Primary cardiac lymphoma (PCL) is defined as non-Hodgkin's lymphoma (NHL) strictly confined to the heart or pericardium (1, 2). PCL of the pericardium represents the minority with 15 of 55 PCL cases reported in the literature (3). Large autopsy studies over a 20-year period have demonstrated only seven cases of PCL in the general population, indicating an incidence of 0.06% (3). Initial clinical signs of PCL patients are often unspecific and point to cardiovascular disease with palpitations, shortness of breath, chest pain, arrhythmia and signs of congestive heart failure (4, 5). The symptoms are typically acute in onset and short in duration, with a high rate of early death. The diagnosis of PCL is most frequently based on echocardiography studies followed by biopsy, and response monitoring is often hampered by residual tumor with unclear significance (5). In our case, cardiac gadolinium-enhanced magnetic resonance imaging (CMR) non-invasively provided information on NHL vitality by perfusion monitoring. The individualized diagnostic and therapeutic approach in patients with PCL, as a rare lymphoma manifestation, is the subject of the present report and review of literature.

Case Report

A 76-year-old female was referred to our department with dyspnea on exertion, chest pain and a 2-month history of progressive fatigue and weight loss. The patient’s past medical history revealed a nodal marginal zone non-Hodgkin’s lymphoma diagnosed 7 years prior to admission, which had never required treatment. On the day of admission, pertinent findings on physical examination were an arrhythmic pulse with 98 beats/min, distended jugular veins and peripheral edema, consistent with congestive heart failure. Routine laboratory tests including white blood cell count revealed a thrombocytosis with 540,000 platelets/µl. FACScan (Becton Dickinson, Heidelberg, Germany) of the peripheral blood revealed a CD4+ T-cell count of 774/µl, a CD8+ T-cell count of 510/µl and a CD19+ B-cell count of 294/µl, indicating normal immuno-competence.

Chest X-ray showed marked cardiomegaly with clear lung fields. Echocardiography and chest computed tomography (CT scan) demonstrated a cardiac mass. CMR imaging revealed a contrast enhancing mass attached to the right atrium and ventricle (Figure 1). Upon CMR, the tumor showed significant first pass contrast perfusion.

Florine-18 fluorodeoxyglucose positron emission tomography (PET) revealed pronounced 18F-FDG accumulation of the large cardiac mass, while less intense hypermetabolic lesions were found in axillary, cervical and abdominal lymph node
regions, most probably representing the previously described nodal marginal zone non-Hodgkin’s lymphoma (Figure 2). Catheter-guided biopsy of the tumor in the right atrium evidenced a CD20-positive immunoblastic B-cell lymphoma (Figure 3). CT scan of the abdomen and pelvis revealed no intra-abdominal lymphadenopathy. Treatment consisted of six cycles of CHOP (Cyclophosphamide, Doxorubicine, Vincristine=Oncovine, Prednisone) chemotherapy, combined with the monoclonal anti-CD20-specific antibody Rituximab. CHOP was given on days 1 to 5, as previously described (6), and 375 mg/m² Rituximab was given on day 0.

Treatment was well tolerated and induced a partial remission, as monitored by echocardiography. Additionally, first pass imaging by CMR displayed hardly any residual perfusion in the lymphoma bulk. Based on this reduced

---

Figure 1. Cardiac MRI in four chamber view of the heart before therapy: steady state gradient echo sequence (A) and T1-weighted contrast enhanced, fat saturated spin echo sequence (B) reveal a large, contrast-enhancing mass (arrow) encasing the right coronary artery. Note pleural effusion on the right (asterisk).

Figure 2. Pre-therapeutic PET projection files (A) show an extensive intra-thoracic ¹⁸F-FDG accumulation depicting the vitality of the cardiac lymphoma. Hypermetabolic lesions were found in axillary, cervical and abdominal lymph node regions with less enhancement as compared to the cardiac lymphoma mass. Additionally, there is physiological FDG-uptake in the kidney, pelvis and urinary bladder. After therapy, FDG-PET does not reveal viable lymphoma manifestations (B). The myocardium of the left ventricle shows moderately increased FDG-accumulation, a benign phenomenon that can regularly be observed after chemotherapy. Note the regular shape of the left ventricle myocardium in comparison to the shapeless thoracic mass of the initial lymphoma. Unchanged, persistent physiological FDG-uptake in the kidney, pelvis and urinary bladder can be seen.
lymphoma perfusion and presumably decreased tumor vitality, no additional therapy was given and the patient was set on observation. Repeated imaging with echocardiography and CMR during follow-up disclosed further reduction of the tumor in all diameters to 10% of the initial size (Figure 4). Nine months after the final treatment, the patient was in sustained remission, as monitored by CMR and validated by FDG-PET.

Discussion

PCL is generally of high grade histology, is diagnosed in 1.3% of all primary cardiac tumors and represents less than 1% of all extranodal lymphomas (1, 2). Other primary malignant tumors of the heart are of sarcomatous or mesenchymal origin, in 50% of the cases (1). Immuno-compromised patients are at a higher risk for PCL, with a
significant increase in HIV-positive individuals (7). The etiology of this increased prevalence in immunocompromized individuals is unclear and, as in our case, is not applicable to all patients. Delay in the diagnosis due to the unspecific cardiac symptoms and infiltration of cardiac structures contribute to the poor clinical outcome. Careful histological and immunohistological assessment of the tumor biopsy is required, since 75% of all myocardial tumors are benign. In most patients, the diagnosis is based on a biopsy of cardiac tissue during an explorative thoracotomy or mediastinoscopy. Furthermore, assessment of cytological sample of pericardial effusion may be beneficial, although it may be difficult to differentiate PCL from benign reactive lymphocytosis. Another route to obtain cardiac tissue is by transvenous endocardiac biopsy under simultaneous echocardiographic guidance (8), which we applied in this case.

In cardiac masses gadolinium-enhanced MRI has proven useful for tumor detection, tissue characterization, depiction of contour, relation with other cardiac structures and is,
Therefore, helpful in differential diagnosis (9, 10). In comparison to cardiac sarcomas, lymphomas have been described to less probably display necrosis or hemorrhage and, therefore, the MRI signal intensity of lymphoma is relatively homogenous (9-11). Lymphoma vitality monitoring by MRI is mostly based on the variation of the tumor size, but also includes other criteria such as fibrosis as a sign of avitality (9-11). Furthermore, gadolinium-enhanced MRI allows for perfusion monitoring with an early and a late perfusion phase (10, 11).

Despite the proven chemosensitivity of PCL and prolonged survival in several reported cases, the prognosis remains poor, with a mortality of 60% within the first 2 months after diagnosis (12). Chemotherapy, according to CHOP and VACOP-B protocols, has been demonstrated to be effective for high grade B-cell lymphoma (6, 13). As in our case of high grade cardiac lymphoma, B-cell lineage PCL are characterized by CD20 expression and, therefore, can be successfully treated with Rituximab (14). In our case, CHOP chemotherapy was combined with Rituximab. The treatment was well tolerated, but induced only a partial remission when applying conventional response criteria. Further investigation with CMR displayed hardly any perfusion of the tumor, which had initially been very well perfused, thus indicating that response monitoring based solely on tumor measurement can be hampered by residual tumor mass with an unclear vitality.

Repeated imaging with echocardiography and CMR during follow-up disclosed a further 80% reduction of the tumor in all diameters. Nine months after the final treatment, the patient was in sustained remission, as monitored by CMR and validated by FDG-PET. In addition to the reduced lymphoma vitality displayed by CMR, the age of our patient was another factor contra-indicating further chemotherapy. Furthermore, the possible complication of cardiac rupture under treatment gave an additional argument for setting our patient on observation. However, such complications associated with tumor regression are characteristically described for the early rather than late stages of anti-tumor treatment.

Although FDG-PET is currently the gold standard for activity monitoring in high grade lymphoma, not every medical center can supply a PET device and we, therefore, believe that our observation that cardiac MRI is of diagnostic value for lymphoma activity monitoring has clinical relevance.

We conclude that the combination of CHOP with Rituximab was effective in our B-lineage high grade cardiac lymphoma case, and that CMR provided valuable insight into the lymphoma perfusion and, presumably, the tumor’s vitality. CMR may, therefore, be a valuable diagnostic means, in addition to FDG-PET, for clinical decision-making on additional therapy.

References

Received March 1, 2005
Accepted May 2, 2005