Case Report

Multiple Metastatic Malignant Melanoma Presenting Intraluminal Gallbladder Bleeding

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We report a case of malignant melanoma of unknown primary origin presenting metastasis in various organs as well as intraluminal gallbladder bleeding due to gallbladder metastasis. A 58-year-old woman was diagnosed with stage IV metastatic malignant melanoma. Because she exhibited acute cholecystitis and hemobilia due to malignant melanoma of the gallbladder, laparoscopic cholecystectomy was performed to relieve the symptoms. The resected gallbladder specimen showed a pedunculated black mass indicating malignant melanoma. Pathologic examination and immunohistochemical analysis revealed malignant melanoma of the gallbladder. Only a few cases of gallbladder malignant melanoma presenting hemobilia have been reported; here we present our case, including the experience of multidisciplinary treatment.

Key words: Gallbladder malignant melanoma – Hemobilia – Laparoscopic cholecystectomy

Malignant melanoma can metastasize to various organs. Metastasis often occurs in the lungs, liver, brain, and gastrointestinal tract; however, reported cases of metastatic melanoma of the gallbladder are rare. Though gallbladder melanoma is usually asymptomatic, acute cholecystitis is the most common presentation among symptomatic

cases. Other symptoms, such as obstructive jaundice, external biliary fistula, and hemobilia, are rare and found in very few reports. Here, we report a case of multiple metastases of malignant melanoma of unknown primary origin, for which we performed laparoscopic cholecystectomy to treat continuous bleeding from the gallbladder. We conclude

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Fig. 1 (A) CT showed a mass in the distended gallbladder. (B) Endoscopic retrograde cholangiopancreatography revealed no protruded lesion in the common bile duct. (C) The bile juice cytology detected malignant melanoma cells.

that cholecystectomy is indicated for symptomatic stage IV gallbladder of melanoma cases, because the patient who underwent cholecystectomy not only experiences resolved symptoms but also maintained a survival benefit with improved quality of life.

Case Report

A 58-year-old woman consulted a local hospital complaining of abdominal and back pain. She was diagnosed with acute cholecystitis and introduced to our hospital for further examination and treatment. Although her laboratory data on admission showed improved inflammation (white cell count, $6700/\text{mm}^3$; C-reactive protein, 0.6 mg/dL), severe liver dysfunction and jaundice were found (total serum bilirubin, 2.31 mg/dL ; Aspartate Aminotransferase (AST), 1207 IU/L ; Alanine Aminotransferase (ALT), 607 IU/L ; Alkaline Phosphatase (ALP)

$\text{ALP} 831 \text{ mg/dL}$; Glutamyltranspeptidase (c-GTP), 556 IU/L ; and AMY, 63 IU/L). An ultrasound scan revealed a sludge-like structure in the dilated gallbladder. Computed tomography (CT) showed a homogeneous enhancing mass (20 mm in diameter) in the distended gallbladder (Fig. 1A and 1B). An endoscopic ultrasound examination of the gallbladder demonstrated a polypoid mass without acoustic shadowing (Fig. 1C). Endoscopic retrograde cholangiopancreatography revealed that a blood clot had become extruded from the duodenal papilla and had filled the common bile duct, resulting in obstructive jaundice and acute cholangitis. However, the protruded lesion was not found in the common bile duct (Fig. 1D). Endoscopic naso-gallbladder drainage (ENGBD) was performed, and continuous bleeding was observed in the ENGBD tube. Bile juice cytology detected malignant melanoma cells (Fig. 1E).

Fig. 2 (A) CT revealed a ring-enhancing mass in the left lateral segment of the liver (arrow). (B, C) CT showed a solid mass in the left lobe of the lung (B) and multiple small masses in the bilateral lobe of the lung (C, arrows). (D, E) Esophagogastroduodenoscopy and colonoscopy found multiple black-pigmented lesions in the stomach (D) and sigmoid colon (E). (F) Bone scintigraphy revealed multiple accumulations in the body.

CT also revealed a ring-enhancing mass (13 mm in diameter) in the left lateral segment of the liver (Fig. 2A), a solid mass in the left lobe of the lung, and multiple small masses in the bilateral lobe of the lung (Fig. 2B and 2C). The histologic diagnosis of the lung tumor by CT-guided biopsy was also malignant melanoma. Furthermore, gastrointestinal tract examinations by esophagogastroduodenoscopy and colonoscopy found multiple black-pigmented lesions in the stomach (Fig. 2D), duodenum, and sigmoid colon (Fig. 2E). Bone scintigraphy also revealed multiple accumulations in the body, suggesting multiple bone metastases (Fig. 2F). Skin and retinal lesions were examined in order to find the primary origin of the malignant melanoma; however, the origin was not detected. She was finally diagnosed with stage IV malignant melanoma of unknown primary origin.

As hemobilia was apparently caused by gallbladder melanoma, we treated her with laparoscopic cholecystectomy after she gave her informed consent. The resected specimen clarified the thickness of the gallbladder wall and the presence of a pedunculated black mass in the gallbladder (Fig. 3A and 3B).

Pathologic examination revealed features of malignant melanoma: numerous melanoma cells with melanin-infiltrated mucosa and submucosa (Fig. 3C). Immunohistochemical staining showed a strong positivity for HMB-45 and MelanA (Fig. 3D and 3E). Fontana-Masson stain showed positive pigmentation, which disappeared after bleaching (Fig. 3F). These findings were compatible with malignant melanoma of the gallbladder. Postoperatively, DAC-Tam chemotherapy [dacarbazine, 200 mg per body; nimustine, 80 mg per body; CDDP (cisplatin), 100 mg per body; and tamoxifen, 20 mg per body] was performed 5 times, and CVD chemotherapy (dacarbazine, 100 mg per body; vindesine, 3 mg per body; and CDDP, 70 mg per body) was performed once, but 8 months later she died of widespread disease.

Discussion

Malignant melanoma can metastasize to any organ, or multiple organs, but is usually asymptomatic, resulting in widely disseminated disease. Because typical symptoms are not specific and show organ-specific outcomes depending on metastasized lesions, it is difficult to suspect malignant melanoma at the outset. Melanoma of the gallbladder is rare, and the distinction between primary and metastasis

is usually difficult. When the disease progresses, the gallbladder presents acute cholecystitis, obstructive jaundice, and external biliary fistula.^{1,2} Because the clinical presentations are common symptoms of gallbladder metastatic involvement for different malignant tumors, the symptoms often do not lead to a definitive diagnosis. In fact, we were not able to determine its primary origin.

A multidisciplinary treatment, including surgery, adjuvant chemotherapy, and radiation therapy, is needed for malignant melanoma. As the role of surgical therapy in the treatment of gallbladder melanoma remains unclear, it seems to be indicated for carefully selected patients who have isolated and resectable cases. According to previous reports, most of the patients who underwent cholecystectomy not only resolved right-upper-quadrant pain but also maintained a survival benefit with improved quality of life.^{1,3,4} In addition to isolated and resectable gallbladder melanoma cases, even if a patient has multiple metastatic lesions, cholecystectomy is indicated in cases where the gallbladder is symptomatic of melanoma.

In the present case, of the multiple metastasized lesions of melanoma, the gallbladder was symptomatic as the patient presented with obstructive jaundice and acute cholecystitis due to intraluminal gallbladder bleeding. To remove the symptoms, we performed a laparoscopic cholecystectomy. Because malignant melanoma had already metastasized to multiple lesions at the first admission, the intent of the cholecystectomy was not radical but mitigation therapy. Therefore, a laparoscopic approach seemed to be adequate for this case.⁴⁻⁶ Despite detailed examination of the skin and retina, we could not determine where the primary site was or whether the gallbladder was a primary or metastatic lesion. However, the malignant melanoma was detected in at least 2 organs and was also suspected in other organs; hence, we diagnosed her with stage IV metastatic malignant melanoma and performed systemic chemotherapy postoperatively. Dacarbazine and high-dose interleukin-2 are usually used for advanced melanoma, although the response rate of both is only 10% to 20%.^{7,8} Recent clinical trials using new targeted immune system drugs and molecularly targeted drugs are expected to improve survival in metastatic melanoma.⁹⁻¹¹

Hemobilia is an abnormal communication between the bile ducts and blood vessels caused by iatrogenic or accidental trauma, gallstones, acalculous cholecystitis, and neoplasm.¹² Among the causes of hemobilia, malignant melanoma is extremely

Fig. 3 (A, B) The resected specimen of the gallbladder showed 1 polypoid melanotic lesion and 2 melanotic lesions. (C) Histopathologic examination revealed black-pigmented melanoma cells infiltrating gallbladder mucosa (H&E stain, $\times 100$). (D) Immunohistochemical staining ($\times 100$) of HMB45 showed a strong positivity. (E) Immunohistochemical staining ($\times 100$) of MelanA showed a strong positivity. (F) Fontana-Masson stain ($\times 100$) showed a strong positivity (left panel), and signals disappeared after bleaching (right panel).

rare and reported only in a few reports.^{13–15} In our case, while symptomatic gallbladder led to the diagnosis of malignant melanoma, we did not initially suspect gallbladder melanoma. As mentioned above, gallbladder melanoma is rare, and it is very difficult to diagnose. In particular, we think that the present case, which involved bleeding from the gallbladder tumor and in which we were able to control the bleeding and improve the patient's quality of life by surgery, is very rare, and the accumulation of case-based reports sheds light on the understanding of the treatment impact on malignant melanoma.

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