



## 초음파 내시경 유도하 조직 검사로 진단된 담낭의 원발성 편평상피암 1예

원광대학교 의과대학 원광대학교병원 <sup>1</sup>내과, <sup>2</sup>병리과

허원각<sup>1\*</sup> · 전형구<sup>1\*</sup> · 최금하<sup>2</sup> · 김태현<sup>1</sup>

### Primary Squamous Cell Carcinoma of the Gallbladder Diagnosed by Endoscopic Ultrasound-Guided Fine Needle Biopsy

Won Gak Heo<sup>1\*</sup>, Hyung Ku Chon<sup>1\*</sup>, Keum Ha Choi<sup>2</sup>, and Tae Hyeon Kim<sup>1</sup>

Departments of <sup>1</sup>Internal Medicine and <sup>2</sup>Pathology, Wonkwang University Hospital, Wonkwang University School of Medicine, Iksan, Korea

Squamous cell carcinoma of the gallbladder (GB) is uncommon and often presents at an advanced stage; therefore, it is associated with more aggressive behavior and a worse prognosis than those of adenocarcinoma. Herein, we report the case of an 82-year-old woman presenting a weight loss of 5 kg and epigastric discomfort over the previous 3 months. Abdominal computed tomography and magnetic resonance cholangiopancreatography revealed an infiltrative mass in the GB with hepatic invasion. Endoscopic ultrasound-guided fine needle biopsy using a 20-G core needle was performed, and the pathological examination revealed keratin pearls and an intracellular bridge, which are characteristics of squamous cell differentiation consistent with squamous cell carcinoma. Endoscopic ultrasound-guided fine needle biopsy was useful for obtaining an accurate histological diagnosis of GB masses without the need for surgery. (Korean J Med 2019;94:371-374)

**Keywords:** Carcinoma, Squamous cell; Gallbladder; Endoscopic ultrasound-guided fine needle biopsy

#### INTRODUCTION

Squamous cell carcinoma (SCC) of the gallbladder (GB) is rare and constitutes approximately 1% of all GB cancer (GBC) cases [1]. Primary SCC of the GB is very aggressive, typically

spreading to the surrounding structures and lymph nodes. More than 85% of SCC cases of the GB are not detected preoperatively. Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) for GB masses is a minimally invasive tool that may be useful for obtaining a correct preoperative diagnosis of SCC of the GB.

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Correspondence to Tae Hyeon Kim, M.D., Ph.D.

Department of Internal Medicine, Wonkwang University Hospital, Wonkwang University School of Medicine, 895 Muwangro, Iksan 54538, Korea

Tel: +82-63-859-2670, Fax: +82-63-855-2025, E-mail: [kth@wku.ac.kr](mailto:kth@wku.ac.kr)

\*These authors contributed equally to this work.

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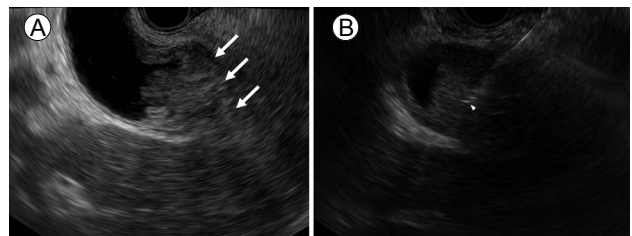
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Most of the reported case series of SCC of the GB were confirmed by histopathological examination of resected GB specimens. Herein, we report a case of primary SCC of the GB diagnosed by EUS-FNB without performing surgery.

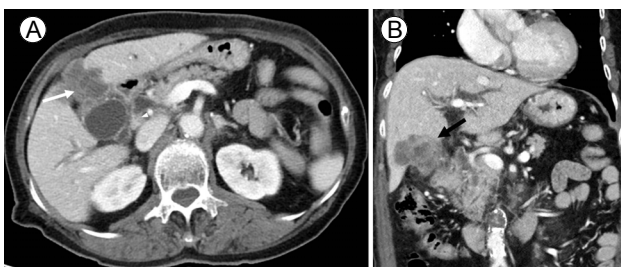
### CASE REPORT

An 82-year-old woman was admitted to Wonkang University Hospital because of a 5 kg weight loss and epigastric discomfort over the previous 3 months. Mild tenderness was noted in the right upper abdomen on physical examination. Her vital signs were a body temperature of 36.8°C, pulse rate of 70 beats/min, and blood pressure of 140/80 mmHg. Laboratory tests revealed the following: leukocyte count, 9,820/mm<sup>3</sup>; hemoglobin level, 11.5 g/dL; platelet count, 179,000/mm<sup>3</sup>; total bilirubin level, 1.03 mg/dL; aspartate aminotransferase level, 67 IU/L; alanine aminotransferase level, 60 IU/L; alkaline phosphatase level, 45 IU/L; C-reactive protein level, 2.99 mg/L; carcinoembryonic antigen level, 13.80 ng/mL; and carbohydrate antigen 19-9 level, 297.8 U/mL. Contrast-enhanced abdominal computed tomography (CT) scan showed a heterogeneous mass emanating from the GB fundus invading the liver, and multiple lymph nodes were enlarged (Fig. 1). There were no abnormal findings on contrast enhanced chest CT. Positron emission tomography-CT revealed intense hypermetabolic activity in the GB fundus and adjacent liver with suspected hepatoduodenal lymph node metastasis. We planned adjuvant chemotherapy after surgical resection, but the patient did

not consent to the operation. Ultrasound guided percutaneous FNB (US-FNB) using the histology of the GB solid mass and adjacent hepatic mass is considered diagnostic, but our patient would not cooperate and held her breath during the procedure because of old age and a mild hearing impairment. The patient was anxious about procedure-related pain. We performed EUS to evaluate a small hepatic metastasis not detected on cross-sectional imaging or in regional lymph nodes, as well as to obtain a pathological diagnosis. No other hepatic metastases were observed, and EUS-FNB using a 20-G core needle (EchoTip ProCore HD US biopsy needle, Wilson-Cook Medical Inc., Bloomington, IN, USA) was performed on the GB mass and adjacent hepatic mass (Fig. 2). Visible whitish core specimens were collected (Fig. 3). Keratin pearls and intercellular bridges,



**Figure 2.** Endoscopic ultrasound (EUS) images. (A) An ill-defined heterogeneous gallbladder (GB) mass with hepatic infiltration (white arrows). (B) EUS-guided fine needle biopsy using a 20-G core needle (white arrowhead) to evaluate the GB mass.



**Figure 1.** Abdominal computed tomography findings. (A) Transverse section showing a hypoechoic mass in the gallbladder (GB) with infiltration in the liver (white arrow) and enlarged lymph nodes (white arrowhead). (B) There was a heterogenous hypoechoic mass (black arrow) along the GB fundus extending to the adjacent liver parenchyma (coronal view).



**Figure 3.** Visible whitish core specimen obtained via endoscopic ultrasound-guided fine needle aspiration using a 20-G core needle.

which are characteristics of squamous cell differentiation, were evident on the histological examination (Fig. 4). Based on the elevated tumor marker levels and histological and radiological findings, the patient was diagnosed with primary SCC of the GB with adjacent hepatic invasion. Unfortunately, the patient refused any treatment other than conservative management.

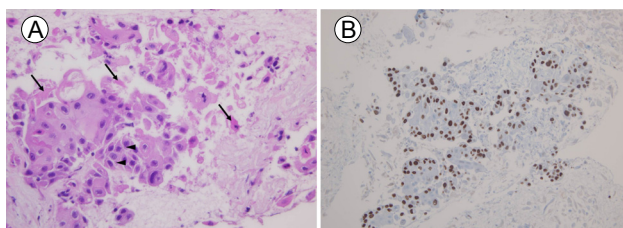
## DISCUSSION

Adenocarcinoma (ADC) of the GB is the most common histological finding of GBC. However, SCC of the GB is very rare and may have a more aggressive behavior than that of ADC. It tends to have poor resectability and to be locally invasive due to a higher tumor growth rate and more aggressive squamous component compared with ADC [2,3]. In a recent retrospective analysis of patients with GBC who underwent surgery, SCC of the GB was associated with a significantly larger tumor size and a higher T stage compared with ADC of the GB. Previous studies also showed a higher incidence of lymph node metastasis in SCC than in ADC of the GB [4]. In concordance with these results, our patient had a tumor infiltrating the adjacent hepatic parenchyma with involvement of multiple lymph nodes.

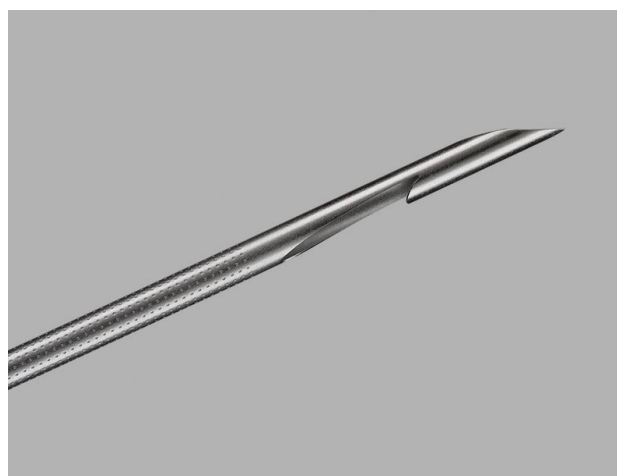
A definite diagnosis of GBC is usually made by histopathological evaluation of a resected specimen. US-FNB is a popular procedure and is reliable and highly accurate for diagnosing GB malignancies [5]. However, the procedure has related complications, such as minor abdominal pain (4.5%) and bile peritonitis (1-6%) [6,7]. Transabdominal US is not reliable for detecting regional lymph node abnormalities or bile duct infiltration. EUS

can also be used to detect small focal liver metastases not detected by cross-sectional imaging. EUS-FNB is a safe and accurate tool for detecting tumors in various organs, including the gastrointestinal tract, sub-epithelial layers, pancreas, and lymph nodes. Furthermore, EUS has been widely used to stage GBC and to distinguish neoplastic lesions from non-neoplastic GB lesions. However, as bile leakage and subsequent bile peritonitis may occur, EUS-FNB should be carefully used for GBC. It is important to avoid puncturing the GB mass through any intervening layer of fluid and to target the mass by effacing the probe and changing the position of the echoendoscope. Several studies have shown that EUS-FNB is a safe, feasible, and accurate modality for diagnosing GBC. The sensitivity, specificity, and accuracy of EUS-FNB are 90%, 100%, and 93.3%, respectively [8,9]. No study has compared US-FNB with EUS-FNB for evaluation of GB malignancies. Although US-FNB may be cheaper than EUS-FNB, EUS-FNB may be less painful than US-FNB because it avoids skin puncture and eliminates breath-holding during the procedure, particularly in elderly patients who may not cooperate, as in our case.

Various needle designs have been evaluated to improve diagnostic accuracy. A newly developed 20-G core needle, which is flexible and has a relatively large bore with a reverse bevel design, is believed to be capable of obtaining quality histological samples from core tissues (Fig. 5). Use of core specimens may



**Figure 4.** Histological findings. (A) Sheets of polygonal cells containing keratin material (arrows) and intercellular bridges (arrowheads) (hematoxylin and eosin staining,  $\times 400$ ). (B) These tumor cells were immunoreactive for nuclear p40 protein (original magnification,  $\times 200$ ).



**Figure 5.** Detailed image of the tip of the 20-G core needle used (figure supplied by Cook Medical Inc.).

improve the diagnostic accuracy due to the preserved tissue architecture and ability to use immunohistochemical staining. Iwashita et al. [10] demonstrated that visible whitish core specimens  $\geq 4$  mm obtained from macroscopic on-site evaluation are adequate histological samples. In the present case, an approximately 4 mm in length macroscopic visible whitish core specimen was obtained using the 20-G core needle, and a definitive diagnosis was made by immunohistochemical staining. Although future studies are needed, EUS-FNB using a 20-G core needle is a feasible and effective modality for evaluating GB masses or other intra-abdominal pathological conditions. In conclusion, SCC of the GB may present at an advanced stage, and EUS-FNB using a 20-G core needle is a useful method for pre-operatively diagnosing GB masses.

**중심 단어:** 편평상피세포암, 담낭, 초음파 내시경 유도하 세침 조직검사

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