Clinical Case Report

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# Surgical treatment for metastasis from lymphoepithelioma-like cholangiocarcinoma in the liver

## A case report

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**Abstract**

**Rationale:** Lymphoepithelioma-like cholangiocarcinoma (LEL-CC) is a rare variant of intrahepatic cholangiocarcinoma (ICC), which is characterized by the better outcome than normal ICC. There is no report about the treatment for the metastasis of the LEL-CC. Here, we describe a rare case of LEL-CC of the liver and report the treatment for metastasis of it.

**Patient concerns:** A 38-year-old woman with a chronic hepatitis B infection was referred to the department of liver surgery in our hospital with a mass in the liver.

**Diagnoses:** A past ultrasound examination had revealed a 28 mm × 16 mm nodular lesion in the right posterior lobe of the liver in May 2013. She had undergone partial resection of the thyroid gland for papillary carcinoma 1 year earlier.

**Intervention:** Suspicious of the metastasis from thyroid cancer, she underwent surgery with liver segmentectomy. The pathologic diagnosis of the lesion was LEL-CC. After surgery, she regularly got checked in our hospital, and in the 6 months after surgery, there was enlargement of lymph node before the inferior vena cava in CT. The doctor did not detect the enlargement of the lymph node until June 2017. The PET-CT was done in June of 2017, which showed the lymph node was hypermetabolic.

**Outcomes:** The patient got her second surgery for lymph node three years after the first surgery, which was proved that the lymph node was metastasis from LEL-CC. The patient was free from recurrence 9 months after surgery.

**Lessons:** We report the first case of surgery for metastasis from LEL-CC in the liver that was diagnosed 3 years after hepatectomy. Our findings suggest that surgery could be an effective way of treating lymph node metastasis of LEL-CC and early PET-CT can help to identify metastasis.

**Abbreviations:** AE = anion exchanger, CK = cell keratin, CT = computed tomography, EBV = Epstein–Barr virus, EMA = epithelial membrane antigen, ICC = intrahepatic cholangiocarcinoma, LEL-CC = lymphoepithelioma-like cholangiocarcinoma, MRI = magnetic resonance imaging, PET-CT = positron emission tomography-computed tomography.

**Keywords:** lymphoepithelioma-like cholangiocarcinoma, metastasis, surgery

## 1. Introduction

Lymphoepithelioma-like cholangiocarcinoma (LEL-CC) is a rare variant of intrahepatic cholangiocarcinoma (ICC), which is defined as tumors arisen in the hepatic tract and composed of undifferentiated epithelial cells with an prominent lymphocytic infiltrate.[1] Because the good outcome of LEL-CC compared with ordinary cholangiocarcinoma, the report of their recurrence was also rare.[2] We had noted that there was no report about the treatment of the metastasis of LEL-CC. To the best of our knowledge, 51 cases of LEL-CC and one case of extrahepatic LEL-CC had been described in the English literature, and only 9 cases had reported the metastasis. They all focused on the histology and pathology of original lesion. This case showed early recurrence of lymphoepithelioma-like cholangiocarcinoma, and we proved that surgery was a good way to treat the metastasis of LEL-CC. Herein, we reported the first case of the growth and treatment of the lymph node metastasis of LEL-CC, and this was the first case to report the PET-CT of the metastasis of LEL-CC.

## 2. Case report

In September 2013, a 38-year-old Chinese woman was referred to the Department of Liver Surgery in our hospital with a mass in the liver. She had undergone partial resection of the thyroid gland for papillary carcinoma 1 year earlier, and had a 10-year chronic hepatitis B infection. When she received a regular physical

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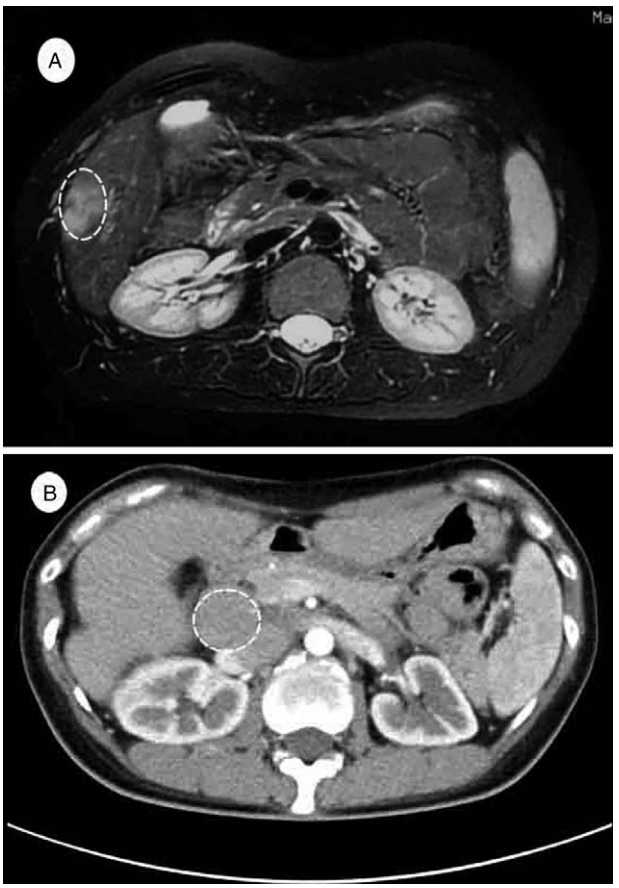


**Figure 1.** (A) Liver magnetic resonance image shows a small lymphoepithelioma-like cholangiocarcinoma at segment 6 of the liver (in-phase T1-weighted image). (B) CT shows metastasis of LEL-CC. CT = computed tomography, LEL-CC = lymphoepithelioma-like cholangiocarcinoma.

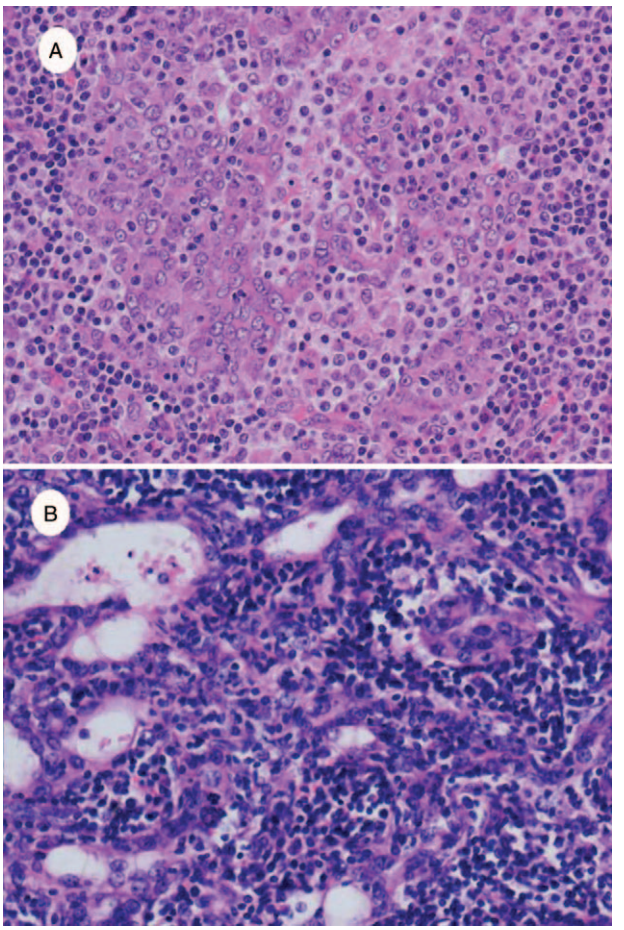


**Figure 2.** Histology of lymph node metastasis. (A) The majority of the tumor was composed of undifferentiated epithelial cells with dense lymphocytic infiltration and scattered lymphoid follicles (hematoxylin and eosin stain, ×200). (B) The majority of the lymph node was composed of undifferentiated epithelial cells with dense lymphocytic infiltration and scattered lymphoid follicles (hematoxylin and eosin stain, ×200).

examination in May 2013, an ultrasound examination showed a 28 × 16-mm nodular lesion in the right posterior lobe of the liver, which was suspected to be hepatic hemangioma. In August 2013, she was rechecked in a local hospital for the nodular lesion by magnetic resonance imaging. This technique showed a focal liver lesion, which was 28 × 10 mm in size in segment 6 of the liver, and could not be excluded from metastasis of thyroid carcinoma (Fig. 1A). The mass showed hypointensity on T1-weighted imaging and an irregular margin with hyperintensity on T2-weighted imaging. In our hospital, we performed dynamic sonography, which showed early heterogeneous arterial enhancement in the arterial phase, washout in the portal venous phase, and a hypoechoic nodule in the delayed phase. Because we suspected metastasis from thyroid cancer, she underwent surgery of liver segmentectomy in September 2013. Histology of a specimen removed from surgery showed poorly differentiated adenocarcinoma with considerable lymphoid infiltrate (Fig. 2A). Immunohistoche-mical studies showed that the epithelial component was reactive for AE1/AE3, CK7, CK19, EMA, and EBV, and was negative for hepatocyte and CK20. The lymphoid infiltrate was positive for CD3 and CD20. A diagnosis of LEL-CC was made. The postoperative course was uneventful, without complications or need for additional treatment.

After surgery, she was regularly checked in our hospital every 6 months. However, enlargement of the lymph node in front of the inferior vena cava was not found until June 2017, which enabled us to study the growth of lymph node metastasis. Lymph node metastasis had appeared 6 months after the first surgery, and computed tomography (CT) images showed that the lymph node had grown in the past 3 years (20 × 10 mm → 20 × 13 mm → 24 × 16 mm → 26 × 24 mm → 26 × 25 mm → 28 × 25 mm) (Fig. 1B). The PET-CT (positron emission tomography-computed tomography) was done in June 2017 and it showed the lesion was hypermetabolic. Because we suspected that the metastasis was from LEL-CC, the patient had a second surgery for lymph node metastasis 3 years after the first surgery. The lymph node was soft, substantial, and gray-white. Histologically, this node was composed of formed of irregular, small glands with lymphoid stroma (Fig. 2B). Immunohistochemically, the lymph node was diffusely positive for AE1/AE3, CK7, CK19, and CK20 and negative for CD20 and hepatocyte. Based on these histopathological and immunohistochemical findings, the diagnosis of metastasis of LEL-CC was made. The patient's postoperative course was uneventful. Due to the success of surgery, there was no necessity for the patient to have chemotherapy or radiotherapy and the patient has been free from tumor recurrence for 6 months.

The study was approved by the Institutional Review Board for the Protection of Human Subjects of Peking Union Medical

College (PUMC) Hospital and adhered to the tenets of the Declaration of Helsinki. The patient provided written informed consent for publication of this report and all accompanying images.

## 3. Discussion

LEL-CC is a rare variant of intrahepatic cholangiocarcinoma (IHCC), which is characterized by intense lymphocytic infiltrate and a lower rate of recurrence after surgery and better overall survival than normal cholangiocarcinoma.[1] Despite the rarity of LEL-CC, these tumors are of general interest, because of its better outcome and its relationship with EBV infection.[2]

After searching PubMed, Embase, and the Web of Science, we found that 52 cases of LEL-CC had been reported in the English literature. Only 8 cases had recurrence. The current case report is the first to report growth and treatment of metastasis of LEL-CC. Additionally, LEL-CC with thyroid cancer is uncommon.

We intended to understand the mechanism of a better outcome of this tumor, and the relationship between this tumor and the immune system, which could be useful for treating cancer. LEL-CC might be associated with EBV infection, but whether it is associated with a better outcome is unclear. Wang et al reported that EBV infection leads to a poorer prognosis in LEL-CC.[3] However, Sun et al showed that EBV-positive IHCC was not significantly different in overall survival compared with EBV-negative IHCC. Further studies were required to investigate the relation between EBV and LEL-CC.[4] We observed that the average followed month of EBV positive and negative was, respectively, 42.4 months and 20.4 months, which may show that EBV infection can be protective aspect for LEL-CC. The case we reported was positive for EBV, and the patient had 3 years survival after the first surgery. It can increase our knowledge about the relationship between EBV and LEL-CC.

The histologic diagnosis of metastatic LEL-CC can be challenging, which can be diagnosed as medullary carcinoma, metastatic melanoma, and lymphoma.[5] Immunohistochemistry was helpful to characterize the origin of these neoplastic cells. In our case, it was diagnosed by immunohistochemistry and histology.

We report the first PET-CT of the metastasis of LEL-CC. Though Park et al[6] has reported that F-18 FDG PET/CT showed high sensitivity for lymphoepithelioma -like gastric carcinoma, and high specificity for both lymph node and distant metastasis. There was no study about the function of PET/CT in LEL-CC. Our case was a good example for the function of PET-CT to detect the metastasis, because the doctor failed to find the metastasis in the early stage through enhanced CT.

Because the limited number of LEL-CC, no consensus on standardized treatment strategy for the tumor had been reported. All cases experienced surgical treatment, but the necessity of lymph node dissection had not been reported. Radical surgical resection was still said to be the most effective treatment. Some reports had suggested that postoperative radiation therapy and chemotherapy may be beneficial.[7] However, the evidence had not been conclusive. And in our case, the metastasis was resected completely at the time of second surgery, so we didn't use radiation therapy and chemotherapy. In our case the patient was still free of disease 9 months after the second surgery for lymph node metastasis, and 3 years after the first surgery. Nine months may not be longer enough to show surgery could be an effective way to treat metastasis of LEL-CC, but we at least proved that LEL-CC patient can have a chance to have a second surgery for metastasis.

In conclusion, we reported the first case of surgery for metastasis from LEL-CC in the liver that was diagnosed 3 years after hepatectomy. Our findings suggested that surgery could be an effective way of treating lymph node metastasis of LEL-CC, HBV could be the protective factor for LEL-CC, and early PET-CT could help to identify metastasis.

## Author contributions

Zhang JW reported the case and wrote the manuscript; Yu SN contributed to the histopathological diagnosis; Huang HC researched the bibliography;Yang HY, Xu yiyao, and Sang XT revised the manuscript; Bian J and Xiong JP collected the data; Lu X provided clinical information and approved submission of the manuscript.

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**Investigation:** Jin Bian, Jianping Xiong.
**Writing – original draft:** Junwei Zhang.
**Writing – review & editing:** Xin Lu, Huayu Yang, Yiyao Xu, Xinting Sang, Hanchun Huang.

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