Abstract

Primary mediastinal neuroendocrine tumors are a rare malignancy that accounts for < 10% of all mediastinal tumors. The case presented here involves a 52-year-old man who had been suffering for 3 mo from chronic cough, anorexia and substantial weight loss, as well as 2 wk of jaundice prior to his admission. A computed tomography scan showed a 4.3 cm × 6.6 cm mediastinal mass with multiple liver nodules scattered along both hepatic lobes. Endoscopic ultrasound showed a large heterogeneous hypoechoic mass at the mediastinum with multiple target-like nodules in the liver. Fine-needle aspiration specimens revealed numerous, small, round cells with hyperchromatic nuclei, scarce cytoplasm, and frequent mitotic features. Immunohistochemical study revealed positive results for AE1/AE3, CD56 and chromogranin A, with negative findings for synaptophysin, CK20, vimentin, CK8/18 and CD45. The patient was subsequently diagnosed with a poorly differentiated neuroendocrine carcinoma, small cell type. A bone marrow biopsy also revealed extensive involvement by the carcinoma.

Key words: Bone marrow metastasis; Liver metastasis; Lymphoma; Mediastinal mass; Neuroendocrine tumor

Core tip: Neuroendocrine tumors are rare tumors that arise from the gastrointestinal tract and broncho-pulmonary system. Primary mediastinal neuroendocrine...
tumors are exceptionally rare malignancies, accounting for < 10% of all mediastinal tumors. The common clinical manifestation of this rare tumor is a mediastinal mass, but the condition can mimic lymphoma in advanced cases. The liver is the most common site of metastasis.

INTRODUCTION

The most common malignancy of the mediastinum is Hodgkin’s lymphoma, which usually involves the anterior mediastinum and typically presents as adjacent organ invasion, superior vena cava obstruction, pleural effusion, or erosion of the sternum. The most common site of metastasis for Hodgkin’s disease is the liver[4], In contrast, primary mediastinal neuroendocrine tumors are a rare malignancy that account for < 10% of all mediastinal tumors, with a reported incidence of 0.2-2.0 per 100000 people. These tumors are typically detected as incidental findings from chest radiography, as 40%-70% of advanced cases present with chronic cough, chest pain, dyspnea, or superior vena cava obstruction syndrome[5].

According to Travis[3], pulmonary neuroendocrine tumors are classified as: (1) typical carcinoid tumors; (2) atypical carcinoid tumors; (3) large cell neuroendocrine carcinomas; and (4) small cell neuroendocrine carcinomas. The prognoses of these mediastinal neuroendocrine tumors differ, with typical carcinoids associated with the best prognosis due to their slow growth and late metastasis, and the worst prognosis found with small cell neuroendocrine tumors[6]. Only a few cases of these tumors have been reported, with the liver as the most common site of metastasis[5,6]. This report describes a rare case involving a mediastinal mass with clinical manifestations mimicking lymphoma. To our knowledge, this is the first case report of primary neuroendocrine carcinoma with bone marrow and liver metastases.

CASE REPORT

A 52-year-old man presented to our hospital with a chronic cough, anorexia and substantial weight loss that had occurred over the previous 3 mo. He also presented with painless jaundice and palpable lymphadenopathy. Laboratory blood tests showed marked anemia with 6.8 g/dL hemoglobin (reference range: 12.0-18.0 g/dL), and normal white blood cell (7.7 × 10^3 cells/μL; reference range: 4-11 × 10^3 cells/μL) and reduced platelet (139 × 10^3 cells/μL; reference range: 150-440 × 10^3 cells/μL) counts. Liver chemistry results were as follows: total bilirubin, 4.2 mg/dL (reference range: 0-1.2 mg/dL); direct bilirubin, 3.7 mg/dL (reference range: 0-0.3 mg/dL); aspartate transaminase, 138 U/L (reference range: 0-32 U/L); alanine transaminase, 141 U/L (reference range: 0-32 U/L); and alkaline phosphatase, 403 U/L (reference range: 35-105 U/L). A markedly elevated lactate dehydrogenase level was noted at 3971 U/L (reference range: 240-480 U/L). Carcinoembryonic antigen measured 3.1 ng/mL (reference range: 0-5.0 ng/mL), with carbohydrate antigen 19-9 at 19-9 at 60.6 U/mL (reference range: 0-37.0 U/mL) and alpha-fetoprotein at 3.02 ng/mL (reference range: 1.09-8.04 ng/mL). The anti-HIV test was negative.

A computed tomography (CT) scan of the chest and upper abdomen showed a 4.3 cm × 6.6 cm mediastinal mass (Figure 1) with multiple liver nodules scattered along both hepatic lobes without any noteworthy pulmonary lesions. The provisional diagnosis was lymphoma, and the patient was therefore scheduled for endoscopic ultrasound and tissue sample collection. After deep sedation was induced using intravenous propofol with full anesthetic monitoring, a curvilinear endoscopic ultrasound scope (EG530UT2; Fujifilm, Minato-ku, Tokyo, Japan) was used for scanning. The echoview showed a large heterogeneous hypoecholic mass > 6 cm in diameter at the mediastinum, with multiple target-like nodules in the liver (Figure 2). Next, fine-needle aspiration of the mediastinal mass was performed with four passes using a 22-gauge needle (EchoTip Procore; Cook Group Inc., Bloomington, IN, United States) (Figure 3). A diagnosis of primary mediastinal lymphoma with liver metastasis was strongly suspected.

The patient’s clinical status worsened despite administration of intravenous corticosteroids. The histopathologic results finally revealed numerous small, individual, round cells with hyperchromatic nuclei, scarce cytoplasm, and frequent mitotic features. An immunohistochemical study was positive for AE1/AE3, CD56 and chromogranin A (Figure 4), but negative for synaptophysin, CK20, vimentin, CK8/18 and CD45. Based on these findings, a diagnosis of poorly differentiated neuroendocrine carcinoma, small cell type was made.

A bone marrow biopsy was also performed, which showed extensive involvement by the carcinoma (Figure 5). However, intravenous chemotherapy was not administered due to the poor performance status at this point. The patient subsequently died a few weeks later, after developing progressive liver failure, edema in both legs, and a sudden onset of dyspnea and cyanosis, due without splenomegaly and a negative finding for peripheral lymphadenopathy.
A 6.6 cm × 4.3 cm mediastinal mass was observed.

A: Echoview showed a large mediastinal mass; B: Liver nodules with target-like appearance were also observed.

Cell-block preparation from fine-needle aspiration of the mediastinal mass showed numerous small, individual, round cells with hyperchromatic nuclei, scarce cytoplasm, and frequent mitotic features. Rare instances of nuclear molding were also observed (hematoxylin-eosin staining, magnification × 10 and × 40, respectively); C and D: Immunohistochemical study revealed that the tumor cells were positive for AE1/AE3 (C) and chromogranin A (D; magnifications × 40).

to a suspected acute pulmonary embolism. No autopsy was performed in this case.
The patient described in this case report had an advanced stage neuroendocrine tumor with fatal outcome. Definitive treatment for this small cell carcinoma should be guided by the definite histopathological and immunohistochemistry results.

COMMENTS

Case characteristics
A 52-year-old man presented with a chronic cough, weight loss, anemia and progressive jaundice.

Clinical diagnosis
Metastatic small cell neuroendocrine tumor with liver and bone marrow involvement.

Differential diagnosis
Lymphoma; Carcinoid tumor; Mediastinal lymphoma; Germ cell tumor of mediastinum; Thymoma.

Laboratory diagnosis
Hemoglobin, 6.8 g/dL; White blood cell count, $7.7 \times 10^3$ cells/μL; Platelet count, $139 \times 10^3$ cells/μL; Total bilirubin, 4.2 mg/dL; Direct bilirubin, 3.7 mg/dL; Aspartate transaminase, 138 U/L; Alanine transaminase, 141 U/L; Alkaline phosphatase, 403 U/L; Lactate dehydrogenase, 3971 U/L; Carcinoembryonic antigen, 3.11 ng/mL; Carbohydrate antigen 19-9, 60.62 U/mL; Alpha-fetoprotein, 3.02 ng/mL.

Imaging diagnosis
Computed tomography scan of the chest and upper abdomen showed a 4.3 cm × 6.6 cm mediastinal mass with multiple liver nodules scattered along both hepatic lobes without any marked pulmonary lesions.

Pathological diagnosis
Poorly differentiated neuroendocrine carcinoma, small cell type.

Treatment
Palliative treatment.

Related reports
Neuroendocrine tumors are a very rare malignancy of the mediastinum, and there are very few reports in the literature.

Experiences and lessons
 Mediastinal neuroendocrine tumors may have a clinical presentation similar to lymphoma of the mediastinum. Histologic diagnosis and immunohistochemical study are crucial for definite diagnosis.

Peer-review
The authors describe a case of primary mediastinal neuroendocrine tumor with liver and bone marrow metastases, which mimicked lymphoma. This is a rare tumor with malignant lymphoma as the primary differential diagnosis.

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