Thymic Hyperplasia Following Successful Chemotherapy for Hodgkin’s Lymphoma: Report of a Case

Tung-Liang Lin, MD; Lee-Yung Shih, MD; Yu-Shin Hung, MD; Tseng-tong Kuo, MD, PhD

A recurrent mediastinal mass in a patient following treatment for Hodgkin’s lymphoma presents a diagnostic challenge. We report a 17-year-old boy with nodular sclerosing Hodgkin’s lymphoma, stage IIIa, who achieved complete response after 6-cycle chemotherapy with doxorubicin, bleomycin, vinblastine and dacarbazine and developed thymic hyperplasia 6 months later. Ten cases have been reported previously. Most patients were young, had the nodular sclerosis subtype of Hodgkin’s lymphoma, were in an advanced stage, and had a latency of 2 to 12 months following successful chemotherapy. It is impossible to delineate radiologically benign from malignant lesions. Resection of the tumor for tissue diagnosis is mandatory to establish an accurate diagnosis and thus avoid further harmful therapy. *(Chang Gung Med J 2009;32:98-103)*

Key words: Hodgkin’s lymphoma, thymic hyperplasia, mediastinal tumor

CASE REPORT

A new or recurrent mediastinal mass in patients treated for malignant disease presents a diagnostic dilemma. The reappearance of a mediastinal mass in a patient in complete remission from Hodgkin’s lymphoma usually indicates a relapse. However, some benign processes, albeit rare, may present similar features. Thymic hyperplasia after successful treatment of malignant disease is a well-documented phenomenon in patients with testicular carcinoma. In those patients, the thymic mass developed 3-14 months after initiation of therapy. *(1)* Thymic hyperplasia has been described sporadically in patients with Hodgkin’s lymphoma. It is postulated that thymus regeneration following involution during chemotherapy represents a rebound phenomenon. *(2,3)* We report another case of thymic hyperplasia following successful treatment for nodular sclerosis Hodgkin’s lymphoma.
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The laboratory data showed a hemoglobin of 8.9 gm/dL, red blood cells 4.06 x 10^{12}/L, mean corpuscular volume 68.4 fl, white blood cells 18.5 x 10^9/L, platelets 297 x 10^9/L, erythrocyte sedimentation rate 126 mm/hr, aspartate transaminase 44 U/L, alanine transaminase 75 U/L, alkaline phosphatase 160 U/L, total bilirubin 0.6 mg/dL, creatinine 0.8 mg/dL, calcium 8.9 mg/dL, uric acid 5.5 mg/dL, lactate dehydrogenase 163 U/L (47-140 U/L), beta 2-microglobulin 2046 µg/L (800-2400 µg/L), serum iron 24 µg/dL, and total iron binding capacity 195 g/dL. Hepatitis B virus surface antigen and anti-hepatitis C virus antibody were both negative. A bone marrow aspiration smear and biopsy specimen showed no involvement of Hodgkin’s lymphoma. A liver biopsy was also negative for lymphoma involvement. A diagnosis of Hodgkin’s lymphoma of the nodular sclerosis type, stage IIIa, was made. He received 6 courses of chemotherapy with doxorubicin (25 mg/m^2), bleomycin (10 mg/m^2), vinblastine (6 mg/m^2) and dacarbazine (375 mg/m^2) over the next 5 months. His liver function returned to normal in May, 2002 and a follow-up chest radiograph revealed no more widening of the mediastinum. A CT scan in October, 2002 revealed complete regression of the previously enlarged nodes and a normal spleen. A follow-up whole body CT in April, 2003 found a soft tissue mass measuring 5 x 2 cm in the anterior mediastinum (Fig. 2A) which was initially suspected to be a recurrence of Hodgkin’s lymphoma. Sonography of the anterior mediastinum showed an elongated hypoechoic area. As the location of the mass was relatively risky for CT-guided biopsy, a thoracoscopy was performed one month later. There was an enlarged encapsulated tumor in the left lower part of the thymus, measuring 5 x 3 x 1 cm. The thymus was completely resected and pathology showed thymic hyperplasia without malignancy (Fig. 2B). Clinically, he had no evidence of myasthenia gravis. The patient has remained in continuous complete remission 45 months after the initial diagnosis of Hodgkin’s lymphoma.

**DISCUSSION**

The reappearance of an enlarged mediastinal mass in our patient was first suspected to be a relapse of Hodgkin’s lymphoma. Thoracoscopy with excision of the mass confirmed thymic hyperplasia, thus avoiding unnecessary further therapy for recurrent disease. The differential diagnosis of recurrent mediastinal tumor after successful treatment of Hodgkin’s lymphoma consists of fibrosis and necrosis of the primary tumor, recurrence of Hodgkin’s lymphoma, thymic cysts, thymic hyperplasia, pulmonary fibrosis, and other hematologic malignancies such as non-Hodgkin’s lymphoma or granulocytic sarcoma. Tissue confirmation is mandatory to make an accurate diagnosis and avoid unnecessary and potentially harmful treatment.

CT scan is the standard method for staging and follow-up of Hodgkin’s lymphoma, but it can not differentiate among the various causes of a mediasti-
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Gallium scan also has been a good tool for follow-up, however, a mediastinum gallium-uptake might persist for 10 weeks after completion of chemotherapy. Moreover, enhanced localization of gallium could occur as a result of thymic regeneration following involution during chemotherapy. Feldges et al. reported that ultrasound-guided transthoracic fine-needle aspiration failed to make a diagnosis of thymic hyperplasia which was later diagnosed by open excision. Furthermore, there were reports of simultaneous occurrence of both benign and malignant lesions coexisting in the same mass. Therefore, it should be emphasized that echo-guided biopsy might fail to reach a definite diagnosis because of the limited tissue obtained.

Thymic cysts usually develop after radiotherapy for Hodgkin’s lymphoma, whereas thymic hyperplasia can occur concurrently at the initial diagnosis of Hodgkin’s lymphoma or following successful therapy for Hodgkin’s lymphoma. Thymic hyperplasia after chemotherapy for Hodgkin’s lymphoma was first reported by Shin and Ho in 1983. Thymic hyperplasia could represent an immunologic rebounding phenomenon, a good sign of immune recovery, and should favor the successful control of Hodgkin’s lymphoma.

A total of 10 patients, including the current case, have been reported in the English literature (Table 1). Six were males, and their ages ranged from 8 to 31 years old. The subtypes of Hodgkin’s lymphoma included 7 nodular sclerosis and 3 mixed cellularity. Two cases were in clinical stage II, 6 cases in stage III, and 2 cases in stage IV. Seven cases had fever as an initial symptom. The duration between completion of chemotherapy to the occurrence of thymic hyperplasia ranged from 2 to 12 months. Their diagnoses were made by pathologic examination on surgical specimens from the recurrent mediastinal tumors in all but one patient who was diagnosed by echo-guided biopsy. Our patient, as well as previously reported patients, were young, and in an advanced stage of Hodgkin’s lymphoma of the nodular sclerosis type, and there was a latency of 2 to 12 months between the diagnosis of thymic hyperplasia and completion of chemotherapy.

There is still controversy regarding whether and how to treat thymic hyperplasia. Stolar et al. suggested that immediate exploration is not necessary and may be deferred for a period of close observation, because the hyperplastic thymus may occasionally regress with oral administration of adrenocorticosteroids. Ford et al. suggested a therapeutic trial of oral prednisolone 60 mg/m²/day for 7 days and then evaluation of the response to steroid therapy; if the mass fails to regress, open biopsy is recommended. As both thymic hyperplasia and recurrence of Hodgkin’s lymphoma would respond to steroids, we think a therapeutic trial with steroids is not appropriate for these patients; on the contrary, a tissue diagnosis is mandatory for accurate diagnosis, which in turn can prevent unnecessary chemo- or radiotherapy. Unnecessary treatment for misdiagnosis of recurrence of Hodgkin’s lymphoma has been described in
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...some patients and has led to at least one death in a patient who died of fibrinous pneumonitis and Nocardia.\(^\text{4}\)

**REFERENCES**


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Table 1. Patients with Thymic Hyperplasia Following Successful Treatment for Hodgkin’s Lymphoma

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Subtype and stage</th>
<th>Initial presentation</th>
<th>Treatment</th>
<th>Duration after completion of chemotherapy to thymic hyperplasia</th>
<th>Size and/or weight of thymic tumor</th>
<th>Reference number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>F</td>
<td>Nodular sclerosis, stage IIIbB</td>
<td>Fever, night sweats</td>
<td>9 cycles of chemotherapy</td>
<td>7 months</td>
<td>3 x 4 x 8 cm, 100 gm</td>
<td>19</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>F</td>
<td>Nodular sclerosis, stage IIIbB</td>
<td>Fever, palpable neck lymph node</td>
<td>6 cycles of alternating courses of BCVPP-Bleo and DBD, then 3 courses of BCVPP-Bleo</td>
<td>10 months</td>
<td>6 x 4 cm</td>
<td>19</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>M</td>
<td>Mixed cellularity, stage IIIaA</td>
<td>Palpable neck lymph node</td>
<td>8 cycles of MOPP</td>
<td>Not available</td>
<td>10 x 6 x 2 cm</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>M</td>
<td>Nodular sclerosis, stage IVB</td>
<td>Fever, low back pain</td>
<td>6 cycles of MOPP</td>
<td>2 months</td>
<td>10 x 8 x 2 cm, 180 gm</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>M</td>
<td>Mixed cellularity, stage IIIb</td>
<td>Fever, weakness, palpable neck lymph node</td>
<td>9 cycles of alternating courses of MOPP and CVPP</td>
<td>6 months</td>
<td>43 gm</td>
<td>18</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>M</td>
<td>Mixed cellularity, stage IVB</td>
<td>Weight loss, fever, palpable neck lymph node</td>
<td>Alternating cycles of MOPP and DBVD, number of cycles not available</td>
<td>6 months</td>
<td>Not available</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>M</td>
<td>Nodular sclerosis, at least stage IIb</td>
<td>Right upper abdominal pain, weight loss, fever</td>
<td>8 cycles of hybrid regimen of MOPP/ABV</td>
<td>12 months</td>
<td>4 x 3 cm (by CT), 8 gm</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>F</td>
<td>Nodular sclerosis, stage IIIb</td>
<td>Fever, cough, night sweats, palpable neck lymph node</td>
<td>Combined CCRT (Swiss Pediatric Oncology Group Hodgkin’s Disease Protocol)</td>
<td>6 months</td>
<td>Not available, biopsy only</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>28</td>
<td>F</td>
<td>Nodular sclerosis, stage IIA</td>
<td>Weakness, pallor</td>
<td>Combined modality (German Hodgkin’s Disease Study Group)</td>
<td>12 months</td>
<td>11 x 6 x 2 cm, 74 gm</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>17</td>
<td>M</td>
<td>Nodular sclerosis, stage IIIaA</td>
<td>Palpable neck lymph nodes</td>
<td>8 cycles of DBVD</td>
<td>6 months</td>
<td>5 x 3 x 1 cm, 10 gm</td>
<td>Current case</td>
</tr>
</tbody>
</table>

**Abbreviations:**
DBD: doxorubicin, bleomycin, dacarbazine; DBVD: doxorubicin, bleomycin, vinblastine, dacarbazine; BCVPP-Bleo: bischloroethylisonitrosourea, cyclophosphamide, vinblastine, procarbazine, bleomycin; CCRT: concurrent chemotherapy and radiotherapy; MOPP: nitrogen mustard, vincristine, procarbazine, prednisone.
何杰金氏淋巴瘤化學治療成功後之胸腺增生：一病例報告

林棟樑 施麗雲 洪玉馨 郭承統

何杰金氏淋巴瘤治療後再度發生的縱膈腔腫瘤，在診斷上是一個挑戰。我們報告一位十七歲的男性患者，診斷為何杰金氏淋巴瘤結節硬化亞型，在化學治療結束六個月後發生胸腺增生的病例。由文獻回顧得知，共有十位同樣的病例被報告出來。大部份病例具有的共同特徵是：年齡較輕，結節硬化亞型，疾病後期，以及發生在化學治療結束後二到十二個月。這樣的縱膈腔腫瘤以放射診斷學的檢查並無法區分出良性或惡性的病灶，因此，腫瘤切除以得到組織學上的診斷是必要的，以避免進一步有傷害的治療。(長庚醫誌 2009;32:98-103)

關鍵詞：何杰金氏淋巴瘤，胸腺增生，縱膈腔腫瘤