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CASE REPORT

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Non-Hodgkin lymphoma with exclusive involvement of the heart and the gastrointestinal tract

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Abstract An extranodal high-grade B-cell lymphoma, centroblastic type, with exclusive involvement of the heart, stomach and small bowel was detected at postmortem examination following the death of an 80-year-old man. Autopsy revealed massive cardiomegaly with a total heart weight of 1800 g owing to an intramyocardial tumour involving the right ventricle, and multiple mucosal tumour plaques and nodules in the stomach and small bowel. The case highlights the difficulties of diagnosing cardiac lymphoma clinically even in the presence of a large tumour mass.

Key words Cardiac tumours · Malignant lymphoma · Histology · Immunohistochemistry

Introduction

The heart is seldom involved by malignant neoplasms [1, 20, 21, 36, 37]. Primary malignant pericardial and myocardial tumours are extremely rare [36], and only a few cases of primary heart lymphoma fulfilling the strict criteria of McAllister and Fenoglio (documented absence of lymphoma outside the pericardium) [21] have been reported in the literature [3, 5–8, 10, 11, 15, 18, 19, 27, 29, 31–33].

Metastatic tumours of the heart are much more frequent than primary tumours [1, 23]. The occurrence of cardiac metastasis has been reported for almost every type of neoplasm [1, 20]. Secondary involvement of the heart by lymphoma is detected in 16–26% of lymphoma patients in systematic autopsy studies, but is rarely recognized before death [11, 13]. Clinically, relevant cardiac involvement can produce markedly variable symptoms, which can mimic a wide range of cardiac and extracardiac diseases [2, 3, 9, 14, 24, 28, 30]. This makes clinical recognition of cardiac lymphoma extremely difficult, and detailed imaging studies and histological or cytological examination are usually required [9, 25, 26, 29, 33].

We present a 80-year-old patient with extensive cardiac involvement by an extranodal high-grade B-cell malignancy that was probably a true primary lymphoma of the heart.

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Clinical history

A 80-year-old man was first admitted to the Department of Internal Medicine, Innsbruck University Hospital, in April 1992 because of dyspnoea and chest pain. He had previously been treated for cardiac failure and a benign gastric ulcer. There was no history of autoimmune disease (rheumatoid arthritis), malignancy or immunosuppression. Physical examination showed severe dyspnoea at rest and tachycardia with arrythmia. The lungs were clear on auscultation, and there was no peripheral oedema, elevated jugular pressure or peripheral lymphadenopathy.

Peripheral blood counts showed a moderate leucocytosis (11,400/μl) with an increase in neutrophils and moderate anaemia. No atypical lymphoid cells were observed. The erythrocyte sedimentation rate was markedly increased (>100 mm in 1 h), and the lactic dehydrogenase highly elevated (1600 U/l).

An electrocardiogram revealed atrial fibrillation at a rate of approximately 140/min. Chest X-ray disclosed a significant enlargement of the cardiac silhouette, consistent with congestive heart failure. The clinical presentation suggested an occult malignancy in addition to the cardiac failure, but the patient declined further examination and his condition improved under symptomatic therapy. He was readmitted twice during the following 6 months, and a continuous deterioration of his condition with dyspnoea, chest pain and weight loss was noted. A detailed cardiac examination, including duplex sonography and echocardiography, performed 3 months before death, revealed marked myogenous biventricular dilatation with consecutive valvular insufficiency and thickening of the epi- and pericardium of the right ventricle, interpreted as residues of pericarditis. Gastroscopy showed a small prepyloric scar and otherwise normal conditions; gastric biopsy material revealed a mild lymphoplasmocytic inflammatory infiltrate. The pa-

tient died of progressive cardiac failure 7 months after primary admission. He had received no specific chemotherapy during the course of his disease.

Materials and methods

All tissues obtained at autopsy were routinely fixed in formalin and embedded in paraffin. Sections were stained with haematoxylin-eosin, Giemsa, PAS and Gomori's reticulin stain. Immunohistochemistry was performed with our routine streptavidin–biotin immunoperoxidase technique. The primary antibodies used were anti-CLA (CD45), L26 (CD20), UCHL-1 (CD45RO), KiM1p (macrophages; gift from Professor Parwaresch, Kiel, Germany), anti-vimentin, BerH2 (CD30), polyclonal anti-CD3, antibodies against immunoglobulin heavy and light chains, the latent membrane protein-1 (LMP) of the Epstein–Barr virus (all antibodies obtained from Dako, Copenhagen, Denmark) and KL1 (cytokeratin; Immunotech, Marseille, France). In situ hybridization for EBV was performed with fluorescein-labelled oligonucleotides complementary to EBER1/2 RNAs (Dako), as previously described [12].

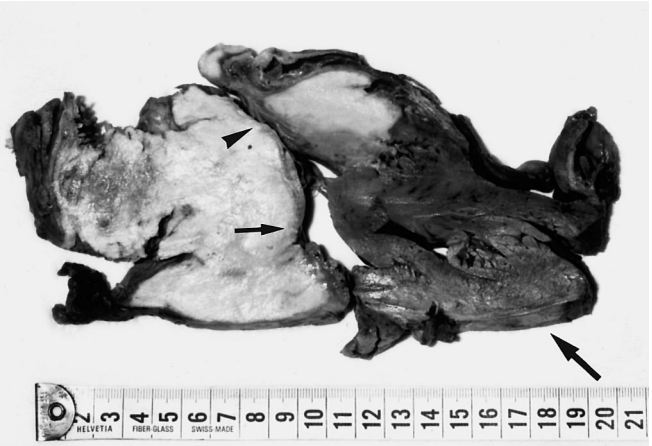

Fig. 1 Whitish tumour masses almost completely replacing both atria (*arrowhead* right atrium) and right ventricle (*small arrow*; *large arrow* left ventricle) of the heart (horizontal section)

Pathological findings

The heart was grossly enlarged, with a total weight of 1800 g. The diaphragmatic aspect and the lateral wall of the right ventricle were almost completely replaced by tumour masses, which also involved both atria and were compressing the outflow tract of the right ventricle. The cut surface of the tumour revealed soft, whitish tissue without gross areas of necrosis (Fig. 1). There was no pericardial effusion or involvement of the parietal sheet of the pericardium. The stomach and the small bowel showed more than 50 sharply circumscribed, mucosal tumour nodules ranging from 0.5 to 5 cm in diameter, the larger ones exhibiting central, shallow ulceration. All lymph nodes, the liver and the spleen appeared normal.

The myocardium (Fig. 2), the epi- and endocardium of the right ventricle and the subepicardial fatty tissue showed diffuse and sheet-like infiltrates composed of large, polymorphous lymphoid cells. These had basophilic cytoplasm and vesiculated nuclei with sometimes marginated, multiple nucleoli, most closely resembling centroblasts. Multinucleated tumour cells, sometimes resembling Reed-Sternberg cells, were frequent, and the number of mitotic figures was increased. The myocyte fibres were separated and partially destroyed by the infiltrate, and even the leaflets of the tricuspidal valve showed neoplastic infiltration. No larger areas of tumour necrosis or myocardial necrosis were seen. The right cor-

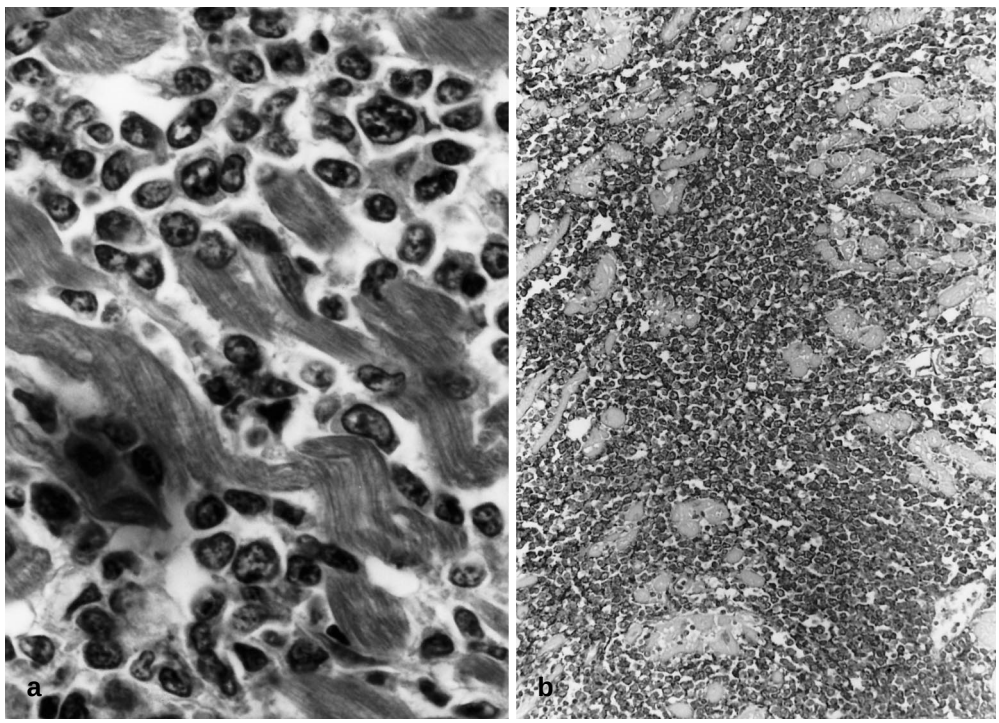

Fig. 2a Diffuse, sheet-like cardiac infiltrate; note prominence of centroblasts between remnants of cardiac smooth muscles. Haematoxylin-eosin, original magnification ×1000. **b** Strong immunoreactivity of cardiac infiltrate with L26 (CD20) dissecting as well as partially destroying myocytic fibres. Harris haematoxylin counterstain, original magnification ×100

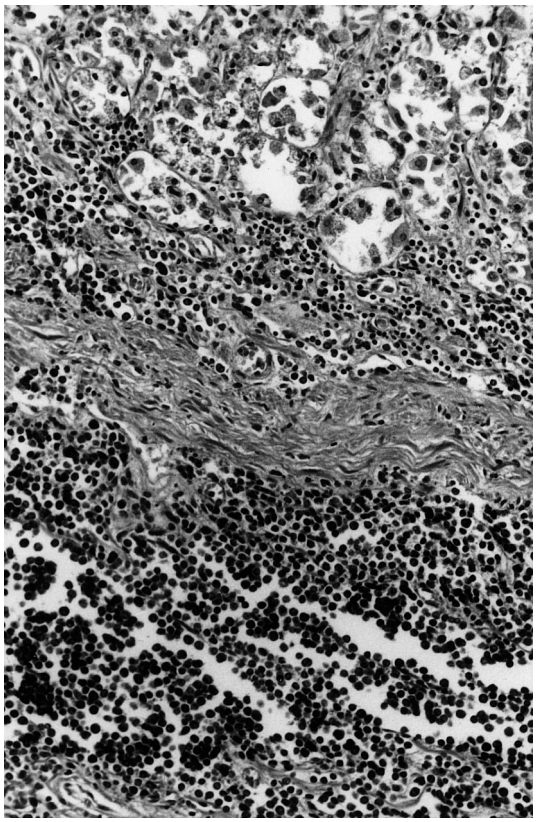

Fig. 3 Diffuse intestinal infiltration of mucosa and submucosa by lymphoma. Haematoxylin-eosin, original magnification ×200

onary artery was completely surrounded by neoplastic cells, but the vessel wall remained intact. No lung involvement was seen.

Histological examination of the gastrointestinal tract (Fig. 3) revealed identical neoplastic lymphoid infiltrates in the mucosa and submucosa of stomach and small bowel, which caused focal ulceration and separation of gastric glands and intestinal crypts, but no formation of lymphoepithelial lesions. The uninvolved intestinal mucosa was unremarkable, without villous atrophy. All lymph nodes and other organs, including the spleen, liver and bone marrow, were free of tumour. The neoplastic cells expressed CD20 strongly (Fig. 2b), and cytoplasmic IgM and the common leucocyte antigen to a lesser degree. Intratumour reactive T-cells labelled with the antibody UCHL-1 (CD45RO) and for CD3. Numerous macrophages, often containing cellular debris, were strongly stained with KiM1p. The reactions for CD30, LMP-1, cytokeratin, vimentin, and immunoglobulin light chains and the in situ hybridization for EBV remained negative.

Discussion

Clinically significant involvement of the heart by malignant lymphoma is infrequent and in most cases due to direct extension of mediastinal lymphoma to the pericardium [20, 22, 36]. The clinical presentation and symptoms of cardiac involvement are extremely variable and nonspecific in most cases, ranging from a complete lack of symptoms to progressive cardiac insufficiency, which is often misinterpreted as congestive heart failure, especially in elderly patients. There are also acute dramatic presentations such as myocardial infarction, myocardial rupture and pulmonary tumour embolism [2, 3, 9, 14, 24, 28, 30]. However, the majority of both primary and secondary cardiac lymphomas, including some cases with large cardiac tumour masses, are not diagnosed until autopsy. In large autopsy studies, involvement by malignant lymphoma has been reported to account for up to 17% of the total metastases from malignant neoplasms to the heart [36], and 16–26% of patients dying with lymphoma are found to have mostly minor cardiac involvement [11].

Primary cardiac lymphoma, defined as involving only myo- and pericardium using the strict criteria of McAllister and Fenoglio [21], has been reported only 28 times in the literature [3, 5–8, 10, 11, 15, 18, 19, 27, 29, 31–33]. Some authors take a broader view and have proposed that cases with the main tumour mass in the heart, as in our case, should also be classified as primary cardiac lymphomas [4, 13, 35]. The predilection site for all these cases is the low pressure system of both atria and the right ventricle.

Although our case does not fulfil the strict criteria for primary heart lymphoma [21], such massive involvement of the myocardium is rare, and a combination with isolated involvement of heart and gastrointestinal tract has not previously been reported. Owing to the distribution of the tumour masses and the apparent absence of lymphomatous involvement on gastroscopy 4 months before the patient's death we consider the heart to have been the primary site of the tumour. The peculiar distribution of the lesions in our case, with complete sparing of lymphoid organs, is similar to the dissemination characteristics of other extranodal lymphomas and might be due to specific homing characteristics of the tumour cells.

Apart from two cases of cardiac T-cell lymphoma [17, 24] all other cardiac lymphomas reported so far have been of B-cell origin. Risk factors for this type of lymphoma are similar to those for other types of extranodal lymphoma and include iatrogenic, autoimmune- or HIV-associated immunosuppression and old age [6, 15, 16, 19, 32, 34, 36]. Old age was the only risk factor identified in our patient, and an association with Epstein Barr-virus, which is common in high risk groups, was not found.

This case highlights the difficulties of diagnosing cardiac lymphoma clinically, even in the presence of a large tumour mass, and emphasizes the need for thorough evaluation of cardiac failure in elderly patients with concurrent signs of an underlying malignancy.

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