We report on a 68-year-old male with a multistation mediastinal lymph node adenocarcinoma, who had no primary lesions occurring within 48 months. After diagnosis by lymph node biopsy via right-sided thoracoscopy, the bilateral mediastinal lymphadenopathy responded to platinum-based chemotherapy. At 30 months after completion of chemotherapy, left mediastinal lymphadenopathy recurred. Left anterior mediastinal dissection via left-sided thoracoscopy was successful. After surgery, the patient did well with no primary lesions for more than a year. The etiology of mediastinal lymph node carcinoma of unknown origin is discussed.

Keywords: lymph node adenocarcinoma, lymph nodal dissection, chemotherapy, thoracoscopy, mediastinum

Introduction

Mediastinal lymph node carcinoma of unknown origin is comparatively rare. It has been reported as having a relatively good prognosis, as compared with primary lung cancer with mediastinal lymph node involvements. However, some cases of multistation lymph node carcinoma have poor prognoses. Herein, we describe a patient with multistation mediastinal lymph node adenocarcinoma who had a good clinical course. After thoracoscopic biopsy and subsequent thoracoscopic surgery for the recurrent lymph nodes, the patient was treated with chemotherapy over a 48-month period.

Case Report

A 68-year-old male presenting with an elevated tumor marker and asymptomatic mediastinal tumors was admitted to our hospital for investigation. At the age of 59 years, the patient had undergone an endoscopic mucosal resection for a rectal carcinoid tumor. Blood tests showed that serum concentrations of carcinoembryonic antigen (CEA) and sialyl Lewis-x antigen (SLX) were elevated to 28.9 ng/ml and 55.7 ng/ml, respectively.

Chest computed tomography (CT) revealed mediastinal lymph nodes that had shortest diameters of 25 mm, 10 mm and 6 mm, located at the right paratracheal site, the ventral side of the brachiocephalic vein and the left side of the ascending aorta, respectively (Fig. 1). There were no abnormal findings in the lung field and other organs, and no lymphadenopathy in other regions. Positron emission tomography (PET) revealed fluoro-deoxy-glucose (FDG) uptake in the lymph nodes described above. The maximum standardized uptake values (SUVs) for these lymph nodes were 8.5, 3.9 and 4.5 at the right paratracheal site, the ventral side of the brachiocephalic vein and the left side of the ascending aorta, respectively.

Right-sided exploratory thoracoscopic revealed a
red-brown elastic enlarged lymph node measuring 30 mm, with no invasion to the superior vena cava (SVC) and azygos vein. The lymph node was well-demarcated and could be excised. Pathological findings related to the right paratracheal lymph node revealed a poorly differentiated adenocarcinoma with gland ductal structure. Immunohistochemical staining was positive for thyroid transcription factor-1 (TTF-1), Napsin A, and cytokeratin 7 (CK7), whereas they showed negativity for cytokeratin 20 (CK20), CD5, and c-kit. These findings suggested the presence of metastatic adenocarcinoma of the lymph node originating from lung cancer.

We selected cisplatin and paclitaxel chemotherapy for the residual lymph node located at the ventral side of the brachiocephalic vein and the left side of the ascending aorta, a treatment used for unresectable non-small cell lung cancer. Using the Response Evaluation Criteria in Solid Tumors (RESIST) method, these lesions showed...
a partial response after three cycles of chemotherapy. Serum concentrations of CEA and SLX were decreased to 4.6 ng/ml and 29.6 ng/ml, respectively. At 30 months after completion of chemotherapy, serum concentrations of CEA and SLX were elevated to 17.0 ng/ml and 61.7 ng/ml, respectively.

PET-CT demonstrated re-enlargement of the mediastinal lymph node situated at the ventral side of the brachiocephalic vein, which showed elevated FDG uptake (SUV max, 9.0) (Fig. 3). There were no primary lesions in the lung field, and no lymphadenopathy other than that which was evident at the ventral side of the brachiocephalic vein. Left-sided thoracoscopy was performed to remove a recurrent lymphadenopathy. It was found to be a pink, oval, smooth-surfaced and enlarged lymph node measuring 15 mm that was attached to thymic tissue removed from the ventral side of the brachiocephalic vein. Video-assisted left hemithymectomy was performed, including dissection of the lymph node located at the left side of the ascending aorta that had been decreased in size due to initial chemotherapy (Fig. 4).

Histological and immunohistochemical pathological analyses suggested a poorly differentiated adenocarcinoma similar to the one described above. This tumor was a single lesion, and there were no tumors present within the left hemithymus, including the dissected lymph node. The serum concentration of CEA decreased to 6.0 ng/ml. PET revealed no primary lesion in the lung field and no lymphadenopathy at 14 months after left thoracoscopic surgery and at 48 months after the onset.

**Discussion**

The frequency of all primary unknown cancers is reported at 0.5%–6.7% and mediastinal lymph node carcinoma constitutes 1.5% of these. In 2007, Hayashi et al. reviewed 31 cases of mediastinal lymph node carcinoma that had been reported in Japan from 1983 to 2006. Twenty-five of the patients were male. Of the total patient population, 17 had adenocarcinoma and seven had squamous cell carcinoma. It can be speculated that two pathogenic mechanisms were involved. First, mediastinal lymph node metastases from minimal lung cancer could not be neglected, because immunohistochemical studies showed positivity for TTF-1 and Napsin A. Second, a malignant transformation of aberrant benign epithelial tissue in the lymph nodes was suspected, because a primary lesion in the lung field or other organs had not
been detected for more than 48 months.

The lymph node situated at the ventral side of the brachiocephalic vein became re-enlarged after its initial reduction due to chemotherapy. There was no differential diagnosis in comparing the multiple lymph node metastases from the right paratracheal lymph node carcinoma and the synchronous multiple primary lymph node carcinoma.

A definitive recommended therapeutic strategy for the disease has not yet been established. Several surgical procedures including, lymph node incisional biopsy, resection, dissection and lobectomy are all in use. There are opinions that if the identification of the primary lesion is unknown, lobectomy should be avoided. Incisional biopsy and subsequent concurrent chemoradiation therapy have shown poor prognosis.

The local recurrence ratio after lymph node dissection is not always lower than that after lymph node resection, and the operative procedure is not well defined. Morio et al. and Masaki et al. reported that the mean survival time of patients with hilar and mediastinal lymph node carcinoma was 28.9–30.7 months, and that the prognoses of these patients were more favorable than those of pN1 or pN2 lung cancer patients. Miyoshi et al. reported that multistation lesion cases have poor prognoses. Patients underwent concurrent chemoradiotherapy after biopsy, and all had died due to cancer within 1 year (mean survival time: 9.3 months). The patient described in this report had multistation mediastinal lymph node adenocarcinoma, which had no nodal recurrence more than 1 year after chemotherapy and subsequent thoracoscopic nodal dissection. Platinum-based chemotherapy was selected for the mediastinal lymph node metastases from minimal lung cancer. Left-sided thoracoscopic hemithymectomy, including lymph node dissection for solitary recurrent lymphadenopathy, was successful.

The patient is doing well after occasional treatments including chemotherapy and lymph nodal dissection for recurrent lymphadenopathy, with no primary lesions occurring over a 48-month period. The development of a definitive therapeutic strategy against primary unknown mediastinal lymph node carcinoma is desirable.

References