ANTICANCER RESEARCH *18:* 1291-1294 (1998)

Cardiac Malignant Lymphoma: A Case Report

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Abstract. *A 76 year old man, who had undergone tonsillectomy for non Hodgkin's malignant lymphoma, died suddenly in rapidly evolving cardiogenic shock with electrocardiographic signs of acute lateral myocardial infarction. Post mortem examination showed three cardiac lesions, two in the left ventricle and one in the right atrium, corresponding to the "crista terminalis". Histologic examination of autopsy samples confirmed the presence of lymphoma in the heart, partially affecting the sino atrial node (NSA) but excluding other sites. There was no evidence of acute myocardial infarction in spite of the clinical signs and symptoms. An infarction-type electrocardiographic pattern associated with conduction disturbances in patients with lymphoma should suggest the possibility of cardiac localization of the disease.*

The incidence of secondary cardiac localizations of lymphoma ranges from 9% to 24% (1-4). Clinical signs and symptoms may be non-specific and cardiac involvement may remain undiagnosed while the patient is alive. The most frequent clinical manifestations are: chest pain, ventricular motility defects, conduction disturbances, congestive heart failure. In particular, the presence of blood in the pericardial sac suggests epicardial involvement (1-5). Numerous non-invasive instrumental tests have proved useful in indicating and defining the extent of cardiac involvement in these tumors (6). However, such tests are not able to provide a definitive diagnosis. Only removal of myocardial lissue by endomyocardial biopsy, thoracotomy or post mortem examination call confirm the diagnosis and allow documentation of the histotype (6). Early diagnosis is essential since these tumors are sensitive to chemotherapy and to chemotherapy associated with radiotherapy (1,6).

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Key Words: Cardiac malignant lymphoma.

Patient and Methods

Case report. A 76 year old man, who had previously undergone tonsillectomy for non-Hodgkin's malignant lymphoma, was admitted to hospilal suffering from cardiogenic shock. Symptoms included a prolonged syncopal episode accompained by sweating, vomiting and severe mesogastric pain irradiating to the back. Arterial pressure was 90/55, heart rate 120/minute. Cardiac tones were rhythmic, rapid with non-assessable pauses. Peripheral pulses were hyposphygmic. Haemogas-analysis showed marked metabolic acidosis. Arterial blood test revealed: ASTGOT) 99 U/l, ALT(GPT) 74 U/l, LDH 362 U/l, CK 48 U/l. Electrocardiogram (ECG) showed: sinus tachycardia, lesion wave in V4-V6 and electric alternation. The patient died in circulation arrest in spite of reanimation attempts. Post mortem examination was requested with clinical diagnosis of rapidly evolving cardiogenic shock and electrocardiographic indications of acute lateral myocardial infarction.

Materials and Methods. A complete autopsy was performed. Multiple samples of all organs including brain were fixed in 10% formalin buffer, processed and embedded in paraffin. 5 μ sections were stained with hematoxylin-eosin. Samples of the common myocardium were also stained with giemsa and azan-Heidenhein trichrome. The cardiac conduction system was removed in two blocks: the first including the sino-atrial node (NSA) and the "crista terminalis", the second contained the atrio-ventricular node (NAV), His bundle and branches. These samples were fixed in 10% formalin buffer for 7 days and subsequently dehydrated by passage through 95° ethanol and four times in pure dioxane. After partial impregnation in a solution made up of 1/3 dioxane and 2/3 paraffin and total impregnation in paraffin, the samples were cut into 8 μ seriated sections with an interval of l20-140 μ for the NSA block and 160-180 μ for the NAV block. The sections were stained alternately with hematoxylin-eosin and azan-Heidenhein trichrome. The following immunohistochemical tests were performed on sections of the common myocardium, according to the ABC (Avidin Biotin Complex) method: neuron specific enolase (NSE), chromogranin (CHR), cytokeratin (CK), leukocytary common antigen (LCA), CD30, CD20, CD45 RO, CD3, kappa and lambda chains.

Results

Post mortem examination of the pericardial sac and heart revealed serous opaqueness, sero-hematic content of the cavity (about 200 cc) and alteration of the form and the aspect of the heart due to the presence of nodular lesions on the surface of the postero-inferior face of the left ventricular

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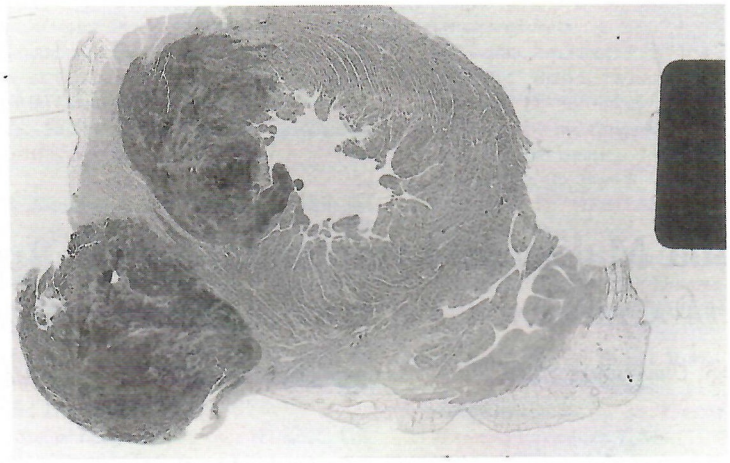

Figure 1. *Cut surface of the heart, evidence of the nodular lesions of the left ventricule.*

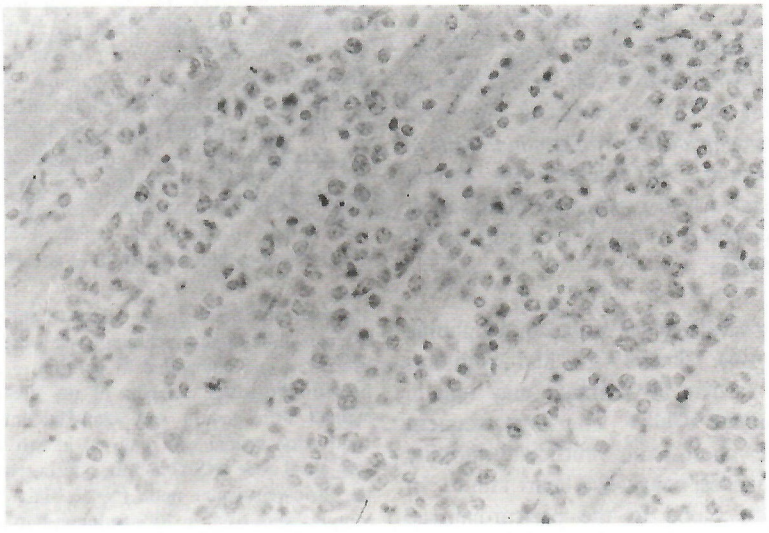

Figure 2. *EE 40X: monomorphous neoplastic lymphoid cells infiltrating the myocardium and dispersed among the fibrocells.*

myocardium. Dissection showed myocardium of the left ventricular lateral wall to be substituted throughout its thickness by a friable greyish-white nodular neoformation, 2,3 cm in diameter. A similar nodular lesion, 2 cm in diameter, affected 2/3 of the left ventricular posterior wall (Figure 1). In the right atrium, corresponding to the "crista terminalis", there was a third, reddish-colored intramural nodular lesion, 1.5 cm in diameter. The rest of the myocardiun was brownish and homogeneous in apparence. The coronaries were rigid and open; the anterior descending branch was 80% occluded by subintimal calcific plaque at the origin. Other significant pathologic findings were as follows: post-hepatitis splenomegalic hepatic cirrhosis with esophageal varices in HCV positive subject, singular absence of lymphoadenomegaly. Histologic examination of the cardiac neoformations showed widespread proliferation of medium size cell elements. These were monomorphous in appearance, infiltrating the myocardium and dispersed among the fibrocells. Necrosis and intratumoral hemorrhages were also present. The neoplastic cells had rounded, hyperchromic nuclei with one or more nucleoles along the nuclear membrane and reduced cytoplasm (Figure 2). The atrial neoformation showed aspects of infiltration of the NSA as well as perigangliar and perineural infiltration. A small neoplastic embolus was observed in the lumen of the right coronary artery. Immunohistochemical investigation of the neoplastic population gave the following results: CK, CHR, NSE negative; LCA and CD20 positive, CD45R0 and CD3

negative. The morphologic aspect, confirmed by immunohistochemical procedures, led to the diagnosis of cardiac localization of non Hodgkin's malignant lymphoma immunofenotype B, diffuse large cell type (G, Working Formulation) (7), diffuse centroblastic (Kiel) (8), diffuse large cells B (REAL) (9). There were no histologic evidence of other localizations. Microscopic examination of the remaining myocardium excluded ischemic lesions.

Discussion

Secondary cardiac localization of lymphoma occurs relatively frequently (1). Clinical symptoms are often generic or completely absent and definitive diagnosis is possible only by autopsy (2-4). Diagnosis is difficult for the following reasons: low index of clinical indications, lack of specific non invasive indicators; moreove, generic signs and symptoms are often located at other sites such as lungs and mediastinum. The most common clinical manifestations of cardiac disfunction in malignant lymphoma patients include not only cardiac tamponade, ventricular disfunction, arrhythmias and cardiac block, but also dyspnea, chest pain, pericardial or pleural effusions, electrocardiographic anomalies such as sinusal tachycardia, alterations of ST and T waves and low voltage (10-17). However, these signs and symptoms are non-specific and are seldom attributed to lymphoma affecting the heart. Bidimensional echography seems to be the most suitable diagnostic technique for evaluating intracardiac tumors; the association of Magnetic Nuclear Resonance provides further information on pathologies of the mediastinum, lungs and great vessels (18-22). Open heart biopsy and endomyocardial biopsy allow precise histopathologic diagnosis, the last one with less risk to the patient and at lower cost (23). Cases of cardiac localization of lymphoma with infarction-type electrocardiographic signs and without histologic alterations due to ischemic myocardial necrosis, have already been reported in the literature (24-26). In the present case, the patient's symptoms and electrocardiographic pattern were compatible with acute lateral myocardial infarction, without enzymatic alterations. The morphologic and immunohistochemical aspects of the cardiac lesions suggest non-Hodgkin lymphoma with immunophenotype B, diffuse large cell type (G, W.F.), diffuse centroblastic (Kiel), diffuse large cell B (REAL). By making a morphologic comparison between the autopsy samples of the cardiac neoformations and the samples of the earlier tonsillectomy it was possible to establish that the same tumoral histotype characterized both. In spite of coronary sclerosis and neoplastic coronary embolus, histologic examination of the tumor free common myocardium did not reveal areas of ischemic necrosis. The lesion wave electrocardiographic sign can be explained by the massive substitution of the myocardial wall due to the neoformations which transmitted an infarction-type electric signal. Neoplastic infiltration of the conduction system, already described in the literature, leads to electrocardiographic alterations, cardiac dysfunction and arrhythmia (27). If it is massive, it causes sudden death due to atrio-ventricular block (27). The present case showed neoplastic infiltration of NSA. Substantial infiltration of subepicardial fat nerves and perisinusal ganglia, as well as direct infiltration of NSA, could have produced conduction disturbances. This could explain the syncopal episodes mentioned above, and also the symptoms present on the patient's final admission to hospital and the sinusal tachycardia prior to decease. In conclusion, the patient's sudden death could have been due, not so much to the diffused neoplastic invasion of the common myocardium, causing a cardiac motility defect (which explains the electrocardiographic pattern), so much as to the involvement of the NSA and intrinsic nervous system, causing conduction disturbances. Diffusion pathways were hematogenic as well as perineural and perigangliar. This case suggests at generic heart symptoms in lymphoma patients could indicate secondary cardiac involvement. Early diagnosis is essential, as these tumors respond well to radiotherapy or radiotherapy and chemotherapy combined (1,6).

Acknowledgements

We thank Mrs. Marina Crippa and Graziella Alfonsi for their excellent technical assistance.

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Received October 13, 1997
Accepted December 8, 1997