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Risk Stratification and Pattern of Cardiotoxicity in Pediatric Ewing's sarcoma

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Background: Improved therapies for childhood cancers have increased the number of survivors; however, they are prone to adverse effects. One of the common effects of treatment is cardiac dysfunction resulting mainly from therapy with anthracyclines.
Patients & Methods: Ewing's Sarcoma patients at Children's Cancer Hospital Egypt (CCHE) from July 2007 till December 2011, were retrospectively evaluated for the incidence, pattern, and severity of cardiotoxicity. Echocardiographic findings at baseline, throughout treatment, and latest follow-up in December 2012. Severity of cardiac disorders were based on Common Toxicity Criteria, 2010. Onset was classified into, acute (developed during protocol treatment), early (within one year from end of treatment), or late (after one year from end of treatment). Results: One hundred and forty nine patients, were treated according to Ewing's sarcoma protocol with alternating courses of vincristine, doxorubicin, cyclophosphamide and Ifosphamide , etoposide with mean age at presentation of 10 years (2-18), 88 males (59%) and 61 were females (41%). 39 patients (26%) developed cardiotoxicity as evaluated by echocardiography based on reduced left ventricular (LV) systolic performance evidenced by reduced ejection fraction (EF%) and fraction shortening (FS%). A statistical significance between the mean EF at initial presentation (mean = 66.6%) and the mean of the lowest EF (mean = 43.6%), was found (p-value < 0.001), with a mean time to develop cardiotoxicity at 17 months (5 - 49 months). The onset of cardiotoxicity was acute in 17 patients (11.4%), early in 14 patients (9.4%), and late in 8 patients (5.4%).
According to the percentage of decline in EF based on CTC criteria, it was found that 13 patients (33%) were classified as grade I (EF drop <10% from baseline), 16 patients (41%) were grade II (EF Drop 10-19%), 9 patients (23%) were grade III (EF Drop 20-29%), and 1 patient (3%) was grade IV (EF drop >29%).
No correlation was found between the incidence of cardiotoxicity and age, gender, onset, cumulative doxorubicin dose, and follow-up duration. However, the onset of cardiotoxicity was significantly correlated with the cumulative doxorubicin dose (p-value= 0.012). Only 4 patients received mediastinal irradiation, 2 of them developed acute cardiotoxicity post-radiotherapy.
Out of 39 patients, seventeen recieved antifailure measures, eighteen presented with clinical manifestations, while only eleven patients (28%) showed improved LV systolic performance, while 6 patients died from cardiotoxicity. The rest remained with impaired systolic function until the latest follow-up.
Conclusion: All patients were affected by dropping their EF, but not all of them (only 26%) had cardiac toxicity, the onset of cardiac toxicity was significantly correlated with cumulative doxorubicin dose. The incidence of cardiac toxicity was not correlated to presumed risk factors. About one third of patients having cardiac toxicity can be salvaged by therapy.

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