

Severe valvular toxicity and pericarditis early after radiation therapy in a patient treated for Hodgkin's lymphoma

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Hodgkin's disease can be cured in most cases by radiotherapy. However, it can increase the risk of cardiotoxicity. Here, we report a patient with Hodgkin's disease and superior vena cava syndrome who was treated with chemotherapy in combination with radiotherapy. Four months after the initiation of this therapy, she developed progressive dyspnea. Pleural and pericardial effusion, severe mitral regurgitation, moderate aortic insufficiency, and mild tricuspid regurgitation were detected in echocardiography, which suggested heart failure. The patient was then treated with intrapericardial drainage and received dopamine and diuretics for congestive heart failure; she responded well to this treatment and was discharged in good condition. After high-dose mediastinal radiation, cardiologic screening is recommended in order to identify patients with radiation-induced heart disease and to assess their need for treatment and follow-up.

Key words: cardiotoxicity, Hodgkin's lymphoma, radiotherapy.

Childhood Hodgkin's lymphoma (Hodgkin's disease) is currently a highly curable disease using standard treatment protocol including multi-agent systemic chemotherapy combined with involved-field low-dose radiotherapy¹⁻³. While most patients respond well to this current treatment approach, survivors can carry some risks for treatment-related effects, which may not manifest until many years later⁴.

Although radiotherapy is a main tool in the management of Hodgkin's lymphoma^{2,3}, it can lead to a wide range of cardiac defects, including different forms of pericarditis, valvular and conduction defects, and coronary artery diseases⁵⁻⁸. In addition, acute myocardial infarction and sudden death have been reported in very young patients following mediastinal irradiation⁹. Thus, cardiotoxicity is considered an important complication of treatment in Hodgkin's lymphoma^{7,8,10}. Among these cardiac abnormalities, the pericardium seems to be the most prominent organ involved shortly after radiation therapy¹¹. However, symptomatic valvular dysfunction following radiation therapy

has been cited infrequently^{5,6} and is considered as a late cardiac sequela occurring within months to years after radiation.

Here, we report a patient with Hodgkin's lymphoma who developed severe valvular dysfunction and concurrent pericardial effusion shortly after radiotherapy.

Case Report

A 16-year-old female patient was referred to our referral center in Tehran, Children's Medical Center Hospital, Pediatrics Center of Excellence in Iran, with a palpable and nontender cervical lymphadenopathy. She had also experienced fever, night sweats and an unexplained weight loss (10% of the body weight) during the six months before admission. An excisional lymph node biopsy from the cervical region was taken and revealed Hodgkin's lymphoma with a lymphocytic predominant type. Thorough investigation revealed involvement of supraclavicular, superior mediastinal and liver, which together categorized the patient as stage 4 Hodgkin's lymphoma. She was then

treated intravenously with the adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) regimen (adriamycin 25 mg/m², bleomycin 10 mg/m², vinblastine 6 mg/m², dacarbazine 375 mg/m² on days 1 and 15 of a 28-day cycle) with a cumulative dose of 175 mg for adriamycin.

A few weeks after the initiation of the therapy, she developed severe headache, facial swelling and dilated neck veins, which was suggestive of superior vena cava (SVC) syndrome. Computed tomography (CT) scan, taken from the chest, revealed a mass in the anterior mediastinum and confirmed the diagnosis of SVC syndrome. While protecting the heart and lungs, she consequently received 35 Gy radiation to the mantle, mediastinal and abdominal regions. She responded completely to the combined chemoradiation therapy and underwent complete remission.

Four months after the initiation of radiotherapy, she developed dyspnea, which was initially observed during exertion, but showed a progressive manner and after a few weeks was observed even at rest. At this time, the orthopnea was so severe that she had to spend the entire night in a sitting position and was therefore re-admitted to the hospital. Her blood pressure was 100/60 mmHg, pulse rate 60 beats/min and respiratory rate 27 per min. Jugular venous distension, coarse crackle in both lung fields, third and fourth heart sounds, and an apical murmur were detected. The chest radiograph showed pleural effusion and enlargement of the cardiac silhouette. An echocardiogram at admission showed mild bilateral pleural effusion and a moderate pericardial effusion. The left ventricular ejection fraction was markedly reduced (35%). Severe mitral regurgitation, moderate aortic insufficiency and a mild tricuspid regurgitation were diagnosed, suggesting heart failure.

The patient was then treated with intrapericardial drainage for the pericardial effusion. The pericardial fluid was exudative, but no microbacteria were detected in the culture. She received dopamine and diuretics for congestive heart failure; she responded well to this treatment and was discharged in good condition. She has not experienced any serious problem during the one-year follow-up.

Discussion

While the effectiveness of radiotherapy in the treatment of Hodgkin's lymphoma has become clear, cardiac involvement after mediastinal radiation therapy has been increasingly reported^{5-8,10-13}. Most of the reported complications, however, have occurred in long-term survivors of Hodgkin's lymphoma; cases in which cardiac abnormalities have been documented shortly after therapy are scarce. In the present report, severe valvular dysfunction and pericardial involvement developed acutely in less than six months post-radiation in our patient.

Shortly after radiation therapy, severe and progressive dyspnea and an abnormal echocardiography revealing severe mitral regurgitation and moderate aortic insufficiency became evident in our patient. Symptomatic valvular dysfunction following radiation has been cited infrequently, and its significant risk in Hodgkin's lymphoma survivors has been estimated to be 5% at the 20-year follow-up¹⁰. The changes are usually mild and without hemodynamic consequences⁵. These valvular abnormalities are more commonly left-sided and the dominant dysfunction is more likely to be stenosis rather than insufficiency¹⁰. Furthermore, abnormalities of the aortic valve are shown to be more common than abnormalities of the mitral and tricuspid valves, which could be a result of the proximity of the aortic valve to the mediastinal radiation field¹⁴. In our patient, however, mitral valve regurgitation dominated the clinical picture and led to the acute heart failure shortly after therapy.

Our patient developed ventricular insufficiency following radiation therapy. While myocardial toxicity is the most significant type of cardiotoxicity, the effect of irradiation on ventricular function differs among studies¹⁵⁻¹⁸. In the majority of these studies, a reduced left ventricular systolic function and fractional shortening have been observed^{15,16}. However, there are studies in which the cardiac functional parameters have remained in the normal ranges and no effect of radiation has been observed^{17,18}.

Moderate pericardial effusion developed in our patient and required intrapericardial drainage for treatment. Pericardial involvement has been considered as the most frequent finding

following mediastinal radiation therapy¹⁹, and around 1% of patients develop pericarditis in an acute form following treatment¹⁹. The process is usually considered self-limiting and most patients indeed would not require specific treatment. However, in the present report, significant effusion was present, which necessitated the need for more invasive therapy.

Superior vena cava (SVC) syndrome was identified in our patient following the initiation of chemotherapy. Mediastinal tumors are the main primary causes of SVC syndromes in childhood and adolescence²⁰. While chemotherapy usually achieves excellent results, radiotherapy has been proven to be the most beneficial form of treatment²¹. In our patient, primary treatment with multi-agent chemotherapy did not alleviate the symptoms, while the addition of radiation resulted in complete resolution of the tumor.

Following mediastinal radiation, cardiologic screening is recommended in order to identify patients with radiation-induced heart disease and to assess their need for treatment and follow-up.

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