Gallbladder Metastasis of Non-small Cell Lung Cancer Presenting as Acute Cholecystitis

Yu-Sook Jeong1, Hye-Suk Han1, Sung-Nam Lim1, Mi-Jin Kim1, Joung-Ho Han1, Min-Ho Kang2, Dong-Hee Ryu3, Ok-Jun Lee4, Ki-Hyeong Lee1, Seung-Taik Kim1

1Department of Internal Medicine, 2Department of Radiology, 3Department of Surgery, 4Department of Pathology, College of Medicine, Chungbuk National University, Cheongju 361-711, Korea

10.1007/s11670-012-0249-x
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ABSTRACT

Although non-small cell lung cancer (NSCLC) can metastasize to almost any organ, metastasis to the gallbladder with significant clinical manifestation is relatively rare. Here, we report a case of gallbladder metastasis of NSCLC presenting as acute cholecystitis. A 79-year-old man presented with pain in the right upper quadrant and fever. A computed tomography (CT) scan of the chest and abdomen showed a cavitory mass in the right lower lobe of the lung and irregular wall thickening of the gallbladder. Open cholecystectomy and needle biopsy of the lung mass were performed. Histological examination of the gallbladder revealed a moderately-differentiated squamous cell carcinoma displaying the same morphology as the lung mass assessed by needle biopsy. Subsequent immunohistochemical examination of the gallbladder and lung tissue showed that the tumor cells were positive for P63 but negative for cytokeratin 7, cytokeratin 20 and thyroid transcription factor-1. A second primary tumor of the gallbladder was excluded by immunohistochemical methods, and the final pathological diagnosis was gallbladder metastasis of NSCLC. Although the incidence is extremely rare, acute cholecystitis can occur in association with lung cancer metastasis to the gallbladder.

Key words: Cholecystitis; Gallbladder; Non-small cell lung cancer; Metastasis

INTRODUCTION

Non-small cell lung cancer (NSCLC) can metastasize to any location in the body, and approximately two-thirds of NSCLC patients present with advanced disease at the time of diagnosis. The frequent metastatic sites of NSCLC are the pleura, contralateral lung, bone, liver, adrenal glands and brain. Extrathoracic metastatic disease is found at autopsy in >50% of patients with squamous cell carcinoma and 80% of patients with adenocarcinoma and large cell carcinoma[1]. By contrast, gallbladder metastasis is extremely rare in NSCLC patients: the gallbladder was recognized as a site of metastasis in only 1.9% of 160 lung cancer cases in large autopsy reviews[2], and there are only a few clinical reports of cases in which metastatic lung cancer of the gallbladder was detected when the patients were alive[3-5]. Here, we report the unusual case of a 79-year-old man with synchronous NSCLC metastasis to the gallbladder presenting as acute cholecystitis. The clinico-pathological features of three previously published cases of NSCLC metastasis to the gallbladder are reviewed in addition to the present case.

CASE REPORT

A 79-year-old man presented in January, 2010 with a 3-day history of progressively worsening abdominal pain in the right upper quadrant, fever and headache. He had no relevant previous medical history. On physical examination, body temperature was 38.9°C, blood pressure 130/75 mmHg, and pulse rate 105/min. Abdominal examination revealed tenderness in the right upper abdomen and rigidity of the abdominal wall with positive Murphy’s sign. Laboratory testing revealed a hemoglobin level of 11.0 g/dl, a white cell count of 17,500/µl with 90.4% neutrophils, and a platelet count of 272,000/µl. Blood chemistry findings were as follows: alanine aminotransferase, 65 IU/L;
aspartate aminotransferase, 40 IU/L; total bilirubin, 0.4 mg/dl; and alkaline phosphatase, 218 IU/L. A computed tomography (CT) scan of the abdomen and pelvis revealed irregular thickening of the gallbladder wall (Figure 1A). A CT scan of the chest showed a 5 cm × 4 cm irregular cavitary mass in the right lower lobe of the lung (Figure 1B) and lymph node enlargement in the right hilar and paraaortic areas. Magnetic resonance imaging of the brain revealed a 1.5 cm well-defined peripheral enhancing necrotic nodule with significant surrounding edema. The patient underwent open laparotomy and cholecystectomy without complication. The tumor was palpable and movable within the body of the gallbladder, without gross involvement of the liver or regional lymph nodes. Examination of the abdominal cavity showed no signs of peritoneal metastases. On gross examination, the gallbladder wall was thickened, with a 3.5 cm palpable mass on the body (Figure 2). There were no gallstones in the bile. Microscopic examination of tumor morphology by hematoxylin and eosin (H & E) staining provided a histological diagnosis of moderately-differentiated squamous cell carcinoma (Figure 3A). Immunohistochemical staining showed that the tumor cells were positive for P63 (1:100; Leica, Newcastle-upon-Tyne, UK) (Figure 3B), but negative for cytokeratin 7 (1:400; NeoMarkers, California, USA), cytokeratin 20 (1:100; Leica) and thyroid transcription factor-1 (TTF-1) (1:200; Leica). A percutaneous needle biopsy of the lung mass was then performed, which revealed a moderately-differentiated squamous cell carcinoma (Figure 3C) with an immuno-histochemical profile consistent with that obtained previously for the gallbladder tumor (Figure 3D). Pathological and immunohistochemical examination revealed that the tumors in the lung and gallbladder were of the same histological type. Therefore, the final diagnosis was NSCLC with synchronous gallbladder and brain metastases.

The patient was treated with palliative whole brain radiotherapy but elected not to undergo palliative chemotherapy. The patient died of progressive disease 4 months after diagnosis.

**Figure 1.** CT scan of the abdomen and chest. A: CT scan of abdomen showing irregular wall thickening of the gallbladder; B: CT scan of chest showing a 5 cm × 4 cm irregular cavitary mass in the right lower lobe of the lung.

**Figure 2.** Resected gallbladder specimen. The resected specimen showed a 3.5 cm polypoid tumor capped with necrotic tissue.

**Figure 3.** Pathological features of resected gallbladder tumor and needle biopsy of the lung mass. Histological examination of the resected gallbladder tumor (A) showed moderately-differentiated squamous cell carcinoma (H & E; ×400), and Immunohistochemistry (B) showed that the tumor cells were positive for P63 (×400), but negative for cytokeratin 7, cytokeratin 20 and TTF-1. Histological examination of needle biopsy of the lung mass (C) also showed moderately-differentiated squamous cell carcinoma (H & E; ×400), and the immunohistochemical profile (D) was consistent (positive for P63, but negative for cytokeratin 7, cytokeratin 20 and TTF-1) with that obtained previously for the gallbladder tumor.

**DISCUSSION**

Metastases to the gallbladder are thought to be rare,