

# The Pathological Features of Dissemination of Lymphoma in the Heart in 42 Autopsy Cases

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**OBJECTIVE** To study the pathological features of dissemination of lymphoma in the heart and understand its influence on cardiac function.

**METHODS** Forty-two patients who died of lymphoma were autopsied and the gross and microscopic pathological changes of the heart observed.

**RESULTS** Eight (19.05%) out of 42 cases had heart dissemination in the pericardium and heart wall. The dissemination features noted were of a nodular type, diffuse type and mixed type, leading to neoplastic myocarditis.

**CONCLUSION** The pathological features of dissemination of lymphoma in the heart are varied, and the different types can produce dissimilar influences in heart function.

**KEYWORDS:** lymphoma, autopsy, heart, dissemination.

**P** rimary cardiac lymphoma is rare, but dissemination of lymphoma in the heart is not uncommon. Reports concerning its pathological features and influence on heart function are few. This study is a summary of 42 autopsy cases from January, 1960 to December, 2000 with the following results.

## MATERIALS AND METHODS

### Cases

The 42 autopsy cases were all in-patients in our hospital including 39 males and 3 females. Their ages ranged from 8 to 61 years (median of 28). The cases consisted of 23 non-Hodgkin's lymphomas and 19 Hodgkin's lymphomas, which were all verified by histopathology corresponding to national criteria.<sup>[1]</sup>

### Methods

The cadavers were dissected with the permission of the patients' relatives. Their thoracic cavity was opened and a "人" incision was performed in the parietal wall of the pericardium, the volume of the pericardial effusion was measured and its nature appraised. The range and degree of the lesions of the heart were observed, after which specimens were taken by incising the pericardium, left atrium, left ventricle, right atrium and right ventricle. The tissue samples were fixed in 10% formalin, then were embedded in paraffin, sectioned and

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stained with H&E, for observation using an optical microscope.

## RESULTS

In a total of 42 autopsied cases, 8 (19.05%) had heart lymphoma dissemination including 6 cases with dissemination simultaneously in the pericardium and heart wall. One case had simplex pericardium dissemination and 1 case had the dissemination of the heart wall alone. There was no dissemination in the endocardium in the cases with heart wall dissemination. The characteristics of the cases were as follows.

### Heart wall dissemination

#### *Diffuse type*

In this type of tumor cells were scattered homogeneously in the epicardium, but sometimes they invaded into the inter-muscle bundles or disseminated into the adipose tissue outside of the heart.

#### *Nodular type*

Tumor cells which were in the epicardium and inter-myocardium formed tumor nodules in this type. The residual myocardial fibers lying in inter-oncocytes were degenerated and necrotized. Some degeneration occurred in other parts of the cardiac muscle and in the myocardium locating near the tumor. This presented with interstitial edema and neoplastic myocarditis developed due to the infiltration of a small number of the mononuclear leukocytes and lymphocytes. In 2 cases the auricular muscle alone was invaded.

#### *Mixed type*

Tumor cells formed tumor nodules and at the same time disseminated between the epicardium and myocardium. Degeneration and necrosis of myocardial fibers were also seen in this type.

### Pericardial dissemination

#### *Direct dissemination*

It originated from the direct involvement of the mass

nearby the mediastinum and presented with intensive adhesion between the pericardium and its peripheral tumor tissue. The appearance of the tumor cells of these 2 sites was similar and in 1 case the formation of neoplastic pericarditis was seen because of the pericardial thickening.

#### *Hematogenous or lymphatic dissemination*

The diffuse tumor nodules in the parietal layer of the pericardium were demonstrated in this condition and the sporadic distribution of oncocytes outside the nodules was also seen.

## DISCUSSION

Primary cardiac tumors are rare, accounting for 0.0017%~0.28% in the general population.<sup>[2]</sup> Primary cardiac lymphomas are even more rare and make up only 1.3% of primary cardiac tumors, but cardiac dissemination of lymphomas is not uncommon<sup>[3,4]</sup> and is seen often in non-Hodgkin's lymphoma.<sup>[5]</sup> It had a high incidence of 19.1% in this study, which may be correlated with the majority of cases seen late in their progression.

There are few reports of the pathological features of lymphomatoid cardiac dissemination due to difficulties in performing autopsies in China. However, this study is of value in that by analyzing the effects of cardiac dissemination we can provide better health care for our patients.

The dissemination of the diffuse type has little influence on cardiac function similar to acute leukemia, although the heart is diffusely infiltrated.<sup>[6]</sup> In general, we believe that cardiac function is affected markedly in the nodular type. Based on our observations, we can infer that the dissemination of the nodular type influences cardiac function in some manner as follows: 1. formation of neoplastic nodules can cause a decline in myocardial compliance and lack of coordination of the timing and the intervals occurring in the contraction of the heart. This can affect the diastolic filling and pumping function of the heart and lead to the heart failure; 2. the degeneration and necrosis of cardiac fibers at the sites of the tumor-cell dissemination can

cause the destruction of the cardiac structure and lead to a decline in the myocardial contractibility; 3. the myocardium adjacent to the disseminating sites of the oncocytes can develop interstitial edema, resulting in a decline of ventricular compliance and abnormal pumping function; 4. the generation of neoplastic myocarditis may also cause destruction of the myocardial structure and a lessening of ventricular compliance. As these events progress, oncocyte dissemination, in some cases, will engender heart failure and even lead to cardiac arrest. Due to the loss of myocardial contractibility caused by the comprehensive degeneration of the myocardial fibers, it is very difficult to treat the problem, so the patients are bound to die of heart failure. Furthermore, it is important to note that we should use digitalis very carefully because it can further suppress the compliance of the myocardium, which is the bases of the pathological changes, and thus accelerate heart failure.

There are only a few reports concerning lymphoma patients complicated with myocarditis, and its pathogenesis has not been elucidated. In our study, tumor cells infiltrated into the myocardium in some myocarditic cases, but in other cases there was only infiltration of inflammatory cells, suggesting that there is no significant correlation between the occurrence of myocarditis and the dissemination of the oncocytes. The role of tumor-cell dissemination in myocarditic occurrence and development has not been solved and should be explored further. Although the patients receiving high-dose cyclophosphamide and/or radiotherapy might suffer from damaging cardiotoxicity,<sup>[7-9]</sup> the pathological features of these patients were hemorrhagic myocardial necrosis associated with the interstitial edema, fibrosis and vascular endothelial injury.<sup>[10]</sup> However we did not see similar pathological changes mentioned above in our autopsy cases, indicating that these changes have no relation with drugs and chemotherapy. The utilization of IL-2 in the autogenous transplantation of bone marrow in some reports, activated Th cells and caused myocarditis due to disorder of cytokines, resulting in apoptosis in the myocardium and infiltration by lymphocytes. These results suggest that immune factors

alone can cause myocarditis. We know that patients with lymphoma frequently can have autoimmune hemolysis etc., indicating that lymphoma might be complicated with autoimmune diseases, and myocarditis might be related to disorders of immune function,<sup>[11]</sup> because of the formation of tumor nodules, pericardial adhesion, hydropericardium and neoplastic pericarditis between the visceral layer and the parietal layer of the pericardium, the pericardial dissemination of lymphoma can also lead to a decline of myocardial compliance, resulting in changes of cardiac function. Severe hydropericardium can give rise to pericardial tamponade; for these reasons, treating the primary disease is the advisable treatment and therapy for the corresponding symptoms should be carried out when needed.

In summary, we learned from our study that lymphoma cardiac dissemination is different from leukemic cardiac infiltration. Myocardial fibers may degenerate and necrotize resulting in neoplastic myocarditis etc., which severely influences cardiac function. Formation of nodular dissemination leads to cardiac insufficiency which, because of the nature of the pathology, is very difficult to treat. Since we have studied only a limited number of cases, further research is needed to understand the pathophysiology involved.

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