Chemotherapy-induced cardiomyopathy

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Articles in this section are inspired by, but not based on, real cases to illustrate the importance of knowledge about ECGs in relation to clinical situations in general practice. Management is not discussed in detail.

Mary is a 61-year-old woman who had a left-sided breast cancer diagnosed and treated two years ago. She had a lumpectomy, left-sided axillary radiotherapy and chose to have chemotherapy. Her baseline cardiac examination and investigations were normal before chemotherapy but afterwards she developed type I cardiotoxicity (which is more serious than type II and irreversible). This manifested at the time as myocarditis, with a small increase in serum troponin level and a reduced ejection fraction of 40%. Mary's condition stabilised and she has since been taking enalapril 10 mg/day. She comes to see you for a routine referral to her cardiologist but mentioned that she has noted some mild, new persistent ankle swelling and mild shortness of breath when walking up stairs. You perform an ECG (see Figure).

Q1. What does this ECG show?

This ECG shows evidence of four-chamber enlargement consistent with dilated cardiomyopathy. The combination of left ventricular hypertrophy (S wave in lead V2 >35 mm) plus right axis deviation indicates biventricular enlargement. There is also evidence of left atrial enlargement (deep, wide negative P wave in lead V1) and right atrial enlargement (peaked P wave in lead II). The ECG also shows nonspecific ST wave changes and T wave flattening, a QT interval of 400 msec and a decreased QRS voltage.

Q2. What is the likely diagnosis?

Based on Mary's history, the most likely diagnosis is a dilated cardiomyopathy after chemotherapy. The new symptoms indicate that Mary's condition has probably progressed and that she has now developed New York Heart Association (NYHA) stage II heart failure.

Q3. What are the NYHA stages of heart failure?

The four classes of the NYHA stages of heart failure and the associated symptoms are shown in the Table.

Q4. What factors predispose an individual to chemotherapy-induced cardiomyopathy?

The crucial factor that can affect an individual's predisposition to developing

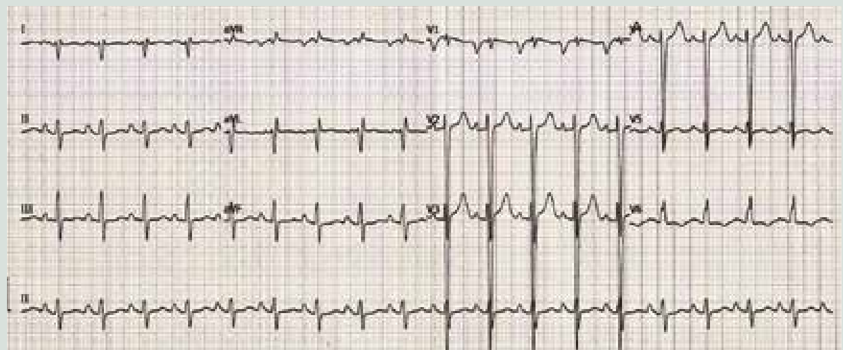

Figure 1. ECG showing dilated cardiomyopathy after chemotherapy.
Image courtesy of Dr Ed Burns and Life in the Fast Lane. http://lifeinthefastlane.com

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Table. The New York Heart Association stages of heart failure

Class	Patient symptoms
I	No limitation of physical activity; ordinary physical activity does not cause undue fatigue, palpitations or dyspnoea (shortness of breath).
II	Slight limitation of physical activity; comfortable at rest; ordinary physical activity results in fatigue, palpitation or dyspnoea.
III	Marked limitation of physical activity; comfortable at rest; less than ordinary activity causes fatigue, palpitation or dyspnoea.
IV	Unable to carry on any physical activity without discomfort; symptoms of heart failure at rest; if any physical activity is undertaken, discomfort increases.

chemotherapy-induced cardiomyopathy is the type of chemotherapy agent used. Anthracyclines (such as doxorubicin are strongly associated with type I cardiotoxicity. Other risk factors include the cumulative dose and rate of anthracycline used, female sex, use of mediastinal radiotherapy, either advanced or younger age, pre-existing hypertension and pre-existing heart disease.

Q5. What are the other causes of cardiomyopathy apart from chemotherapy?

Causes of cardiomyopathy may be classified as either primary or secondary. Primary causes include hereditary genetic factors (especially hypertrophic obstructive cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy), muscular dystrophy, valvular heart disease and familial idiopathic cardiomyopathy syndromes.

Secondary causes include chronic myocardial ischaemia, diabetes, hypertension, radiation, haemochromatosis, aortic valve stenosis, hypothyroidism, alcoholism, autoimmune disease (lupus), muscular dystrophy, toxins (e.g. heavy metal poisoning), malnutrition (especially vitamin B1 or thiamine deficiency), electrolyte imbalance and infiltrative disease (e.g. amyloidosis, sarcoidosis, Gaucher disease).

Q6. What other investigations would be indicated to further examine Mary's cardiovascular and respiratory systems?

A complete physical examination is required (including positional blood pressure measurements), and the results may guide further investigations. A chest x-ray and a echocardiogram should be arranged. Factors that affect Mary's overall cardiovascular risk should be reassessed (e.g. levels of fasting cholesterol, triglycerides, high- and low-density lipoproteins and blood glucose). In addition, urinalysis, serum electrolyte levels, liver function tests, full blood count, iron studies and thyroid-stimulating hormone and vitamin B_{12} levels should be ordered.

Q7. When would it be appropriate to test B-type natriuretic peptide and serum troponin levels?

Measurement of B-type natriuretic peptide and serum troponin levels may be of prognostic use during chemotherapy to identify individuals at increased risk of chemotherapy-related myocarditis and cardiomyopathy. At this later stage, in a case such as Mary's, the ECG, physical examination and past medical history suggest chemotherapy-induced cardiomyopathy and consequent stage II heart failure. The chest x-ray and echocardiogram will be most useful in confirming diagnosis and severity of the condition.

Outcome: Mary's echocardiogram confirmed the diagnosis of cardiomyopathy and she had an ejection fraction of 35%. She commenced frusemide 40 mg/day, potassium 600 mg/day and bisoprolol 2.5 mg/day (the dose to be uptitrated as tolerated over subsequent weeks), and continued with enalapril 10 mg/day. In the unlikely situation that Mary fails to respond to this management plan after three months and if her ejection fraction remains under 35%, she would be eligible for an implantable cardioverter defibrillator as she would then fall into a high-risk group for sudden cardiac death. CT

Key points

- **Chemotherapy-induced cardiotoxicity may be severe and develop into cardiomyopathy (type I) or may be transient (type II).**
- **Common ECG abnormalities due to chemotherapy-induced cardiomyopathy include nonspecific ST wave changes and T wave flattening and a decreased QRS voltage. Other more significant abnormalities may include left ventricular hypertrophy (S wave in lead V2 >35 mm) and right axis deviation indicating biventricular enlargement; left atrial enlargement (deep, wide negative P wave in lead V1); and right atrial enlargement (peaked P wave in lead II).**
- **The ECG is also useful to exclude other possible causes of cardiac symptoms, such as ischaemia, conduction abnormalities and atrial arrhythmias.**
- **Risk factors for type I chemotherapy-induced cardiotoxicity include cumulative dose and rate of chemotherapy (especially when the anthracycline doxorubicin is used), female sex, use of mediastinal radiotherapy, either advanced age or younger age, and the presence of pre-existing hypertension or pre-existing heart disease.**

COMPETING INTERESTS: None.

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