A Long-Term Survival Of Small Cell Lung Cancer Developed Diffuse Large B-Cell Lymphoma

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Citation

D Feng, D Laib, E Santos, M Korkmaz. *A Long-Term Survival Of Small Cell Lung Cancer Developed Diffuse Large B-Cell Lymphoma*. The Internet Journal of Pulmonary Medicine. 2013 Volume 14 Number 1.

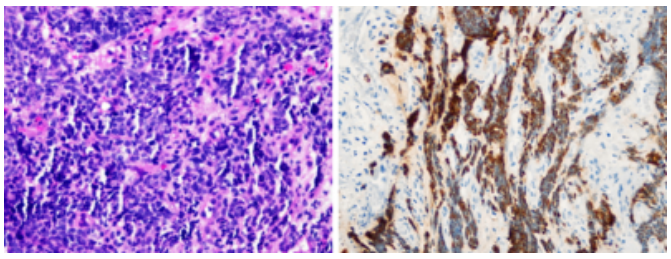
Abstract

We are reporting a rare case of a patient with a long-term survival of a small cell lung cancer (SCLC) who later developed a diffuse large B-cell lymphoma in the left neck. The patient was a smoker, and at age 50, was diagnosed with limited-stage small cell lung cancer. He was treated with chemotherapy and concurrent radiation therapy, and received prophylactic cranial irradiation resulting in a complete remission. Now, eight years later, he has developed an 8 cm mass at the supraclavicular lymph node. Biopsy confirmed a diffuse large B-cell lymphoma. His bone marrow was not involved. With treatment of intense chemotherapy and involved field radiation of the left neck, he is now in complete remission. Long-term survivors of SCLC may develop a second cancer including high-grade lymphoma. Thus, closely following up patients with SCLC is essential.

INTRODUCTION

SCLC is the fifth most common cause of cancer death in the United States; each year, almost 40,000 new cases are diagnosed.[1-3] At the diagnosis, approximately 30% of patients with SCLC will have tumor confined to the hemithorax of origin, the mediastinum, or the supraclavicular lymph nodes. These patients are designated as having limited-stage SCLC. Patients with tumors have spread beyond the supraclavicular areas are stated to have extensive-stage SCLC. The majority of these patients will die of the disease.[1-3] With intensive chemotherapy and radiation therapy, long-term survivors with SCLC are increasing.[1-4] However, developing a second cancer is increasing including mainly non-small cell lung cancer, but rarely is a lymphoma.

Figure 1



CASE REPORT

We are reporting a rare case of a male patient with an 8 year long term survival of limited-stage small cell lung cancer (SCLC) prior to a diagnosis of diffuse large B-cell lymphoma of the left supraclavicular lymph node. When this patient was 50 years old with a history of smoking for years, he developed chest pain, malaise, weight loss, and hemoptysis. Computed tomography (CT) of the chest and abdomen identified a tumor located in the left hilum and left aortopulmonary window. A bronchial washing and transbronchial biopsy were performed. Clusters of small malignant cells were identified in a bronchial washing cytology. The transbronchial biopsy confirmed an infiltrating carcinoma with prominent necrosis. Morphologically the tumor showed a classic picture of SCLC, and was composed of invasive sheet-like small malignant cells with markedly increased nuclear to cytoplasmic ratio, scant cytoplasm, nuclear molding, and indistinct nucleoli (Figure on the left). Scattered mitoses and apoptosis were present. An immunohistochemical staining profile showed that the tumor was strongly positive for pan-keratin (Figure on the right) and synaptophysin while it was negative for LCA and chromogranin. Thus, a diagnosis of SCLC was rendered. Thereafter the patient was treated with chemotherapy, radiation therapy, and prophylactic cranial irradiation. Though the treatment was complicated with radiation-induced pneumonitis, he survived and was closely followed up. Now, eight years later, the patient has developed a mass in his left supraclavicular area. CT images revealed the tumor to be 8 x 6 cm in size with thrombosis of the left jugular vein. Lymphadenopathy was identified in the

bilateral axillary lymph nodes. A needle biopsy of the large mass showed a non-caseating granulomatous lesion. An open biopsy demonstrated a tumor with a nodular and diffuse pattern composed of large atypical lymphoid cells expressing CD20, PAX-5, BCL-6 and MUM-1. Focal sheet-like necrosis was present. Ki-67 identified a high proliferative index, with about 60% of nuclei stained. A diagnosis of diffuse large B-cell lymphoma was rendered by the Mayo Clinic through a consultation. The lymphoma was negative for CD10 and BCL-2. Epstein-Barr virus in situ hybridization was also negative. He was, therefore, treated with CHOP-R for four cycles and thereafter CEPP-R another two cycles. He was admitted to the emergency room for intractable cough, low grade fever, severe neutropenia and thrombocytopenia secondary to intense chemotherapy treatment. Thereafter, the patient received IV antibiotic with Meropenem and Neupogen subcutaneously. Also he received a platelet transfusion due to underlying cirrhosis and variceal bleeding. Currently, he has had a complete remission after intensive treatment of this high-grade lymphoma.

DISCUSSION

In the United States nearly one in four deaths is caused by cancer. Appropriately one-third of these deaths are due to cancers of the lung.[1-3] Small cell lung cancer (SCLC) represents 15-25% of all lung carcinomas in the United States and is the fifth most common cause of cancer death in the United States. SCLC is highly associated with smoking and the median age of patients with SCLC is about 60 years old.[1-5] The most common symptoms for SCLC are worsening cough, shortness of breath, and dyspnea. Other presenting symptoms include chest pain, hoarseness, malaise, anorexia, weight loss, and hemoptysis. SCLC is the most aggressive cancer among lung cancer subtypes, and has a poor prognosis. Without therapy, the median survival is only 2-4 months. With platinum-containing chemotherapy, the response rate of SCLC approaches 85-95% in limited-stage SCLC and 75-85% in extensive-stage SCLC. With combined modality therapy including chemotherapy and irradiation, long-term survivors of SCLC are increasing.[3-5]

Most of the long-term survivors of SCLC are patients with limited-stage SCLC who have been treated with chemoradiation therapy and have achieved a complete remission. One recent article reported a summary of 156 patients (mean age was 56 years old, ranging from 34 to 72 years old) with limited-stage SCLC following up to 15 years after treatments. One hundred fifty one (97%) of the 156 patients were smokers. Forty-eight (31%) of the original 156 patients died within the first year of treatments. Thirty-three (21%) patients survived 3 to 5 years. Twenty-three (15%) patients survived beyond 5 years without evidence of recurrence. Nine patients (6%) were asymptomatic or mildly symptomatic until they developed second cancers after 6 to 14 years.[4] One of these patients was successfully treated for squamous cell carcinoma of the lip at 11 years and was still alive without evidence of lung cancer after 15 years. The remaining eight patients developed respiratory symptoms arising from non-small cell lung cancer.[4]

Extensive-stage SCLC usually has a worse prognosis with a short-term survival. One recent article documented that a five-year disease-free survival for SCLC was only 3% in 139 of 4574 patients including limited-stage and extensive-stage SCLC. Twenty-two (15.8%) of those developed a second SCLC over the next 7 years of follow up.[5] However, long term survivors with extensive-stage SCLC are increasing. A 73-year-old female with extensive disease of SCLC was given six courses of chemotherapy with adriamycin, cyclophosphamide and oncovin, which led to complete remission of the disease. The patient had also been treated with thalidomide (angiogenesis inhibitor) orally on a daily basis for 2 years and 5 months to the day of publication.[6] A 67-year-old man with stage IV SCLC and early-stage centrally located squamous cell cancer died of SCLC with multiple metastases to the ipsilateral lung 8 years after initiation of treatment. Post mortem examination confirmed complete disappearance of the squamous cell cancer.[7] One patient with SCLC survived 14 years without achieving a complete remission since the first episode. During those 14 years, he had two lymph node metastases and a single metastasis to the brain. His SCLC had been well controlled each time by chemotherapy, radiotherapy, and surgery.[8] SCLC usually occurs in old patients with a history of smoking. However one paper reported an 18-year-old female nonsmoker who presented with a left pulmonary mass, an enlarged mediastinum and left hilum. A transbronchial lung biopsy of the lesion revealed limited-stage SCLC, clinical stage IIIA. She received chemoradiation therapy along with salvage surgery. She was well 4 years after therapy to the date of publication.[9]

Long term survival of SCLC patients has a higher risk for developing non-small cell lung cancer than developing a subsequent relapse of SCLC. Development of non-Hodgkin lymphoma is very rare.[10] In a 1993 report of 81 patients with SCLC, only one patient developed non-Hodgkin lymphoma

of the small intestine at 7 years after treatment of SCLC.[10] No further classification was given for that patient. The long term survival of SCLC patient we reported developed a diffuse large B-cell lymphoma in the supraclavicular lymph node with bilateral axillary lymphadenopathy. It is very rare. However we need to be aware of the increased possibility of second malignancy including diffuse large B-cell lymphoma in the long term survival of SCLC patients. Thus, closely following up patients with SCLC is essential.

CONCLUSION

Long term survival with SCLC is increasing, especially for patients with a diagnosis of limited-stage small cell lung carcinoma who received early chemoradiation therapy with a complete response. However, the possibility of second malignancy is also increasing, including diffuse large B-cell lymphoma.

ACKNOWLEDGEMENT

Authors thank Dr. David Smith for review of the manuscript.

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