Progressive conduction disease late after adriamycin treatment of lymphoma, despite normalised ejection fraction

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Adriamycin (doxorubicin) chemotherapy is known for its acute and late cardiotoxic complications1. In up to 2% of patients they manifest in the form of suppressed ventricular systolic function with its well known consequences, raised filling pressures and mitral regurgitation. Its potential direct effect on conduction disturbances, however, has not been systematically described. We present a case of a patient who had severe heart failure following adriamycin lymphoma treatment who despite full recovery of systolic left ventricular (LV) function developed progressive conduction disease that required life saving cardiac pacing.

A 56-year old male with known asthma presented with skin rash and was diagnosed with T-cell lymphoma. He was commenced on chemotherapy with CHOEP (including doxorubicin 50 mg/m² and 90 mg at a time) and by the end of the fourth cycle (four months of treatment) he was admitted with cardiogenic shock with raised inflammatory markers and liver enzymes. The patient received full heart failure treatment and antibiotics for secondary pneumonia. Three weeks later the cardiopulmonary function was stabilized and he was moved to a rehabilitation unit. During admission, LV ejection fraction was less than 40%, which recovered over time and 3 years later increased to 70%. In contrast, during admission QRS duration was 118 ms with normal axis which progressively broadened, becoming 155 ms associated with first degree heart block (P-R interval >260ms) and right axis deviation, consistent with bilateral Bundle Branch Block (Fig 1). As a result of the progressive conduction disease, the patient developed significant LV asynchrony that compromised his total filling time to 150 ms (normal 400 ms). A pacemaker implantation was recommended for prognostic reasons.

Conventional assessment of cardiac function before treatment is based mainly on ECG and non-invasive measurement of LV ejection fraction2. Our patient followed this protocol, having had normal ECG and ejection fraction before chemotherapy but developed severe cardiac dysfunction following the fourth cycle. The likely explanation of such complication is progressive subendocardial fibrosis related to the adriamycin cardiac toxicity. This is supported by the known prolonged adriamycin concentration in the myocardium in these cases3 as well as the published histological evidence for subendocardial fibrosis4. There was no evidence for additional coronary artery disease.
as a potential cause for the conduction disease. The only risk factor this patient had was smoking and when presented with tachycardia he did not have any ECG manifestation of ischaemic pathology. It seems therefore that the late progressive conduction disease parallels that known after radiotherapy, when patients develop significant myocardial, pericardial or valve disturbances.

Discussion

Current clinical practice in this scenario supports the use of ejection fraction as the hallmark for the follow up of LV function, which, once regained warrants no further attention. The paradox we have in this case is the progressive deterioration of electric cardiac function which ended with a picture of bilateral bundle branch block. These patients are known to have their ventricle activated solely via the Maheim fibres at the top of the interventricular septum. With such degree of heart block, prolongation of PR interval, and delayed depolarisation, broad QRS duration, they become electrically and mechanically unstable and require permanent cardiac pacing for prognostic purposes, even if not for symptoms. These patients are known to have severe dyssynchrony and compromised stroke volume and cardiac output. In addition, early diastolic dyssynchrony itself, compromises coronary flow, resulting in perpetual subendocardial ischaemia and instability.

Thus, although ejection fraction recovers after chemotherapy in these patients, a simple routine ECG may indicate progressive conduction disease that has serious mechanical consequences irrespective of symptoms. Since the core disturbances are electromechanical and of known poor prognosis, they can only be managed by cardiac pacing with optimum time intervals, enough to secure adequate stroke volume.

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