

—Report on Experiments and Clinical Cases—

A Case of Recurring Hepatocellular Carcinoma with
a Solitary Virchow's Lymph Node MetastasisNobuhiko Taniai, Hiroshi Yoshida, Yasuhiro Mamada, Yoshiaki Mizuguchi,
Takeo Fujihira, Koho Akimaru and Takashi Tajiri¹Surgery for Organ Function and Biological Regulation, Nippon Medical School Graduate School of Medicine**Abstract**

A 73-year-old male with C type liver cirrhosis and poor liver function reserve was diagnosed with hepatocellular carcinoma (HCC) (Segment V, 2 × 2 cm in diameter) and underwent open microwave coagulation therapy (MCT). Ten months later, a movable hard mass about the size of a quail egg was palpable at the left supra-clavicular lymph node (LN) (Virchow's LN) and blood tests revealed an elevated serum α -fetoprotein (AFP) level of 26.7 ng/dl. Abdominal and chest CT showed no evidence of recurrence in liver or lung, and no metastases of abdominal LN. Barium and bone scintigraphy revealed no abnormal spots. The affected left supra-clavicular LN was extirpated. The tumor was confirmed to be an LN metastasis from HCC by histopathological examination. After the operation, the patient developed uncontrollable pleural effusion and ascites, and intrahepatic and abdominal LN metastases were visible on abdominal CT with great haste. He died 1.5 months after the LN was extirpated. We herein report a case of HCC treated by MCT which later resulted in a solitary Virchow's LN metastasis in the absence of any abdominal LN or recurrence in the liver or lung.

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Key words: hepatocellular carcinoma (HCC), Virchow's lymph node metastasis**Introduction**

Hematogenous metastases from hepatocellular carcinoma (HCC) are well known. The most frequent site of hematogenous metastases is the lung, followed by the adrenal gland and skeleton^{1,2}. On the other hand, lymph node (LN) metastases from HCC are considered to be uncommon. A prevalence of 2.2% was reported in a series of Japanese patients who underwent hepatic resection². We report a patient treated for HCC by open microwave

coagulation therapy (MCT) who later developed a solitary left supra-clavicular LN (Virchow's LN) metastasis in the absence of any abdominal LN or recurrence in the liver or lung.

Case Report

An intrahepatic tumor was detected by follow-up abdominal computed tomography (CT) in a 73-year-old male under treatment for C type liver cirrhosis at the Department of Internal Medicine in our hospital. The patient was promptly admitted to the

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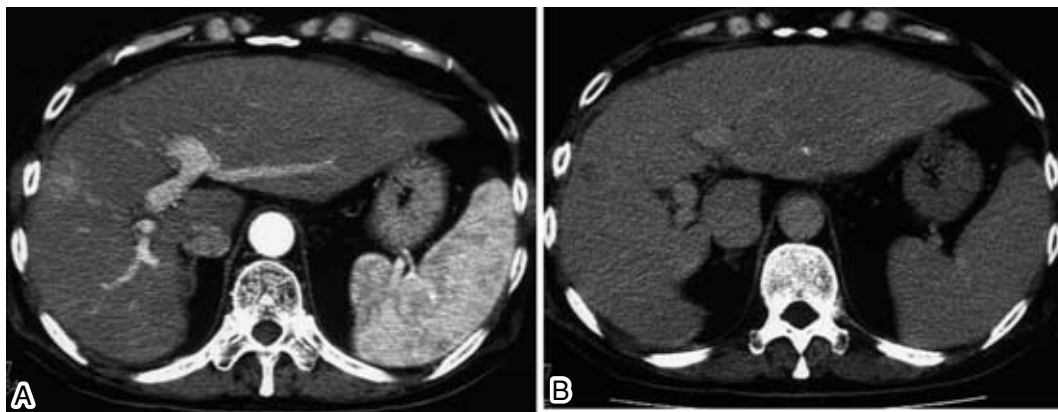


Fig. 1 Abdominal computed tomography showed an enhanced tumor measuring 2×2 cm in diameter in the early phase (A) and a washed-out tumor in the late phase (B) in the anterior-superior segment (S5) of the liver.

Department of Surgery for investigation of the tumor. He appeared to be in excellent health on admission, with no remarkable findings on physical examination. Laboratory investigations on admission showed a white blood cell count of 4,100/mm³, a red blood cell count of 422×10⁴/mm³, a hemoglobin concentration of 13.4 g/dl with a normal differential, and a platelet count of 8.0×10⁴/mm³. Tests on serum enzymes revealed an aspartate aminotransferase level of 87 IU/L, alanine aminotransferase level of 78 IU/L, γ -glutamyltransferase level of 80 IU/L, and cholinesterase level of 182 U/L. Other laboratory tests revealed a serum total bilirubin level of 2.4 mg/dl, serum direct bilirubin level of 1.7 mg/dl, albumin level of 2.9 g/dl, and prothrombin time of 39.6%, indicating a Child-Pugh class C status. ICGR15 estimated by the indocyanine green dye retention rate 15 min after injection of a 0.5-mg/kg dose was 35.5%. The patient had a poor liver function reserve and an elevated serum α -fetoprotein (AFP) level of 40.9 ng/ml (normal range \leq 10 ng/ml). However, PIVKA-II was normal.

Abdominal CT showed an enhanced tumor measuring 2×2 cm in diameter in the early phase and a washed-out tumor in the late phase at the anterior-superior segment (S5) of the liver (**Fig. 1A and B**, respectively). Angiography revealed a hypervascular tumor mainly fed by the anterior-superior branch of the right hepatic artery (A5).

Based on these findings, the patient was diagnosed with HCC at segment V with liver

cirrhosis, and sent to surgery. Laparotomy revealed heavy adhesion of the liver, duodenum, and transverse colon as a remnant effect from an operation for acute peritonitis due to duodenal ulcer perforation performed three years earlier. The surface of the liver appeared roughened and irregular due to the liver cirrhosis. The patient underwent MCT in lieu of a hepatectomy in view of the heavy adhesion and poor liver function reserve. Histopathological examination of the biopsied tissue revealed a pattern of abnormal cell growth. The tumor cells exhibited a compact (solid) growth pattern without a distinct trabecular arrangement (**Fig. 2**). The patient's postoperative course was uneventful and he was discharged from the hospital 14 days after the operation. He remained in what appeared to be good condition for 10 months after the surgery with no signs of recurrence.

Ten months after the operation, a movable hard mass about the size of a quail egg was palpable at the left supra-clavicular LN and blood tests revealed an elevated serum AFP level of 26.7 ng/dl. A neck CT revealed an irregular enhanced mass measuring 3×4 cm in diameter at the left supra-clavicle (**Fig. 3A**). Abdominal and chest CT showed no metastases of abdominal LN and no evidence of recurrence in the liver or lung (**Fig. 3B**). Barium and bone scintigraphy revealed no abnormal spots.

The left supra-clavicular LN was extirpated and closely inspected. Histopathological examination of the LN revealed a trabecular structure of abnormal

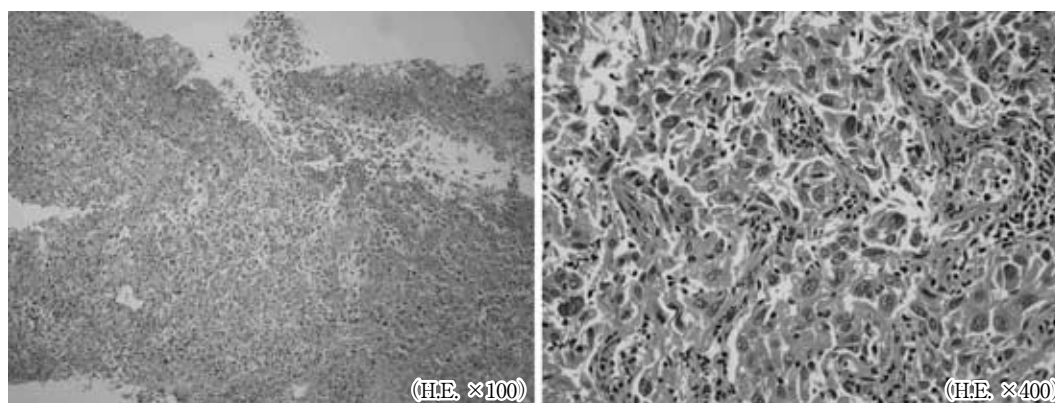


Fig. 2 Histopathological examination of biopsied tissue revealed a pattern of abnormal cell growth. The tumor cells were arranged in a compact (solid) growth pattern without a distinct trabecular pattern.

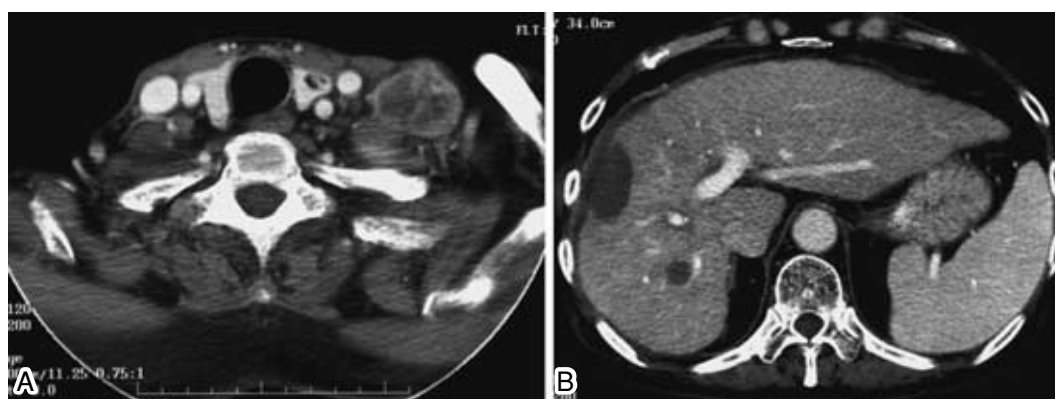


Fig. 3 Neck computed tomography revealed an irregular enhanced mass measuring 3×4 cm in diameter at the left supra-clavicular (A). Abdominal and chest computed tomography taken at the same time showed no metastases of abdominal lymph nodes or evidence of recurrence in the liver or lung (B).

cell growth with massive necrosis (Fig. 4). The tumor was confirmed to an LN metastasis from HCC.

After the operation, the patient developed uncontrollable pleural effusion and ascites in spite of massive doses of furosemide, potassium canrenoate, and albumin. Intrahepatic and abdominal LN metastases were visible on abdominal CT with great haste. The patient died of progressive liver failure and metastases from the HCC 1.5 months after the LN was removed.

Discussion

Autopsy studies have clarified the frequency of LN metastases from HCC (25~42%)²⁻⁴. Unlike the case with other cancers, however, surgeons

operating for HCC rarely find LN metastases. A prevalence of only 2.2% was reported in a series of Japanese patients who underwent hepatic resection². Two points may help to explain this discrepancy. Firstly, LN metastases usually occur in patients with advanced and poorly differentiated HCC who do not receive surgical treatment. Secondly, most surgeons do not routinely perform LN dissection or pay attention to LN metastases during the operations⁵. The hepatic lymphatic system has been well elucidated⁶. Much of the lymph flow towards the hepatic hilum runs through the hepatoduodenal ligament, while smaller amounts communicate with the diaphragmatic and intrathoracic lymphatic system through the bilateral triangular ligaments. Here we must note that some of HCCs lead to what has been termed “skip LN metastases,” that is, LN

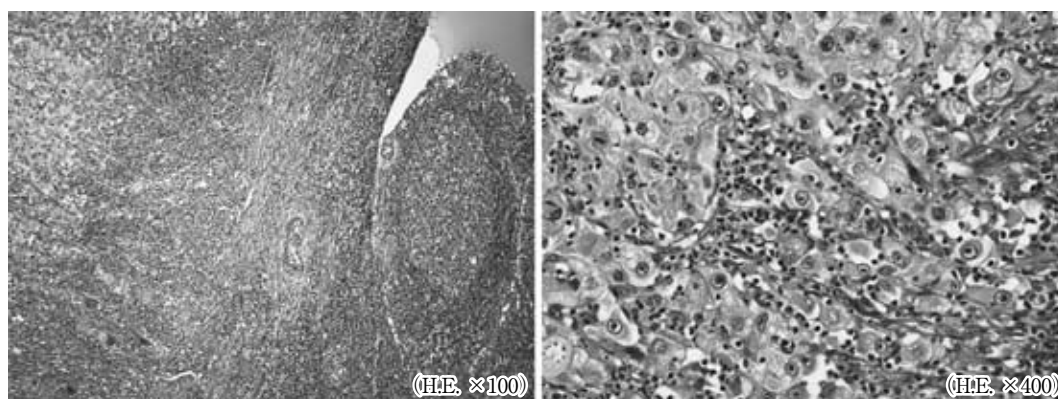


Fig. 4 Histopathological examination of the extirpated lymph node revealed a thickened trabecular structure of abnormal cell growth with massive necrosis. The tumor was confirmed to be a lymph node metastasis from hepatocellular carcinoma.

metastases at distant sites without metastases in the hepatoduodenal ligament^{4,6}.

Virchow's LN has been identified as the last point of lymphogenous metastases from various carcinomas. Cases of Virchow's metastases from HCC are very rare⁷. The present case was detected as a solitary Virchow's LN metastasis. When this LN was palpable, we found no evidence of other LN metastases of the hepatic hilum, hepatoduodenal ligament, or other areas on abdominal CT.

In histopathological studies of primary HCCs, most extrahepatic LN metastases occur in patients with poorly differentiated HCC⁴. The histopathologic findings on patients treated at our hospital generally reveal poorly differentiated HCC.

The prognosis of patients with LN metastases from HCC is generally poor⁸⁻¹⁰. Patients with a solitary metastasis from a controlled intrahepatic tumor are indicated for operation and have been reported to have a favorable prognosis⁸. Patients with multiple metastases or uncontrolled intrahepatic or extrahepatic tumors are indicated for radiation therapy or chemotherapy and are reported to face a poor prognosis^{9,10}. Although external radiation therapy for abdominal LN metastasis has proven effective in relieving symptoms and obtaining some degree of tumor shrinkage, it is not curative¹¹. Moreover, HCC has low chemo sensitivity¹². One patient with a solitary Virchow's LN metastases was reported to recover quite well⁷. In the case of patients with multiple Virchow's LN metastases, however, the prognosis is usually poor,

as it was for our patient. This may be due to the possible development of multiple metastases of abdominal LNs before the Virchow's metastases are detected. Virchow's LN is the final point in every lymph system.

The survival rates of patients with LN metastases should be improved not only by planning out combined therapies with extirpation, radiation therapy and chemotherapy, but also taking steps to prevent the worsening of the liver function reserve.

References

1. Katyal S, Oliver 3rd JH, Peterson MS, Chang PJ, Baron RL, Carr BI: Extrahepatic metastases of hepatocellular carcinoma. *Radiology* 2000; 216: 698-703.
2. The Liver Cancer Study Group of Japan. Primary liver cancer in Japan. Clinicopathologic features and results of surgical treatment. *Ann Surg* 1990; 21: 277-287.
3. Kaczynski J, Hansson G, Wallerstedt S: Metastases in cases with hepatocellular carcinoma in relation to clinicopathologic features of the tumor. An autopsy study from a low endemic area. *Acta Oncol* 1995; 34: 43-48.
4. Watanabe J, Nakashima O, Kojiro M: Clinicopathologic study on lymph node metastasis of hepatocellular carcinoma. Retrospective study of 660 consecutive autopsy cases. *Jpn J Clin Oncol* 1994; 24: 37-41.
5. Uehara K, Hasegawa H, Ogiso S, Sakamoto E, Ohira S, Igami T, Mori T: Skip lymph node metastases from a small hepatocellular carcinoma with difficulty in preoperative diagnosis. *J Gastroenterol Hepatol* 2003; 18: 345-349.
6. Magari S: Hepatic lymphatic system: Structure and function. *J Gastroenterol Hepatol* 1990; 5: 82-93.

7. Omuraya M, Beppu T, Ishiko T, Matsuda T, Ishidori H, Hirota M, Fujiyama S, Yamashita Y, Ogawa M: Lymph node excision with laparotomy and chemoradiation therapy for hepatocellular carcinoma patient with multiple lymph node metastases. *Jpn J Cancer Chemother* 2001; 28: 1699–1703. (in Japanese with an English abstract)
8. Une Y, Misawa K, Shimamura T, Ogasawara K, Masuko Y, Sato N, Nakajima Y, Uchino J: Treatment of lymph node recurrence in patients with hepatocellular carcinoma. *Surg Today* 1994; 24: 606–609.
9. Uenishi T, Hirohashi K, Shuto T, Kubo S, Tanaka H, Sakata C, Ikebe T, Kinoshita H: The clinical significance of lymph node metastases in patients undergoing surgery for hepatocellular carcinoma. *Surg Today* 2000; 30: 892–895.
10. Schoniger-Hekele M, Muller C, Kutilek M, Oesterreichere C, Ferenci P, Gangl A: Hepatocellular carcinoma in Central Europe: Prognostic features and survival. *Gut* 2001; 48: 103–109.
11. Chen SC, Lian SL, Chuang WL, Hsich MY, Wang LY, Chang WY, Ho YH: Radiotherapy in the treatment of hepatocellular carcinoma and its metastasis. *Cancer Chemother Pharmacol* 1992; 31 Suppl: 103–105.
12. Shimada M, Takenaka K, Kawahara N, Yamamoto K, Shirabe K, Maehara Y, Sugimachi K: Chemosensitivity in primary liver cancers: evaluation of the correlation between chemosensitivity and clinicopathological factors. *Hepato-gastroenterology* 1996; 43: 1159–1164.

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