World Journal of Clinical Cases

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DOI: 10.12998/wjcc.v3.i10.915

World J Clin Cases 2015 October 16; 3(10): 915-919
ISSN 2307-8960 (online)

CASE REPORT

Mediastinal small cell carcinoma with liver and bone marrow metastasis, mimicking lymphoma

Napaporn Nawarawong, Tawatchai Pongpruttipan, Pitulak Aswakul, Varayu Prachayakul

Napaporn Nawarawong, Varayu Prachayakul, Siriraj GI Endoscopy Center, Division of Gastroenterology, Department of Internal Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Tawatchai Pongpruttipan, Division of Hematopathology, Department of Pathology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Pitulak Aswakul, Liver and Digestive Institute, Samitivej Sukhumvit Hospital, Bangkok 10120, Thailand

Author contributions: Nawarawong N and Pongpruttipan T performed the data collection; Nawarawong N, Aswakul P, and Prachayakul V drafted and reviewed the article; Aswakul P and Prachayakul V revised the article and approved the version to be published.

Institutional review board statement: This article was approved by the Siriraj Internal Review Board.

Informed consent statement: The patient provided written informed consent before this procedure was performed.

Conflict-of-interest statement: The authors have no conflicts of interest related to this article.

Correspondence to: Varayu Prachayakul, Associate Professor, Siriraj GI Endoscopy Center, Division of Gastroenterology, Department of Internal Medicine, Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkok 10700, Thailand. kaiyjr@gmail.com
Telephone: +66-818654646
Fax: +66-24115013

Received: February 8, 2015
Peer-review started: February 10, 2015
First decision: April 24, 2015
Revised: June 12, 2015
Accepted: August 28, 2015
Article in press: September 7, 2015
Published online: October 16, 2015

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 bronchopulmonary 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.

Nawarawong N, Pongpruttipan T, Aswakul P, Prachayakul V. Mediastinal small cell carcinoma with liver and bone marrow metastasis, mimicking lymphoma. *World J Clin Cases* 2015; 3(10): 915-919 Available from: URL: http://www.wjgnet.com/2307-8960/full/v3/i10/915.htm DOI: http://dx.doi.org/10.12998/wjcc.v3.i10.915

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[1]. 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[2].

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[4]. 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 that had appeared 2 wk prior to his admission. He reported that he was a heavy smoker and had not experienced fever or shivering. His physical exam showed marked pallor and moderate jaundice, with a normal chest examination. The abdominal examination revealed hepatomegaly without splenomegaly and a negative finding for peripheral 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 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 hypoechoic 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

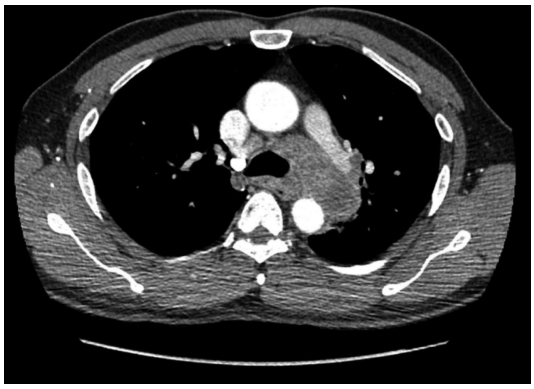

Figure 1 Computed tomography findings. A 6.6 cm × 4.3 cm mediastinal mass was observed.

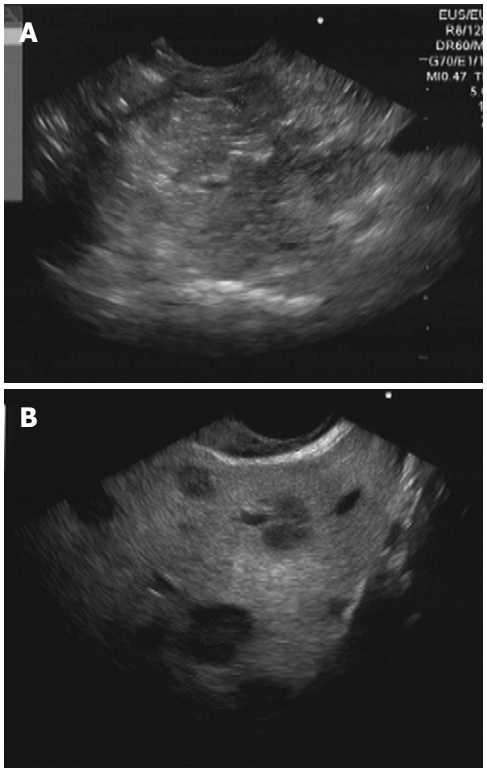

Figure 2 Endoscopic ultrasound findings. A: Echoview showed a large mediastinal mass; B: Liver nodules with target-like appearance were also observed.

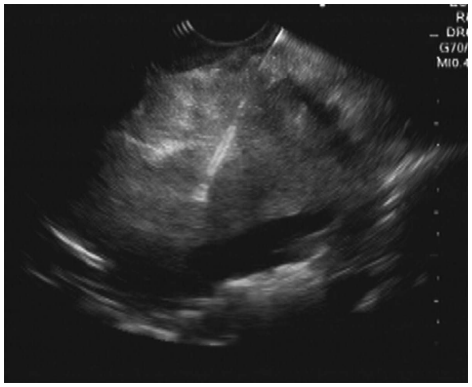

Figure 3 Fine-needle aspiration cytology was performed.

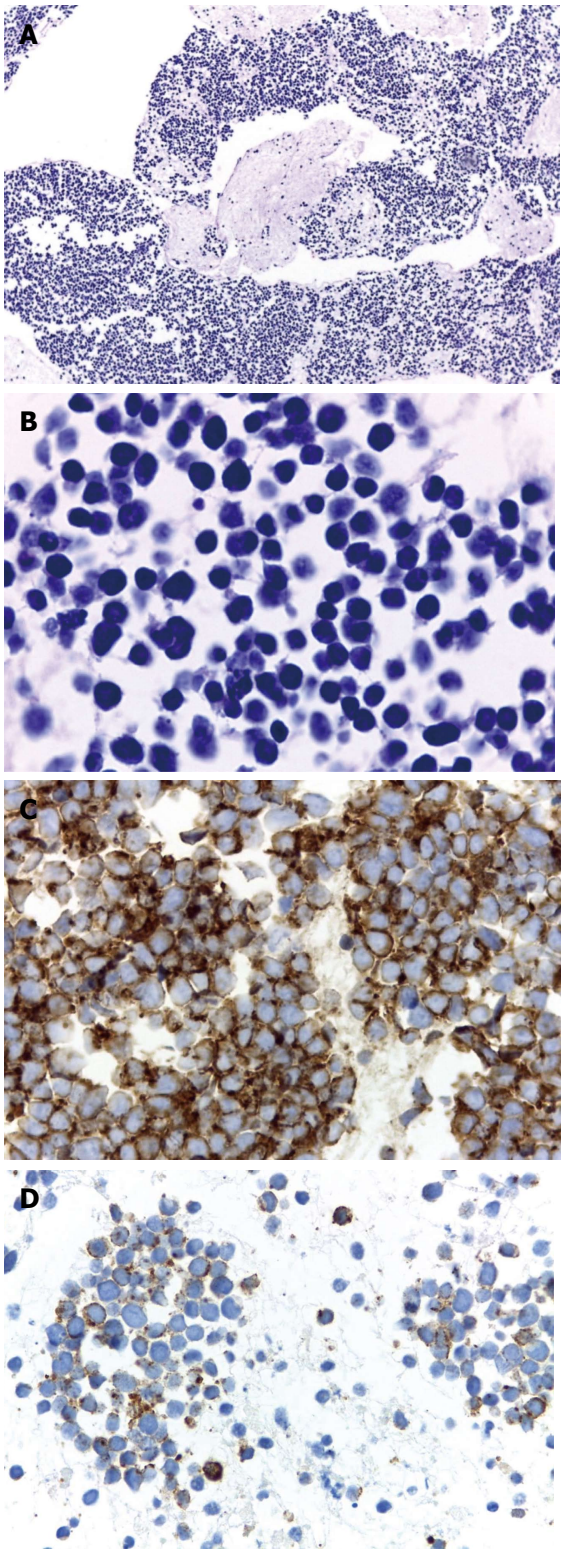

Figure 4 Histopathologic findings. A and B: Cell-block preparation from fine-needle aspiration of the mediastinal mass showed numerous small, individual, round cells with hyperchromatic nuclei, scarce cytoplasm, and frequent mitotic features. Rare instances of nuclear molding were also observed (hematoxylin-eosin 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.

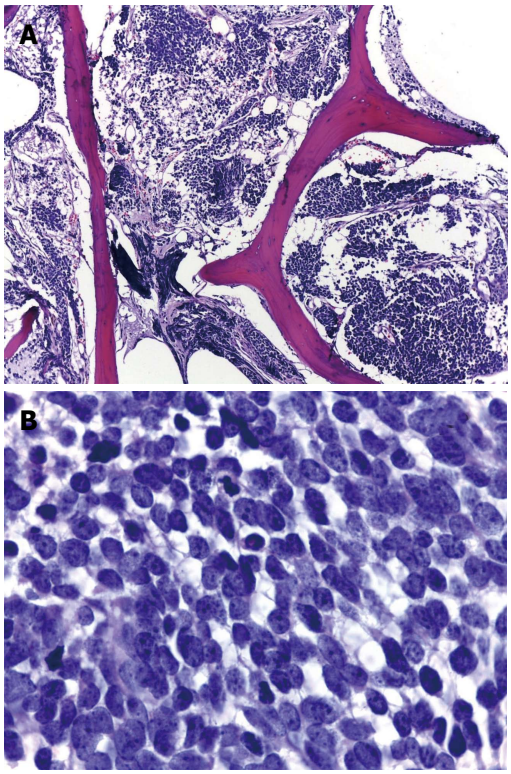

Figure 5 Bone marrow biopsy showed extensive infiltration by cohesive sheets of small, round cells with fine granular chromatin and scarce cytoplasm.

DISCUSSION

Neuroendocrine tumors are rare tumors that typically involve the gastrointestinal tract and the broncho-pulmonary system. Primary mediastinal neuroendocrine tumors are extremely rare[7-13], and can present as lymphoma, particularly Hodgkin's type. Indeed, the case described here initially presented with similar clinical symptoms, such as chronic cough, anorexia, weight loss, and a bulky mediastinal mass with liver metastasis. However, a final diagnosis of a poorly differentiated neuroendocrine tumor, small cell type was made after histopathologic and immunohistochemical study. The multiple liver nodules were strong indicators of liver metastasis, and this is the first reported case of mediastinal neuroendocrine tumor with liver and bone marrow metastases.

Li *et al*[14] reported a case series of six patients with primary small cell neuroendocrine carcinoma and found that most of the cases were in advanced stages, with tumors > 6 cm. Moreover, more than two-thirds of those cases involved the anterior-middle mediastinum with 44% scattered punctate calcification on CT. However, the immunohistochemical studies were positive for different markers, indicating the tumors had differentiated from a carcinoid tumor, mediastinal lymphoma, germ cell tumor of mediastinum, and thymoma. The poor prognosis for primary small cell neuroendocrine carcinoma was demonstrated by only half of the cases responding to chemotherapy, and the 2-year mortality rate of 50%[14].

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 × 10^3 cells/μL; Platelet count, 139 × 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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P- Reviewer: Moyana TN, Zhao HD
S- Editor: Yu J **L- Editor**: O'Neill M **E- Editor**: Jiao XK

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