ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.clinicalimagingscience.org

Journal of Clinical Imaging Science

Case Report *Diagnostic Radiology*

Small-cell cancer of the perihilar bile duct with bleeding esophageal varices: A report of a rare case

Ho Xuan Tuan[1], Dau Quang Lieu[2], Dao-Thi Luan[3], Nguyen Minh Duc[4]

[1]Department of Medical Imaging, Da Nang University of Medical Technology and Pharmacy, Da Nang, [2]Department of Internal Medicine, Hanoi Medical University Hospital, [3]Department of Pathology, Hanoi Medical University, Ha Noi, [4]Department of Radiology, Pham Ngoc Thach University of Medicine, Ho Chi Minh, Vietnam.

***Corresponding author:**
Nguyen Minh Duc,
Department of Radiology,
Pham Ngoc Thach University of Medicine, Ho Chi Minh, Vietnam.

bsnguyenminhduc@pnt.edu.vn

Received: 02 June 2023
Accepted: 19 September 2023
Published: 29 September 2023

DOI
10.25259/JCIS_53_2023

Quick Response Code:

ABSTRACT

Small-cell cancer is an uncommon histological subtype of neuroendocrine carcinoma. It frequently has a poor prognosis because of distant metastasis. It is diagnosed using histopathological and immunohistochemical tests. We report the case of a 29-year-old female with small-cell cancer in the perihilar bile duct who presented with bleeding esophageal varices. This case report aims to improve physicians' understanding of small-cell cancer, thereby helping to reduce the frequency of missed clinical diagnoses.

Keywords: Bleeding esophageal varices, Small-cell cancer, Perihilar tumor

INTRODUCTION

Extrapulmonary small-cell cancer (EPSCC), often referred to as high-grade neuroendocrine tumors (NETs), is a malignancy that develops from cells in the amine precursor uptake and decarboxylation pathway. Small-cell lung cancer (SCLC), which is most frequently caused by these cells and originates in the lungs, can occur anywhere in the body.[1] Duguid and Kennedy described for the 1st time EPSCC in a mediastinal lymph node.[2] Since then, cases have been reported of small-cell carcinoma in numerous locations, including the esophagus, stomach, small intestine, colon, rectum, anal canal, appendix, pancreas, gallbladder, and biliary tree[3] and salivary glands, oral cavity, tongue, nasal cavity, and paranasal sinuses[4] as well as the head and neck.[3,4] There are reports of small-cell carcinoma in both the gallbladder[5] and the pancreas.[6] A few studies have reported small-cell cancer of the ampulla of Vater.[7] However, reports of small-cell carcinoma of the liver or common bile duct are extremely rare.

We report the case of a 29-year-old female with small-cell cancer of the perihilar bile duct, presenting as bleeding esophageal varices, and review the relevant literature on this condition.

CASE REPORT

An otherwise healthy 29-year-old woman with no relevant family or medical history of liver diseases presented at our hospital with a sudden onset of hematemesis. The patient was conscious and had vague epigastric pain. All results of cardiopulmonary examinations were negative. There was no yellowing of the skin or sclera, no spider nevus, no edema in both lower limbs, and no

vascular murmur. The liver and spleen were not palpable under the ribs and there was no percussion pain in the liver and spleen. Murphy's sign and shifting dullness were negative. All neurological investigations were also normal.

Routine blood tests showed a significant decrease in hemoglobin concentration (79 g/L) and red blood cell count (3.04 T/L). Laboratory investigations showed normal prothrombin time, increased blood urea nitrogen (14.9 mmol/L), normal liver and renal function, normal electrolytes, and negative hepatitis serology. An upper gastrointestinal endoscopic examination showed evidence of ruptured esophageal varices. Endoscopic variceal ligation with one rubber band was performed successfully on the 1st day of the patient's admission [Figure 1].

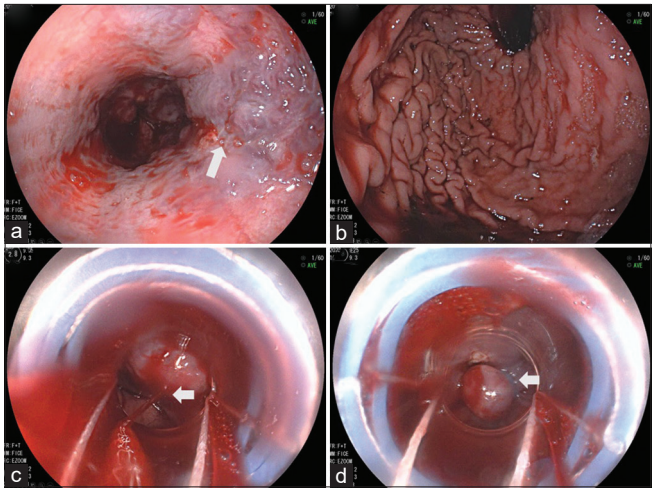

Figure 1: A 29-year-old woman with small-cell cancer of the perihilar bile duct who presented bleeding esophageal varices. (a) Upper gastrointestinal endoscopy showed the esophageal varices (white arrow), (b) gastric retroflexion experienced the blood in fundus, (c) esophageal endoscopic imaging showed the position of bleeding esophageal varices (white arrow), and (d) endoscopic variceal ligation with one rubber band (white arrow) was done.

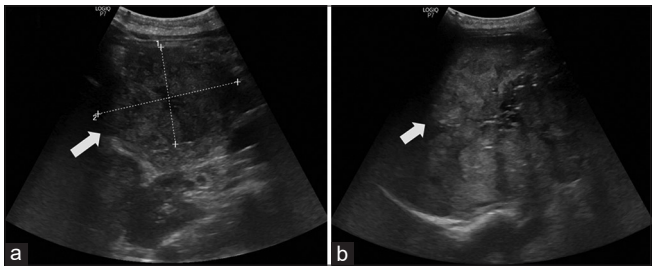

Figure 2: A 29-year-old woman with small-cell cancer of the perihilar bile duct who presented bleeding esophageal varices. (a) Abdominal ultrasonography revealed a 9 × 12 cm sized heterogeneous mass located in the perihilar bile duct (white arrow), (b) multiple hyperechoic mass were experienced in ultrasound imaging of the liver (white arrow).

Abdominal ultrasound revealed multiple hyperechoic masses in the liver and a large heterogeneous mass in the perihilar bile duct [Figure 2]. Enhanced computed tomography (CT) of the whole abdomen showed multiple calcified intra-abdominal lymph nodes, with a larger mass located in the hepatic hilar region and thrombosis of the main portal vein. No lesion was found on chest CT [Figure 3].

A percutaneous needle biopsy of the tumor was performed. Histological examination showed a malignant tumor with small round to oval cells with minimal cytoplasm, fine chromatin, and no distinct nucleoli; necrosis predominated. The tumor cells were positive for synaptophysin and Ki-67: 85% and negative for chromogranin A and CD56. The tumor was then classified as small-cell cancer based on histological and immunohistochemical findings [Figure 4].

These findings led us to diagnose small-cell carcinoma. The tumor was unresectable; therefore, palliative chemotherapy was considered to be the best treatment option. However, the patient died 8 weeks after the diagnosis was confirmed because of a recurrence of bleeding esophageal varices.

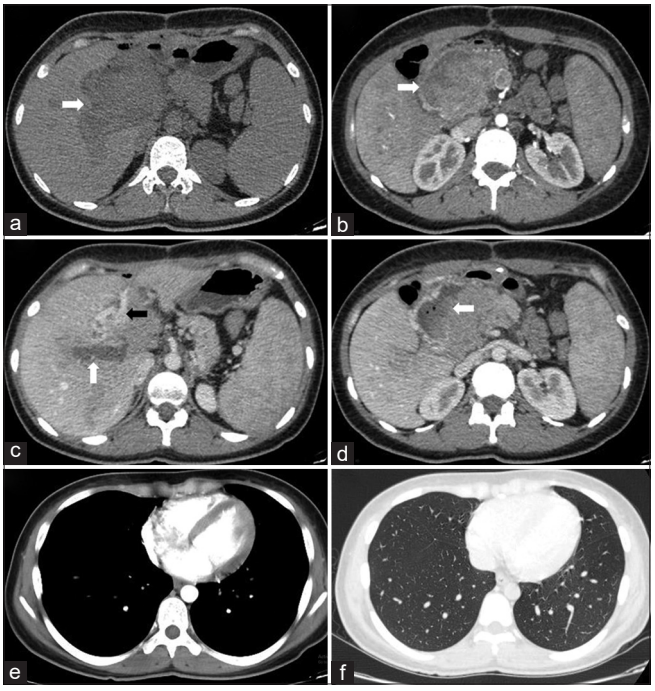

Figure 3: A 29-year-old woman with small-cell cancer of the perihilar bile duct who presented bleeding esophageal varices, (a) abdominal computed tomography (CT) scan revealed the low-density perihilar bile duct mass (white arrow), (b) the tumor gradually improved the density in the arterial (white arrow), (c) the tumor invaded portal vein (white arrow), and caused liver collateral circulation to enlarge (black arrow), and (d) The tumor invaded the duodenum and pancreas (white arrow), (e and f) the chest CT was normal.

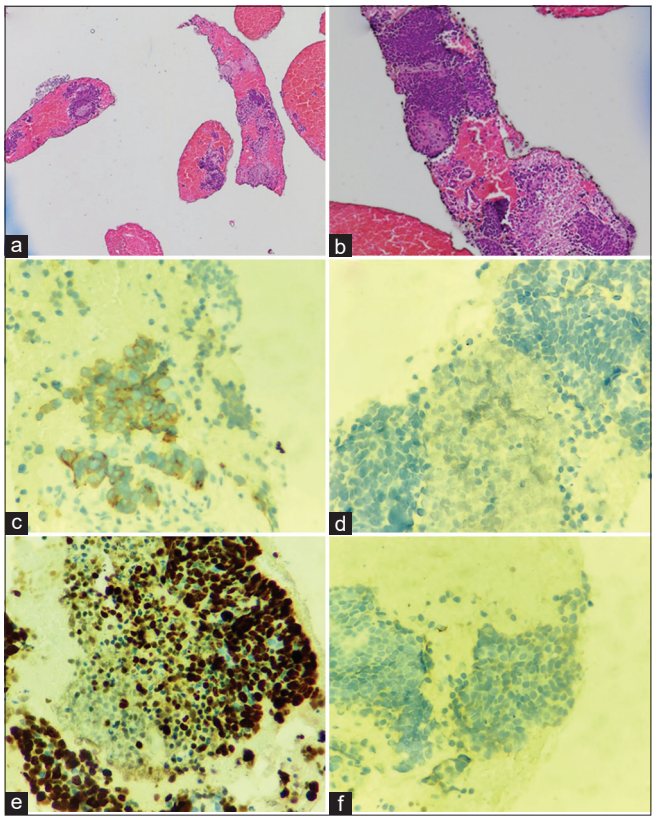

Figure 4: A 29-year-old woman with small-cell cancer of the perihilar bile duct who presented bleeding esophageal varices. A low-density perihilar bile duct mass was detected on an abdominal computed tomography scan. The tumor underwent a percutaneous needle biopsy. Histologic findings of the liver biopsy in the described patient with small-cell cancer. (a and b) Images illustrate hematoxylin and eosin staining, ×10 and ×40, respectively, the tumor consists of round, oval small cells with minimal cytoplasm, fine chromatin, and no distinct nucleoli; necrosis is predominant. Immunohistochemistry for positive synaptophysin (c), Ki67: 85% (e); negative for chromogranin A (d) and CD 56 (f).

DISCUSSION

A case of EPSCC, which was called oat cell carcinoma of the mediastinal glands, was first described as a distinct clinicopathologic disease entity in 1930, which was 34 years after the first of small-cell carcinoma of the lung.[2] Since that time, it has come to be recognized more often. Although 20–25% of bronchogenic carcinomas are small-cell carcinomas, primary locations outside the lung are substantially less common.[8] EPSCC accounts for 2.5–5% of all small-cell carcinomas in the United States.[9] The median age of EPSCC patients in the biggest study was 70 years.[10] The male-to-female sex ratio in this study was also slightly out of balance (1.3:1); nonetheless, the previous studies demonstrated that males are more likely to get cancer than women.[10,11]

To the best of our knowledge, no case of portal hypertension brought on by small-cell carcinoma of the perihilar bile duct has been documented in the literature. Obstructive jaundice has been reported in certain cases; however, there have not been any cases of portal hypertension leading to gastrointestinal bleeding from tumors in the liver and perihilar bile duct. However, this case's therapy of gastrointestinal bleeding is the same as that given to patients who have cirrhosis-related gastrointestinal bleeding. The tumor's existence, however, makes the prognosis worse.

Immunohistochemistry is used in conjunction with morphological diagnostics to confirm EPSCC. The neural cell adhesion molecule is also known as CD56, which is the most sensitive neuroendocrine marker. The neurosecretory granule protein chromogranin A, with <50% reactivity, is the least sensitive and most specific marker for neuroendocrine differentiation in EPSCC. The neuron-specific enolase and synaptophysin are two additional sensitive neuroendocrine markers.[1] NETs are separated into well-differentiated (low-to-intermediate grade) NETs and poorly-differentiated (high-grade) neuroendocrine carcinomas (NECs) based on morphological characteristics and proliferation rate (Ki-67 proliferation index).[12] Those that have a Ki-67 proliferation index of more than 55% are considered small-cell carcinomas.[13] The diagnostic criteria for EPSCC need small-cell carcinoma histological hallmarks to be present in the tumor in the absence of clinical symptoms of SCLC, which imaging investigations rule out.[14] Our patient's sputum cytology test findings for malignancy were negative, and a chest CT indicated no indications of lung cancer; thus, there was no need for a bronchoscopy. Chromogranin A and CD56 were negative in our patient, but synaptophysin was positive, supporting our conclusion. Over 80% of the Ki-67 cells were in mitosis, and 5 mitotic cells/10 HPF were found. Our investigation enabled us to identify small-cell cancer. We classified the carcinoma as a grade 3 (G3) NEC (small-cell type) according to the World Health Organization's 2010 classification of NETs/NECs.

It is generally agreed on that adjuvant chemotherapy followed by a sufficient surgical resection is the best line of action for EPSCC. Surgery does not increase survival in either EPSCC or SCLC, according to Levenson. This could be the case since the most important prognostic factor for EPSCC patients is the severity of the disease on diagnosis, when the majority of them already have concealed metastases.[8] A poor prognosis for small-cell carcinoma is caused by the frequent presence of distant metastases. The long-term survival rate of EPSCC patients is hence frequently poor.

CONCLUSION

Extrapulmonary small-cell carcinoma is an uncommon type of cancer. Due to the lack of disease specificity

in clinicomorphological findings and serological and radiological investigations, diagnosis can only be made through pathology and immunohistochemistry studies. Small-cell carcinoma frequently shows distant metastasis and, consequently, has a poor prognosis. Therefore, the long-term survival of patients with EPSCC is generally poor.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Frazier SR, Kaplan PA, Loy TS. The pathology of extrapulmonary small cell carcinoma. Semin Oncol 2007;34:30-8.
2. Duguid JB, Kennedy AM. Oat-cell tumours of mediastinal glands. J Pathol Bacteriol 1930;33:93-9.
3. Brenner B, Tang LH, Klimstra DS, Kelsen DP. Small-cell carcinomas of the gastrointestinal tract: A review. J Clin Oncol 2004;22:2730-9.
4. Gelot R, Rhee TR, Lapidot A. Primary oat-cell carcinoma of head and neck. Ann Otol Rhinol Laryngol 1975;84:238-44.
5. Eriguchi N, Aoyagi S, Noritomi T, Imamura M, Sato S, Fujiki K, *et al.* Adeno-endocrine cell carcinoma of the gallbladder. J Hepatobiliary Pancreat Surg 2000;7:97-101.
6. Nakamura Y, Tajiri T, Uchida E, Arima Y, Aimoto T, Katsuno A, *et al*. Changes to levels of serum neuron-specific enolase in a patient with small cell carcinoma of the pancreas. J Hepatobiliary Pancreat Surg 2005;12:93-8.
7. Sugawara G, Yamaguchi A, Isogai M, Watanabe Y, Kaneoka Y, Suzuki M. Small cell neuroendocrine carcinoma of the ampulla of Vater with foci of squamous differentiation: A case report. J Hepatobiliary Pancreat Surg 2004;11:56-60.
8. Kim JH, Lee SH, Park J, Kim HY, Lee SI, Nam EM, *et al*. Extrapulmonary small-cell carcinoma: A single-institution experience. Jpn J Clin Oncol 2004;34:250-4.
9. Van der Heijden HF, Heijdra YF. Extrapulmonary small cell carcinoma. South Med J 2005;98:345-9.
10. Wong YN, Jack RH, Mak V, Henrik M, Davies EA. The epidemiology and survival of extrapulmonary small cell carcinoma in South East England, 1970–2004. BMC Cancer 2009;9:209.
11. Haider K, Shahid RK, Finch D, Sami A, Ahmad I, Yadav S, *et al.* Extrapulmonary small cell cancer: A Canadian province's experience. Cancer 2006;107:2262-9.
12. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system. 4th ed. Geneva: WHO Classification of Tumours Editorial Board; 2010.
13. Raj N, Reidy-Lagunes D. Systemic therapies for advanced pancreatic neuroendocrine tumors. Hematol Oncol Clin North Am 2016;30:119-33.
14. Berniker AV, Abdulrahman AA, Teytelboym OM, Galindo LM, Mackey JE. Extrapulmonary small cell carcinoma: Imaging features with radiologic-pathologic correlation. Radiographics 2015;35:152-63.

How to cite this article: Xuan Tuan H, Quang Lieu D, Luan D, Minh Duc N. Small-cell cancer of the perihilar bile duct with bleeding esophageal varices: A report of a rare case. J Clin Imaging Sci 2023;13:30.