

Severe acute cardiotoxicity following two intravenous doses of cyclophosphamide in an adolescent treated for rapidly progressive glomerulonephritis

Ostra kardiotoxyczność dwóch dożylnych dawek cyklofosfamidu u młodej chorej z gwałtownie postępującym kłębuszkowym zapaleniem nerek

Dariusz Runowski¹, Monika Brzezińska², Monika Kowalczyk², Ryszard Grenda¹

¹Department of Nephrology, Kidney Transplantation, and Hypertension, The Children's Memorial Health Institute, Warsaw, Poland

²Department of Cardiology, The Children's Memorial Health Institute, Warsaw, Poland

Here we report the case of 16-year-old female adolescent, who developed acute, life-threatening cardiotoxicity after two intravenous doses of 0.5 g/m² of cyclophosphamide (CYC), given for therapy of rapidly progressive glomerulonephritis (RPGN) in combination with plasmapheresis. She was treated for acute kidney injury related to biopsy-proven RPGN. The baseline two-dimensional echocardiography (ECHO2D) was normal, and the ejection fraction (EF) was 53%. The patient was put on plasmapheresis (n = 12), methylprednisolone pulses (0.5 g/dose; n = 13), and CYC pulses, scheduled on a monthly basis (6 × 0.5 g/m²). There was no improvement in the renal function during 10 weeks, and consecutive biopsy showed end-stage kidney disease. Regular dialysis was initiated. Overall only two doses of CYC were given. Two months later the patient presented heart failure. The Holter electrocardiogram showed sinus tachycardia and ventricular extrasystoles with the aberration of the repolarisation period. ECHO2D confirmed dilated cardiomyopathy with decreased EF (to 25%) and tricuspid (II grade) and mitral valves (II/III grade) insufficiency (Figs. 1, 2). The patient was put on intravenous milrinone (15 µg/kg/min) and carvedilol orally (0.5 mg/kg/day). Haemodialysis was switched to continuous veno-venous haemodiafiltration (CVVHDF). Despite this therapy, three consecutive episodes of cardiogenic pulmonary oedema had occurred. MIBI heart scintigraphy showed decreased EF of left ventricle (27%) and generalised disturbances of left ventricular function (Fig. 3). Mild fibrosis was present in myocardial biopsy (Fig. 4). After two months of treatment she recovered. Repeated ECHO2D showed the EF increase (up to 40%) and improvement in the function of the valves. CVVHDF was subsequently changed to regular haemodialysis and milrinone was stopped. Two months later the patient presented an episode of ventricular fibrillation. Heart function deteriorated again and the patient was regarded as candidate for combined heart–kidney transplantation. Echocardiography showed

further deterioration. Ivabradine (0.17 mg/kg/day) was initiated and the implantable cardioverter-defibrillator was surgically inserted. The patient's general condition and heart function stabilised over time. Final ECHO2D was normal. The qualification to heart–kidney transplantation was then limited to renal only. The case shows that acute, severe, CYC-related cardiotoxicity, reported so far mainly in oncologic adults > 60 years of age, may also occur in young renal patients with no history of previous cardiac disease and may be not dose-dependent. The mechanism of CYC-related cardiotoxicity is associated with direct oxidative injury of cardiomyocytes by acrolein, the toxic CYC metabolite.



Figure 1. Two-dimensional echocardiography during acute phase: low ejection fraction

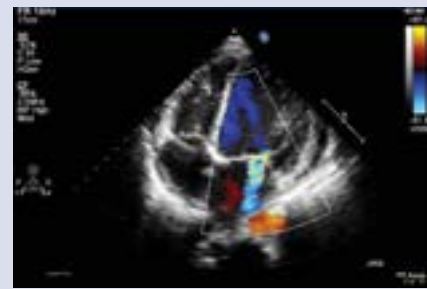


Figure 2. Two-dimensional echocardiography during acute phase: valvular insufficiency

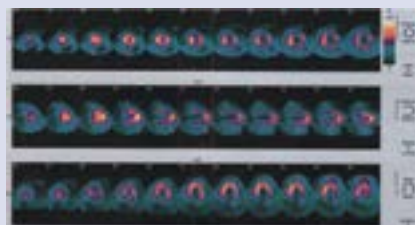


Figure 3. 99mTc-MIBI: generalised defect of perfusion and dyskinesia of left ventricle

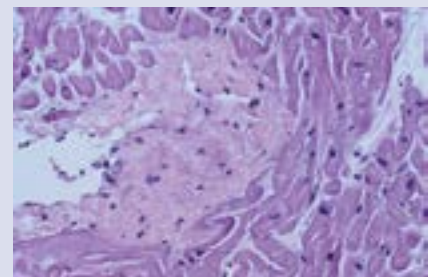


Figure 4. Myocardial biopsy — mild fibrosis

Address for correspondence:

Prof. Ryszard Grenda, MD, PhD, The Children's Memorial Health Institute, Aleja Dzieci Polskich 20, 04-730 Warszawa, Poland, e-mail: r.grenda@ipczd.pl

Conflict of interest: none declared

Kardiologia Polska Copyright © Polskie Towarzystwo Kardiologiczne 2016