Primary malignant fibrous histiocytoma of the left atrium

Surgical and chemotherapeutic management

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SUMMARY A primary malignant fibrous histiocytoma of the left atrium was diagnosed in a 27 year old woman. After surgical excision the tumour recurred together with enlargement of the right hilar lymph nodes. The patient was then treated with nine courses of chemotherapy using a combined drug regimen. During the first course the tumour regressed, and after nine courses almost complete remission was achieved. Subsequently, the residual tumour was removed by resection of the right lung, the right hilar, paratracheal, and paraesophageal lymph nodes and by cardiectomy with partial resection of the right and left atria and atrial septum followed by a reconstruction of the atrias. To date, more than two years after initial presentation, the patient is alive and well.

Case report

FIRST ADMISSION

A 27 year old woman was admitted on 16 April 1981 with a one month history of increasing dyspnoea on exertion, a pleural effusion, and palpitation accompanied by persistent low grade fever and general lassitude. M mode and cross sectional echocardiography as well as cardiac catheterisation showed a large left atrial tumour, which also compressed the right atrium. At cardiac catheterisation, pressures in the right atrium, the right ventricle, and the pulmonary artery were increased. The pulmonary capillary wedge pressure was also raised (30 mm Hg). Function of both ventricles was normal.

At cardiac surgery the left atrium was opened and a sessile tumour measuring 10 × 10 cm was found attached to the superior posterior wall of the atrium. The intra-atrial septum was intact. The right superior pulmonary vein was almost completely occluded. The tumour was removed and on histological examination showed the characteristic mixture of spindle cells arranged in a storiform pattern, polygonal cells resembling histiocytes, and malignant giant cells, which are all features of malignant fibrous histiocytoma (Fig. 1).

SECOND ADMISSION

After an uncomplicated postoperative recovery her clinical condition deteriorated quickly. A recurrence of the tumour was suspected and on 17 July 1981 she was admitted for further treatment. On admission she had dyspnoea at rest. Her blood pressure was 100/80 mm Hg, pulse rate 100 beats/min. The point of maximal impulse was in the fifth intercostal space in the mid-clavicular line. The first heart sound (S₁) was loud and split and the second heart sound (S₂) was physiologically split, the pulmonary component (P₂) being accentuated. A grade 2/2 pansystolic murmur was heard at the apex radiating to the axilla. Haemoglobin concentration was 8.5 g/dl, white blood cell count $9 \times 10^9/l$ ($9000/cm^3$), and the erythrocyte sedimentation rate 74 mm in the first hour (Westergren). The electrocardiogram showed normal sinus rhythm and left atrial enlargement. Chest x ray films showed a normal sized heart, a right and left pleural effusion, increased interstitial markings at both lung bases, and enlarged right hilar lymph nodes. M mode echocardiography strongly suggested a recurrence of the left atrial tumour.

Computed tomography was performed with a Siemens Somatom (Siemens, Erlangen, FRG), a scanner with an exposure time of 4.8 s and a slice thickness of 8 mm. The patient was scanned in the supine position, and inspiration was suspended during each single scan. The images were obtained

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Fig. 1 Histological appearance of malignant fibrous histiocytoma showing the mixture of spindle shaped fibroblasts arranged in a storiform pattern, polygonal pleomorphic histiocytes, and malignant giant cells. Haematoxylin and eosin, $\times 310$ original magnification.

through the heart in continuous slices from the left diaphragm to the aortic arch immediately after rapid bolus injections of 100 ml of an iodine-containing contrast medium (Telebrix 300, Byk Gulden, Konstanz, FRG). The tomograms through the heart after intravenous injection of contrast medium showed a large tumour like mass attached to the atrial septum, which nearly filled the entire left atrium, extended to the left ventricle, and compressed the right atrium. The right pulmonary vein was occluded and the superior vena cava was compressed (Figures 2 ai, bi, and ci). Extensive investigations including bone marrow biopsy, bone scan, computed tomography of the abdomen, and several x ray examinations failed to detect metastases.

As the fibrous histiocytoma belongs to the soft tissue sarcomas, we decided to treat the patient with the combined regimen of cyclophosphamide, vincristine, adriamycin, and imidazol carboxamide (CYVADIC).¹⁻³ Nine courses of this regimen were given. During the first course the tumour regressed, and after all nine almost completely resolved. The final tomograms performed on 16 March 1982 showed a tissue mass of 2 cm in diameter at the former site of the tumour, which appeared to consist of connective tissue judging by its radiodensity (Fig. 2 aii, bii, and cii).

THIRD ADMISSION

After an uneventful recovery the patient presented on 30 June 1982 again complaining of shortness of breath. The tomograms showed an increase in the tissue mass to a diameter of 4 cm at the former site of the tumour. The intra-atrial septum seemed to be infiltrated, the right pulmonary vein was occluded,

and the superior vena cava was again compressed (Fig. 2 aiii, biii, and ciii). At recatheterisation, pressures in the right heart and the pulmonary artery were raised, as was the pulmonary capillary wedge pressure (15 mm Hg). Left ventricular end diastolic pressure was normal. The mean transmitral gradient was 4 mm Hg and the calculated valve area 2.01 cm². The left ventricular angiogram showed normal left ventricular function and a filling defect in the left atrium.

The patient underwent further surgery. The thorax was opened by a lateral incision and dense adhesions resulting from the previous operation were found in the mediastinum. Cardiopulmonary bypass was instituted, and both atria were opened. The tumour was attached to the lateral wall of the left atrium and to the junction of the atrial septum. The entire intra-atrial septum and a full thickness section of the left atrial wall were removed and all visible tumour excised. As the tumour occluded the right lung veins, the right lung was totally removed. All visible paratracheal and paraeosophageal lymph nodes were excised. The intra-atrial septum and the left atrial wall were reconstructed using patches of Gore-tex.

At histological examination only minor parts of the excised tissue contained areas of active tumour, which were identical to those of the tumour removed at the previous operation. Most parts consisted of scar tissue, as often occurs after successful chemotherapy. The left atrial wall was infiltrated. The atrial septum, the lung, and all excised lymph nodes, except a hilar node, were free of tumour.

The postoperative course was uneventful. During intensive investigations for metastases in February 1983 a single right parieto-occipital intracranial metastasis was localised and surgically removed. The

Fig. 2 Contrast enhanced computed tomograms (a) through the base of the heart showing (i) a tumour recurrence after the first operation—compression of the superior vena cava (SVC) by the tumour, (ii) partial remission after chemotherapy—no evidence of a tumour, and a normal size and configuration of the ascending aorta (AA), superior vena cava (SVC), pulmonary trunk (PT), and pulmonary veins, (iii) tissue increase after postchemotherapeutic recovery—compression of the SVC and occlusion of the right pulmonary vein by tumour, and (iv) complete remission after the second operation—no evidence of tumour, a normal size and configuration of the AA, SVC, and PT, and the right lung removed; (b) through the centre of the heart chambers showing (i) tumour recurrence after the first operation—a tumour (T) in the left atrium (LA) compressing the right atrium (RA) and extending to the left ventricle (LV), a small LV, and enlargement of the RV; (ii) partial remission after chemotherapy—tissue regression at the former tumour site, and a normal size and configuration of LV, RA, and RV, (iii) tissue increase after postchemotherapeutic recovery—tissue regression at the former tumour site, and a normal size and configuration of LV, RA, and RV, (iv) complete remission after the second operation—no evidence of tumour in the LA, Gore-Tex patches at the former site in the left atrial wall, and the right lung removed; and (c) through the heart chambers above the diaphragm showing (i) tumour recurrence after the first operation—compression of the right atrium by the tumour and enlargement of coronary sinus (CS) and RV, (ii) partial remission after chemotherapy—no evidence of tumour and a normal size and configuration of CS, LV, RA, and RV, (iii) tissue increase after postchemotherapeutic recovery—no evidence of tumour and a normal size and configuration of CS, LV, RA, and RV, (iv) complete remission after the second operation—no evidence of tumour, a normal size and configuration of LV and RV, and the right lung removed. S, interventricular septum; PE, pericardial effusion.

heart showed no tomographic evidence of tumour (Fig. 2 aiv, biv, civ). To date, more than two years after the initial presentation she is alive and well.

Discussion

The heart reacts to injury by degenerative rather than regenerative phenomena. The paucity of mitotic activity in cardiac muscle may contribute to the rarity of primary tumours in the heart,⁴⁻⁸ which are found at less than 1/1000 necropsies.⁹ Metastases to the heart are more than three times as common as primary malignant tumours.⁵ Primary malignant neoplasms of the heart are almost exclusively sarcomas and these soft tissue malignancies form the second commonest group of cardiac tumours.^{5,8} Like myxomas they occur most frequently in the atria. Their site of origin is more likely to be the right atrium than the left. They most often infiltrate the myocardium, and metastases to the vertebral column and parenchymal organs frequently occur.¹⁰

Malignant fibrous histiocytoma is a relatively recently recognised diagnostic entity, characterised histologically by the mixture of spindle cells arranged in a storiform pattern, polygonal cells resembling histiocytes, and malignant giant cells. The basic cell type is fibroblast-like and histiocyte-like. The occurrence of this kind of soft tissue sarcoma in the heart was reported by McAllister and Fenoglio in five cases¹¹ and recently in a further case.^{12,13} We believe our case represents the first description of the successful chemotherapeutic management of a malignant fibrous histiocytoma in the heart. In the case reported by Shah *et al* and Gabelman *et al* the site of tumour origin was the left atrium.^{12,13} The patient, a 37 year old black woman, underwent surgery and subsequently was irradiated with a total dose of 50 Gy (5000 rad) to the whole heart followed by a booster dose of 8 Gy (800 rad) to the left atrium. Six months later the tumour recurred; she underwent further surgery and finally died of cardiac failure after a total of five intracardiac tumour recurrences about three years after initial presentation. At necropsy there were no metastases.

Recurrence of malignant fibrous histiocytoma after local excision is not uncommon.^{14,15} The response of soft tissue sarcomas to radiation is variable, and radiation treatment is therefore not always successful.¹⁶ Chemotherapy is generally accepted to be the most successful treatment for advanced tissue sarcomas. Of the different regimens, the combined CYVADIC regimen is appreciably superior both in terms of response and survival.¹ In our opinion every surgical excision of cardiac soft tissue sarcomas should be followed by adjuvant chemotherapy immediately. Chemotherapy may be supplemented by radiation if

complete remission is achieved. A dose of at least 50 Gy (5000 rad) should be delivered to the former site of the tumour. The use of radiation treatment alone in the management of soft tissue sarcomas is controversial, and the first reported fibrous histiocytoma in the heart did not respond to irradiation.^{12,13} If there is only a partial remission with chemotherapy, a further operation and radical resection of the residual tumour, as performed in our patient with success, seems therefore to be necessary.

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