Case Report
pISSN 1738-2637 / eISSN 2288-2928
J Korean Soc Radiol 2017;77(4):217-221
https://doi.org/10.3348/jksr.2017.77.4.217

대한영상의학회지

Intrahepatic Cholangiocarcinoma Initially Presented as a Distant Metastatic Lymph Node without Demonstrable Hepatic Mass: A Case Report

간내 담관암에서 원발부위 불명암으로 나타난 전이성 림프절의 낭성 변화: 증례 보고

Lyo Min Kwon, MD[1], Hong Il Ha, MD[1]*, Min-Jeong Kim, MD[1], Kwanseop Lee, MD[1], Mi Jung Kwon, MD[2]

Departments of [1]Radiology, [2]Pathology, Hallym University Sacred Heart Hospital, Anyang, Korea

This report describes a rare case of intrahepatic cholangiocarcinoma, initially presented as a distant metastatic lymph node without demonstrable hepatic mass, in a 37-year-old man. Initially, a solitary cystic mass around the common hepatic artery was detected; two years later, a mass-forming intrahepatic cholangiocarcinoma developed in the left lobe of the liver. The cystic mass showed no change in shape and size for two years, which was then confirmed as a distant metastatic lymph node of cholangiocarcinoma after surgery. This was an extraordinary clinical manifestation of the intrahepatic cholangiocarcinoma, which presented as a cavity lymphadenopathy with unknown primary site, in addition to favorable clinical course with stable size and shape for 2 years. After literature reviews, we discuss in this paper the possible mechanism of cancer of unknown primary in intrahepatic cholangiocarcinoma, and the prognostic factors involved.

Index terms
Cholangiocarcinoma
Lymph Nodes
Metastasis
Prognosis

Received June 15, 2016
Revised March 23, 2017
Accepted May 15, 2017
***Corresponding author:** Hong Il Ha, MD
Department of Radiology, Hallym University Sacred Heart Hospital, 22 Gwanpyeong-ro 170beon-gil, Dongan-gu, Anyang 14068, Korea.
Tel. 82-31-380-3880 Fax. 82-31-380-3878
E-mail: ha.hongil@gmail.com

INTRODUCTION

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary hepatic malignancy in human adults, and several studies have reported a worldwide rapid increase in the rates of ICC over the last few decades (1). According to the current 8th edition of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) staging manual, lymph node metastasis beyond the hepatoduodenal ligament is regarded as a distant metastasis in primary liver carcinoma (2). Cancer of unknown primary (CUP) is a heterogeneous group of cancers when the site of primary origin is not revealed (3). In case of a single distant metastatic lymph node metastasis being detected, it would be considered as CUP (3). ICC presented as CUP has rarely been reported. Herein, we report a case of distant metastatic lymphadenopathy of the ICC, presented as a cystic mass around the common hepatic artery (CHA). We further discuss possible prognostic factors of our patient.

CASE REPORT

A 37-year-old man, without any underlying disease, present-

ed at the emergency room complaining of pain in the right flank. A right ureteral stone was noted on the abdominopelvic computed tomography (CT) scan. Incidentally, a 2.7 cm well-defined mass with lobulating contours had been detected around the common hepatic artery (Fig. 1A). The CT number of the mass on precontrast scan had been 11 Hounsfield units, which represents fluid density. The mass showed a few thin septa and eccentric thin peripheral enhancing portions. No demonstrable hepatic lesions were observed on the CT scan. The cystic mass was considered to have a low malignancy potential; therefore, no further evaluation had been performed at that time. One year later, the patient underwent annual screening for abdominal ultrasound, which revealed no significant interval change in size and shape of the cystic mass. Another year later, the screening abdominal ultrasound detected a 4.5 cm hepatic mass in the left lateral section of the liver. Serum level of CA 19-9 was mildly elevated (84.95 U/mL; normal range 0–27.0 U/mL).

For further evaluation of the hepatic mass, enhanced abdominopelvic CT and gadolinium-enhanced magnetic resonance imaging (MRI) were performed. On the enhanced CT scan, the ill-defined 4.5-cm sized hepatic mass showed a heterogeneous enhancement, associated with surrounding arterioportal shunts and adjacent hepatic capsular retraction (Fig. 1B); minimal dilatation of B2 and B3 intrahepatic bile ducts was noted. The presumed cystic mass around CHA showed no significant change in size and shape (Fig. 1B); however, density of the mass had increased up to 48 Hounsfield units on the precontrast scan. On abdominal MRI, the hepatic mass showed iso-signal intensity on the T1-weighted image and heterogeneous intermediate intensity on the T2-weighted image, indicating that the diffusion coefficient value of the hepatic mass had apparently increased. On the dynamic gadolinium-enhanced axial T1-weighted imag-

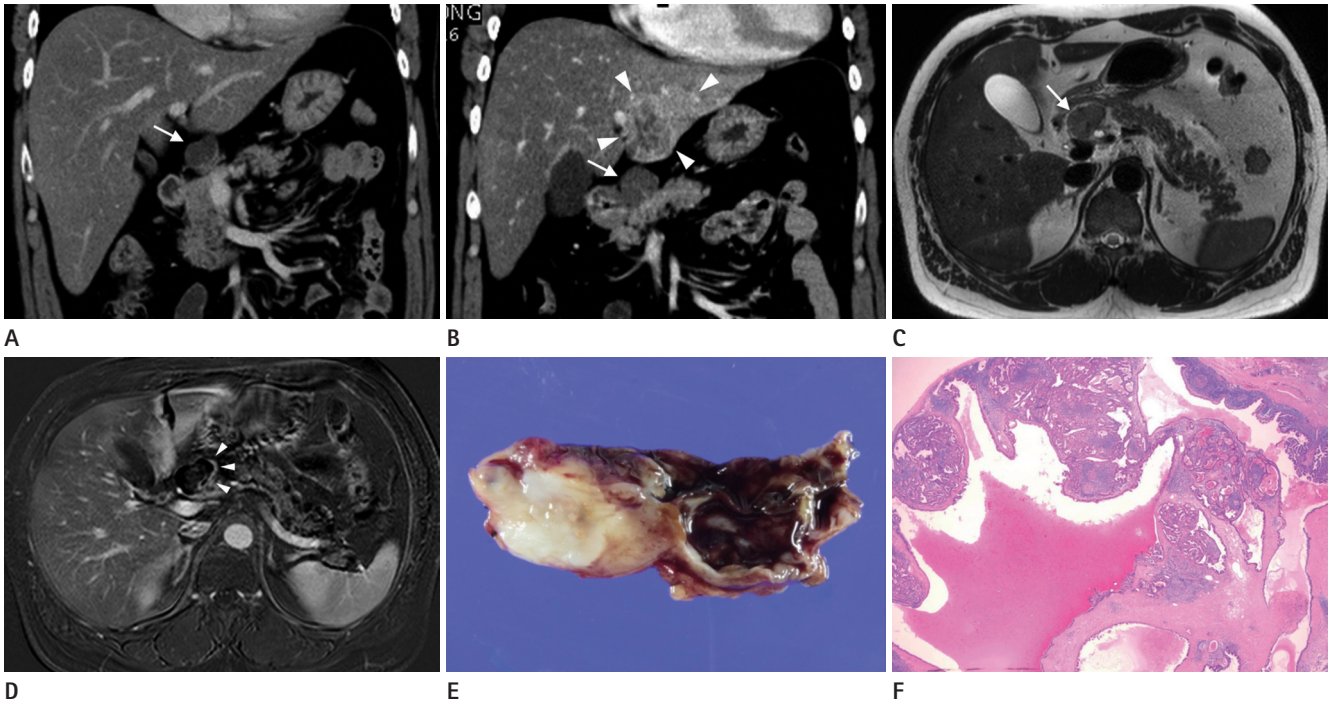

Fig. 1. Intrahepatic cholangiocarcinoma in a 37-year-old man, initially presented as a distant metastatic lymph node without demonstrable hepatic mass.
A. Contrast-enhanced CT scan shows a 2.7-cm well-defined cystic mass (arrow) around the common hepatic artery, with no demonstrable hepatic mass.
B. After two years, follow up contrast enhanced CT scan reveals a presumed cystic mass around the common hepatic artery without interval change (arrow). However, an approximately 4.5-cm hepatic mass (arrowheads) is newly identified.
C. The newly identified cystic mass shows intermediate signal intensity on axial T2-weighted MR image (arrow).
D. The newly identified cystic mass shows focally eccentric enhancing wall thickening on contrast-enhanced axial T1-weighted MR image (arrowheads).
E. The gross specimen photograph of the cystic mass shows cavitary mass with irregularly thickened wall, and having internal hemorrhage.
F. Photomicrograph (hematoxylin and eosin staining, × 100) of the cystic mass confirms the necrotic and hemorrhagic change of metastatic lymph node.

ing, the mass showed peripheral enhancement on the arterial phase, with gradual and centripetal progression on the portal to delayed phases. With this enhancing pattern, bile duct dilatation and capsular retraction, the hepatic mass was radiologically consistent with a mass forming ICC. Conversely, the presumed cystic mass around the CHA showed high signal intensity on the T1-weighted image and intermediate signal intensity on the T2-weighted image (Fig. 1C), which represented hemorrhagic change. The eccentric peripheral solid component showed a strong enhancement on gadolinium-enhanced subtraction image (Fig. 1D). Grossly, the mass showed no interval change in size and shape, compared with the previous CT scan two years back.

The ultrasound-guided percutaneous needle biopsy for hepatic mass was performed, and the result was moderately differentiated adenocarcinoma.

The patient underwent left hemihepatectomy with regional lymph node dissection and excision for the cystic mass around the CHA. The hepatic mass was pathologically confirmed as ICC; it was poorly differentiated, measuring 4.5 × 4 cm with lymphatic tumor emboli. The regional lymph nodes were free of tumor. On the gross specimen, the cystic mass around the CHA was grossly irregular, having a thick wall cavity with internal hemorrhage and necrosis (Fig. 1E). The pathology confirmed the mass as metastatic lymph nodes of adenocarcinoma (Fig. 1F). Immunohistochemistry of the mass was positive for cytokeratin (CK) 7, CK 19, and CK 20 staining, which is compatible with metastasis of cholangiocarcinoma. Therefore, the final diagnosis was an ICC with a distant lymph node metastasis, compatible with stage IVB. Currently, at 28 months after surgery, the patient remains in the disease-free state.

DISCUSSION

An intra-abdominal cystic mass around the CHA was found incidentally; the mass proved to be a distant metastatic lymph node, and no primary tumor was observed at initial presentation. This type of clinical presentation is broadly regarded as CUP. This case is considered as CUP of ICC, with latent visualization of the primary tumor two years after initial presentation.

CUP is relatively common in clinical medicine, and has been reported to comprise 2–5% of all cancer cases (3). It was reported that primary sites were found in about 73% of the CUP patients on autopsy, with the lung, liver, pancreas and gastrointestinal tract being the most common sites (4). On the other hand, in a recent retrospective study by Greco et al. (5), latent primary sites were found in 38 of 501 CUP patients (7.6%) during their lifetime, months to years after their initial diagnosis (median time: 12.25 months).

The common histopathologic types of CUP are adenocarcinoma, poorly differentiated carcinoma, squamous carcinoma, and neuroendocrine cancers (3). Of these, adenocarcinoma is the most common CUP, accounting for about 60% of all CUPs (6). The cholangiocarcinoma is a subtype of an adenocarcinoma arising from the epithelial lining or peribiliary glands of the biliary tract. The prevalence of cholangiocarcinoma of CUP is regarded as very rare, and has not been analyzed so far. In previous literature on CUP, cholangiocarcinoma is stated as one of the differential diagnoses in CUP of adenocarcinoma (7). However, to the best of our knowledge, this is the first case report of a CUP of ICC with clinical presentation, clinical course, radiologic finding and pathology.

CUP usually shows unfavorable prognosis due to its characteristics; early metastatic dissemination, invasive nature of small primary tumor, diagnostic challenge and limited treatment effect of empirical broad spectrum agent (8). According to Hemminki et al. (6), the CUP of adenocarcinoma has a poor prognosis, with a 12-month survival rate of 41% and median survival time of 8 months. The CUP of lymph node involvement only (nodal CUP) shows worse prognosis, with a 12-month survival rate of 18% and median survival time of 4 months, compared to that of extranodal involvement type (4). However, in our patient, the nodal CUP shows no significant interval change for 24 months, and the patient remains disease-free till date, i.e., 12 months after surgery. This is an extraordinarily favorable clinical course as a case of a nodal CUP of adenocarcinoma.

Previous reports state that nodal CUP shows a more favorable prognosis than extranodal CUP (4). The reason suggested was that the vital organ was preserved in the case of nodal CUP, and hence no vital functions are immediately threatened in nodal CUP (4). Hence, we believe that the nodal CUP may be a factor contributing to favorable prognosis of our case. Our patient had a 4.5-cm ICC in the left hemiliver with a single metastatic lymph node around CHA, which was compatible with distant metas-

tasis. No metastasis to the regional lymph node, such as hepatoduodenal ligament, was noted. The TNM stage was IVB, according to the AJCC/UICC classification. This manifestation of metastasis would be stated as a skip distant metastasis (2). According to the analysis of nodal metastasis of ICC by Nozaki et al. (2), a skip distant metastasis was found in 18% of patients with lymph node metastasis in ICC. All patients with a skip distant metastasis had ICC in the left hemiliver, and none of the patients were noted with ICCs in the right hemiliver. An interesting aspect of the report is that there was no difference in survival rate between the patients with only a regional lymph node metastasis, and those with a skip distant metastasis (2). Also, the survival rate of patients with skip metastasis was more favorable than that of patients with both regional and distant lymph node metastases (2). The authors explained these findings by the possibility of the existence of two main lymphatic drainage routes of the left lobe: one through the hepatoduodenal ligament, and the other through the cardinal portion of the stomach or along the CHA. As a result, the authors suggest that a skip distant metastasis of ICC in the left hemiliver may not suggest a worse prognosis than regional lymph node metastasis only, and may suggest a better prognosis than when both regional and distant lymph node metastases are involved (2). Our case could be a representative case of ICC in the left hemiliver with a skip metastasis. Although the TNM stage of our patient was IVB, this skip distant metastasis may suggest a relatively favorable prognosis, compared to other stage IVB patients having a combination of regional and distant lymph node metastases.

We admit that this case had some limitations. No percutaneous biopsy or endoscopic ultrasound-guided fine needle aspiration was performed two years prior to the final diagnosis. This is because immediate pathologic confirmation is not always performed for an incidentally detected cystic lesion or a single enlarged lymph node, particularly without evidence of malignancy. However, we tracked one of them, and finally it was pathologically confirmed as nodal CUP.

In conclusion, the present study reports a case of a nodal CUP along CHA with cystic change in ICC, having an extraordinarily favorable prognosis. If a nodal CUP was detected around CHA, cholangiocarcinoma should be considered as one of differential diagnosis of primary tumor. In particular, nodal CUP was proved to be an adenocarcinoma on biopsy.

REFERENCES

1. Bridgewater J, Galle PR, Khan SA, Llovet JM, Park JW, Patel T, et al. Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. *J Hepatol* 2014;60:1268-1289
2. Nozaki Y, Yamamoto M, Ikai I, Yamamoto Y, Ozaki N, Fujii H, et al. Reconsideration of the lymph node metastasis pattern (N factor) from intrahepatic cholangiocarcinoma using the International Union Against Cancer TNM staging system for primary liver carcinoma. *Cancer* 1998;83:1923-1929
3. Varadhachary GR. Carcinoma of unknown primary origin. *Gastrointest Cancer Res* 2007;1:229-235
4. Pentheroudakis G, Golfinopoulos V, Pavlidis N. Switching benchmarks in cancer of unknown primary: from autopsy to microarray. *Eur J Cancer* 2007;43:2026-2036
5. Greco FA, Lennington WJ, Spigel DR, Hainsworth JD. Molecular profiling diagnosis in unknown primary cancer: accuracy and ability to complement standard pathology. *J Natl Cancer Inst* 2013;105:782-790
6. Hemminki K, Bevier M, Hemminki A, Sundquist J. Survival in cancer of unknown primary site: population-based analysis by site and histology. *Ann Oncol* 2012;23:1854-1863
7. Hammar SP. Metastatic adenocarcinoma of unknown primary origin. *Hum Pathol* 1998;29:1393-1402
8. Greco FA. Cancer of unknown primary site: still an entity, a biological mystery and a metastatic model. *Nat Rev Cancer* 2014;14:3-4

간내 담관암에서 원발부위 불명암으로 나타난 전이성 림프절의 낭성 변화: 증례 보고

권려민[1] · 하홍일[1]* · 김민정[1] · 이관섭[1] · 권미정[2]

37세 남자 환자에서 간내담관암이 간종괴 없이 총간동맥부근의 원격림프절 전이로 첫 발현한 드문 증례를 보고하고자 한다. 우연히 총간동맥 부근의 낭성종괴가 발견되었고 당시에 간에 국소병변이 발견되지 않았으나 2년 후 간좌엽에서 간내담관암이 발견되었다. 총담관주변의 낭성종괴는 2년 동안 크기와 모양에 변화가 없었으며, 수술로 간내담관암의 원격전이 림프절로 진단되었다. 간내담관암이 원발병소 없이 전이성 림프절로 발현하였고, 2년 동안 변화가 없다는 것은 일반적인 간내담관암의 임상경과에서는 보기 어려운 예외적인 현상이다. 이에 본 증례보고를 통해 원발병소 없이 림프절 전이로 나타난 간내담관암과, 이러한 예외적인 임상경과에 영향을 미칠 수 있는 인자들에 대해서 문헌고찰을 통해 살펴보고자 한다.

한림대학교 성심병원 [1]영상의학과, [2]병리과