Case reports


Myeloma of the heart

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A case of IgA myeloma is presented in which one of the main clinical problems was digoxin-resistant atrial fibrillation. This was due to a large interatrial deposit of myeloma involving the site of the sinoatrial node. This has not previously been described.

There are a number of recognized causes of digoxin-resistant atrial fibrillation, one of which is infiltration of the heart by malignant tumour. Extraosseous deposits of myeloma can be found in about 70 per cent of cases by careful necropsy (Hayes, Bennett, and Heck, 1952; Churg and Gordon, 1950), the liver, spleen, and lymph nodes being by far the commonest sites. Cardiac involvement at necropsy is particularly uncommon. When it occurs it may predominantly involve either the pericardium (Goldberg and Mori, 1970; Derechin, Goldberg, and Herron, 1970) or the myocardium (Morse, 1920; Pinney and Riach, 1931; Carlisle, 1938). Clinically detectable extraosseous deposits during life seem to be no particularly associated with IgD (Hobbs and Corbett, 1969) and IgA (Edwards and Zawadzki, 1967) myelomas. They are, however, rare, and indeed significant clinical manifestations due to myelomatous cardiac deposits were not reported until 1970, when 2 cases of cardiac tamponade were described (Goldberg and Mori, 1970; Derechin et al., 1970). A case of IgA myeloma is presented in which digoxin-resistant atrial fibrillation, due to a deposit of myeloma involving the sinoatrial node, posed a major therapeutic problem. This is a previously undescribed manifestation of cardiac myeloma.

Case report

The patient was a 62-year-old English woman. She complained of nausea and vomiting, and pain in the hips and ribs. She was pale and in atrial fibrillation, but showed no other physical abnormalities. Investigations revealed hypercalcaemia due to an IgA Kappa myeloma. Haemoglobin was 8·8 g/100 ml; urea 83 mg/100 ml; calcium 14·6 mg/100 ml, phosphorus 3·7 mg/100 ml; alkaline phosphatase 14 King-Armstrong units; total protein 10·5 g/100 ml, IgA 550 mg/100 ml, IgG 380 mg/100 ml, IgM 27 mg/100 ml; immunoelectrophoresis showed a monoclonal IgA paraprotein and Kappa light chains; Bence-Jones proteinuria was not detected. A bone-marrow aspirate showed infiltration by malignant plasma cells. Lytic deposits were present in the skull, mandible, clavicles, scapulae, femora, and pelvis. There was a dense right mediastinal shadow on the admission chest x-ray: this was thought to be either a paravertebral mass or an abnormal left atrium, though it was too dense to be wholly characteristic of the latter. An electrocardiogram on admission revealed atrial fibrillation with a ventricular rate of 140 a minute, horizontal ST depression in leads V5–6, and T wave inversion in leads V2–6. No further investigations were undertaken at this time. The hypercalcaemia was brought under control by rehydration with normal saline, potassium supplements, prednisolone, and oral inorganic phosphate. Seven days after admission biventricular heart failure developed, almost certainly precipitated by the saline infusions and prednisolone. Recovery from this with digoxin and diuretics was uneventful, but maintenance therapy with bendrofluazide and digoxin 0·25 mg daily alternating with 0·25 mg twice daily was required. The myeloma was treated with oral cyclophosphamide 150 mg daily. On discharge the total protein value was 9·0 g/100 ml, calcium, 9·6 mg/100 ml, and urea 30 mg/100 ml.

She remained more or less well for the next 4 months, but was readmitted in February 1972 with severe dyspnoea. The only abnormalities on physical examination were dyspnoea at rest, and an apex rate of 150 beats a minute. The electrocardiogram was unchanged. On the chest x-ray there was shadowing at the left base suggestive of linear atelectasis, as well as the previously noted shadow in the right mediastinum. Mediastinal tomography (Fig. 1) showed this to be an oddly-shaped left atrium. There was slight posterior displacement of the oesophagus by the left atrium on a barium swallow, but no evidence of valvular calcification on cardiac screening. A lung scan was within normal limits. A serum digoxin level on the maintenance digoxin regimen
beats per minute. Investigations to exclude other causes of digoxin-resistant atrial fibrillation revealed nothing abnormal. The dyspnoea gradually disappeared, but over the next 2 months, while taking cyclophosphamide, she developed tender lumps arising from her skull and ribs, and subcutaneous nodules on her trunk. These were deposits of myeloma. A trial of melphalan was given, but a rapidly downhill course followed, and the patient died 8 months after her presentation with hypercalcaemia. The white cell differential count had been normal on 5 occasions during those months, but on one occasion had shown 4 per cent plasma cells.

Necropsy findings

Four soft, white fairly discrete myeloma nodules were present in the anterior atrioventricular groove, the largest of which was 8 mm in diameter. These were largely confined to the epicardium. A larger tumour deposit (4 cm maximum diameter) lay at the root of the superior vena cava extending to the right beyond the cardiac outline and to the left between the atria to the fossa ovalis (Fig. 2). Histologically, tumour cells extended from epicardium through the atrial myocardium to the endocardium so involving and surrounding the sinoatrial node (Fig. 3). The only other cardiac abnormality was moderate coronary atheroma but without significant stenosis or myocardial damage.

Myeloma nodules were numerous in the skull, ribs, and vertebra. Small extramedullary deposits (up to 2 cm in diameter) were present in the mediastinal connective tissue close to, but not involving lymph nodes; the subpleural connective tissues (multiple); the thyroid (1 nodule); the gastric submucosa (3 nodules); the skin (multiple); each kidney (1 nodule); the fat around the left ureteric pelvis; the dura mater (multiple).

FIG. 1 Anteroposterior mediastinal tomogram. February 1972. The abnormal left atrial shadow is well seen.

(0.25 mg daily alternating with 0.25 mg twice daily) was 1.2 ng per ml. (Normal therapeutic range taken as 0.5–2.0 ng per ml.) Serum potassium was 3.4 mEq per litre, and the blood urea 54 mg/100 ml. The dose of digoxin was increased to 0.25 mg twice daily, and digoxin levels of 2.0 ng and 1.1 ng per ml were achieved. Despite this, the apex rate was usually in the region of 110 beats per minute. Investigations to exclude other causes of digoxin-resistant atrial fibrillation revealed nothing abnormal. The dyspnoea gradually disappeared, but over the next 2 months, while taking cyclophosphamide, she developed tender lumps arising from her skull and ribs, and subcutaneous nodules on her trunk. These were deposits of myeloma. A trial of melphalan was given, but a rapidly downhill course followed, and the patient died 8 months after her presentation with hypercalcaemia. The white cell differential count had been normal on 5 occasions during those months, but on one occasion had shown 4 per cent plasma cells.

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FIG. 2 The heart at necropsy. The upper pointer delineates the myeloma deposit extending into the cardiac muscle between the base of the superior vena cava and the fossa ovalis. The lower pointer delineates the other half of the deposit after sectioning of the interatrial septum.
The largest single deposit extensively replaced the pancreas becoming continuous with a 5 cm thick tumour extending into the splenic hilum without involving the spleen. Liver, spleen, and lymph nodes were not infiltrated by tumour.

The kidneys showed mild nephrosclerosis and nephrocalcinosis but not tubular casts or epithelial proliferation. There was considerable pulmonary congestion and oedema but no significant infection.

In all sites the tumour consisted of moderately well-differentiated neoplastic plasma cells with little necrosis. No evidence of amyloid production was seen.

Discussion

Although this patient showed electrocardiographic changes consistent with ischaemic heart disease, the atrial fibrillation was relatively digoxin-resistant; we were unable to explain this, though recurrent pulmonary emboli were considered a possible cause. There was no clinical or biochemical evidence of hyperthyroidism; she was not in persistent heart failure, nor was there any clinical evidence of pericarditis. She did not show the typical clinical manifestations of amyloid cardiomyopathy, and a rectal biopsy showed no amyloid. She was not suffering from digitalis intoxication, nor any of the electrolyte disturbances that render myocardial cells more digoxin-resistant, namely hyperkalaemia, hypocalcaemia, hyponatraemia; there were no electrocardiographic changes indicative of the Parkinson-White syndrome: the remaining possibility was myelomatous involvement of the heart.

Extraosseous deposits of myeloma can be found by careful necropsy in about 70 per cent of cases of myeloma (Churg and Gordon, 1950; Hayes et al., 1952). The liver, spleen, lymph nodes, and kidney are the commonest organs involved. Cardiac involvement is especially uncommon: Churg and Gordon (1950) found 1 instance in 30 necropsies (epicardium); Hayes et al. (1952) found no instance of it in 38 necropsies; Innes and Newall (1961) found 1 instance of myocardial and 2 of pericardial involvement in 45 necropsies; Pasmantier and Azar (1969) found no instance in 57 necropsies. Reviewing necropsy reports, Hayes et al. (1952) found 10 cases of cardiac involvement out of a total of 182 cases reviewed.

In clinical studies cardiac involvement is even less common. In a 16-year review, Edwards and Zawadzki (1967) found no cases with cardiac manifestations out of 78 reviewed, though there were 6 patients with other prominent extraosseous lesions. Herskovic, Andersen, and Bayrd (1965) reviewed 21 cases of intrathoracic plasmacytomas, 19 of which had disseminated disease: none had cardiac manifestations. Indeed no clinically significant cardiac manifestations due to myeloma deposits were described until 1970, when Derechin and Goldberg, in 2 separate reports, described cardiac tamponade.
due to pericardial deposits. Goldberg’s case developed tamponade while receiving warfarin.

It is known that there is a high incidence of extraosseous deposits in IgD myeloma (Hobbs and Corbett, 1969). The apparent preponderance of IgA myelomas in some of the cases with extraosseous manifestations referred to in this article is of interest: 5 of the 6 cases described by Edwards had immunological studies performed, and 3 of the 5 had an IgA myeloma. Derechin’s case with tamponade had an IgA myeloma, as had our own case. Pasmantier divided his cases into 3 stages: stage 1 having gross skeletal nodules with or without microscopical distant metastases; stage 2 had gross skeletal and paraskeletal nodules; stage 3 had gross distant metastases. Of 8 cases in stage 1 there were 5 with microscopical distant metastases – all had an IgA myeloma. There were 3 without microscopical distant metastases – all had an IgG myeloma. Immunological studies were only done in 8 stage 3 cases: 4 had an IgA, and 4 an IgG myeloma.

Atrial fibrillation due to infiltration of the sinoatrial node area is previously undescribed. It is not unduly surprising that it proved relatively digoxin-resistant. It is possible that radiotherapy to the heart might have been of value in both this case, and the 2 cases of tamponade, and the possibility of tumour involvement should be remembered in cases of myeloma with cardiac problems who have no clinical or pathological evidence of amyloid.

References
Morse, P. F. (1920). The peroxidase reaction in three cases of multiple myeloma of the bones: with remarks concerning the nosological position of these tumors. Journal of Cancer Research, 5, 345.

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