfunction in our patient. Endomyocardial biopsy was not indicated. The patient responded auspiciously to routine treatment of heart failure and we assumed that it would not provide information that would affect further treatment procedure. He is currently stabilized, but with a low LV ejection fraction of 30% (based on echocardiography in October 2019). After assessing the prognostic markers (good exercise tolerance, NYHA class II, improvement of LV ejection fraction, almost normal level of NT-proBNP), the short-term prognosis is considered good, and so the conservative treatment procedure is continued. The patient met the criteria for primary prevention of sudden cardiac death and was implanted with the ICD. Due to the narrow QRS complex on the ECG, cardiac resynchronization therapy (CRT) was not indicated. Heart transplantation is not excluded to be considered in the future. However, the presence of CADASIL syndrome may prevent the transplantation (12, 13). CADASIL syndrome is associated with possible serious neurological and psychiatric dysfunction at a young age. Authors Lesnik Oberstein et al. published a study on the possible association between CADASIL and myocardial infarction in 2013. In this study, NOTCH3 mutation was confirmed in 41 individuals. Thirty-two of the 41 mutation carriers had neurological symptoms, ranging from 1 transient ischemic attack to multiple strokes and cognitive decline. The evidence of myocardial infarction was found in 10 of 41 (24.4%) mutation carriers, 3 had a history of acute myocardial infarction and current Q/QS ECG abnormalities, 2 had a history of acute myocardial infarction but no current Q/QS abnormalities, and 5 had current Q/QS abnormalities without a history of acute myocardial infarction (silent myocardial infarction) (14).

In addition, the aetiology of restrictive ventilation disorder needs to be dealt with. It may involve paresis of the left diaphragm, which was noted by auscultation findings on admission and the chest X-ray. Symptoms of late anthracycline toxicity may also include arrhythmias. (2) In case of our patient we found frequent premature ventricular contractions (PVCs). PVCs may contribute to LV dysfunction and manifestation of heart failure. Interventional radiofrequency ablation therapy is currently available and can affect the ventricular ectopy substrate and eliminate or significantly reduce PVCs. As the number of ventricular extrasystoles decreased and LVEF improved, the intervention was indicated. The present case is similar to another 4-year old patient (published by us in 2010) who was treated with standard doses of chemotherapy containing cardiotoxic daunorubicin (at a cumulative dose of 375 mg/m^2), mitoxantrone, and with an allogeneic bone marrow transplantation. Twelve years after the diagnosis of acute myeloid leukemia, and following a viral infection of an unknown cause, he developed symptoms of heart failure. Severe dilated cardiomyopathy; and severe, left ventricular dysfunction with ejection fraction of 12% were found on echocardiography. The patient required a heart transplant 19 years after the diagnosis of leukemia at the age of 23 (15).

Conclusion

Late cardiac consequences after anthracycline therapy may become a complicated therapeutic problem even many years after successful anticancer therapy.

Although the treatment of heart damage is constantly improving, long-term follow-up of high-risk cancer survivors should focus on subclinical cardiotoxicity before the onset of such complications, in particular on possible progressive left ventricular dysfunction, by regular monitoring of levels of serum cardiac biomarkers and using of modern imaging methods. If the cardiac dysfunction has already progressed into a heart failure, no treatment guarantees a complete restoration of the heart function. In order to better understand the pathogenesis and dynamics of late cardiovascular complications after anticancer treatment and the possibilities of its primary and secondary prevention, further randomized studies are necessary.

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