Fatal cardiovascular complication 19 years after treatment for fibrosarcoma

Malcolm Galloway, Dominic MacLeod, Mike Sheaff, Jadwiga Wedzicha

CASE REPORT

A 34-year-old fork-lift truck driver was referred to the casualty department of the Royal London Hospital by his general practitioner with chronic cough productive of green sputum, dyspnoea and pleuritic chest pain. He had recently been treated as an inpatient with pneumonia. Despite an initial response to erythromycin, symptoms had recurred soon after discharge, and further erythromycin prescribed by his general practitioner had not resulted in any improvement.

The only past medical history of note was that 19 years previously he had a poorly differentiated fibrosarcoma of the left tibia diagnosed. He was successfully treated with an above knee amputation, radiotherapy for pulmonary metastasis to the left upper lobe, and adjuvant chemotherapy. The radiotherapy consisted of 20 Gy to the whole of both lungs using anterior and posterior megavoltage beams, divided into fifteen treatments over 21 days. A boost of 28 Gy was directed at the metastatic lesion in the left upper lobe concurrently with the final eight treatments of the whole lung radiotherapy. The boost field did not include the myocardium. Before the radiotherapy adjuvant chemotherapy consisting of methotrexate, vincristine and adriamycin was given. Following the radiotherapy further chemotherapy with methotrexate, vincristine and adriamycin was administered. The total cumulative dose of adriamycin was 1200 mg and the total cumulative dose of methotrexate was 650 mg.

Examination

Physical examination revealed jaundice, mildly tender hepatomegaly and reduced air entry at the left lung base. Oximetry on air showed an oxygen saturation of 98%. The patient was normotensive, afebrile and appeared well perfused. His left above knee amputation was noted. The initial differential diagnosis included:

1. Pneumonic illness
2. Recurrence of disseminated fibrosarcoma or a secondary malignancy
3. Possible hepatocellular dysfunction as a result of hepatitis A, B or C, or Weil's disease.

Investigations

Chest radiography demonstrated cardiomegaly and abnormal shadowing in the left upper lobe. This shadowing had been noted on a previous admission and had been interpreted as fibrosis following treatment for his earlier pulmonary metastasis. Recent abdominal ultrasound had been reported as normal and a cardiac transthoracic ultrasound showed a dilated left ventricle with moderate dysfunction.

Management

The patient was treated with intravenous ciprofloxacin and clarithromycin as he had a history of penicillin allergy. Within 12 hours his condition deteriorated rapidly with hypotension, hypoglycaemia, disseminated intravascular coagulopathy and later a cardiac arrest with electromechanical dissociation. He was successfully resuscitated and transferred to the intensive care unit, but despite inotropic support and invasive monitoring including jugular bulb oximetry, died within 48 hours with multiorgan failure.

Postmortem findings

At postmortem severe chronic fibrosing myocardial disease with acute myocardial injury and ventricular mural thrombosis was found (*Figure 1*). Embolic infarction was noted in the lung, kidney and adrenal glands. There was severe centrilobular necrosis of the liver consistent with severe hypotension. No histopathological evidence of septicaemia was found.

It was concluded that a recent chest infection had exacerbated chronic myocardial disease related to his previous treatment for fibrosarcoma and had led to cardiogenic shock, secondary ischaemic organ damage and systemic emboli.

INTRODUCTION

Fibrosarcoma accounts for 3% of all primary bone tumours. It most commonly occurs in the metaphyseal areas of long bones around the knee, and may metastasize to the lungs (Neff, 1991). Here we report a case of a fatal cardiovascular complication 19 years after successful treatment of fibrosarcoma with chemotherapy and radiotherapy.

DISCUSSION

This case highlights the importance of considering the possibility of myocardial dysfunction in any patient who has had previous chemotherapy or radiotherapy.

Adriamycin is a chemotherapeutic agent classically associated with cardiac toxicity. It intercalates between base pairs of DNA, forming high affinity complexes leading to single and double stranded breaks. It is also a generator of free radicals. Adriamycin is associated with three forms of cardiotoxicity:

1. Acute effects including supraventricular tachycardias and conduction delays
2. Pericarditis and myocarditis after 24–48 hours, leading to congestive heart failure
3. Chronic dilated congestive cardiomyopathy, which is dose and schedule dependent.

The risk of chronic cardiomyopathy is lower than 10% with less than

Dr Malcolm Galloway is Senior House Officer in Histopathology, University College London, London WC1E 6JJ, **Dr Dominic MacLeod** is Senior Registrar in the Department of Respiratory Medicine, Royal London Hospital, and **Dr Jadwiga Wedzicha** is Reader in the Academic Department of Respiratory Medicine, London Chest Hospital, London, and **Dr Mike Sheaff** is Consultant in the Department of Histopathology, Royal London Hospital, London

Correspondence to: Dr M Galloway

450 mg total dose of adriamycin per square metre (Larson and Ramsey, 1989). The patient in this case received a total of 1200 mg of adriamycin. At the time the patient was treated his prognosis was considered very poor, and repeated electrocardiograms at the time did not show any evidence of cardiac toxicity, so the use of unusually high doses of adriamycin was felt to be justified. Methotrexate in high doses and vincristine have also been postulated as cardiotoxins. Both of these drugs were used in combination with adriamycin in this patient. Mediastinal radiation also predisposes to the development of adriamycin-associated cardiomyopathy.

Radiotherapy can cause cardiovascular complications, including pericardial disease (effusion, acute pericarditis, constrictive pericarditis and fibrosis), endocardial fibrosis, valvular dysfunction, coronary artery disease, conduction system abnormalities and, as was found in this case, a diffuse myocardial fibrosis (Veinot and Edwards, 1996; Lund et al, 1996; Benoff and Schweitzer, 1995).

This case illustrates the need for great caution in the assessment of the severity of infective illnesses in any patient with a previous history of chemotherapy or radiotherapy which may have affected the cardiovascular system. HM

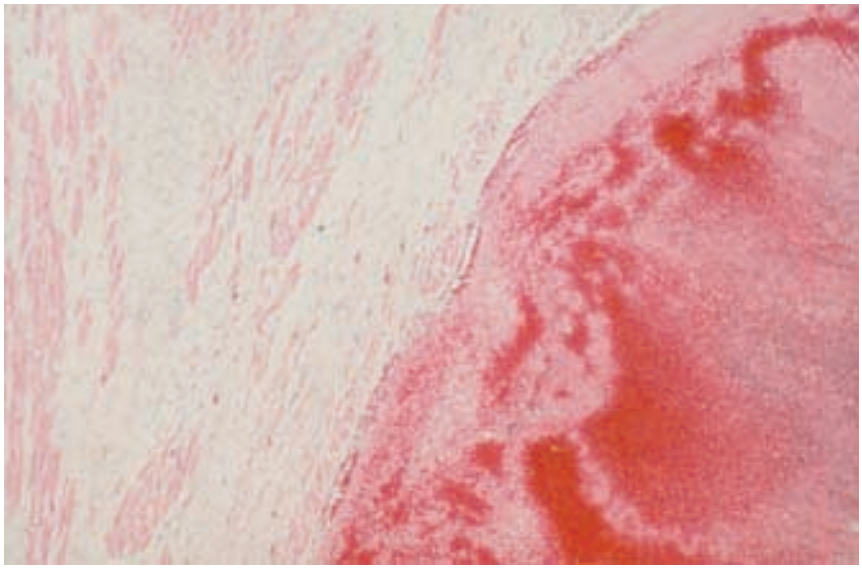

Figure 1. Section of myocardium showing extensive myocardial fibrosis with mural thrombus adherent to the endocardium.

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