Giant Hepatic Biloma Following Transcatheter Oily Chemoembolization in a Patient with Hepatic Metastases from Malignant Pheochromocytoma

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A 48-year-old woman developed hepatic metastases from malignant pheochromocytoma resected 8 years previously. Angiography revealed multiple tumor stains in the liver. Transcatheter oily chemoembolization using styrenemaleic acid neocarzinostatin and iodized oil was performed. The patient complained of severe right upper quadrant pain immediately following the transcatheter oily chemoembolization. Necrotizing cholecystitis developed on the 4th day post-transcatheter oily chemoembolization, hepatic infarction on the 12th day, and a biloma on the 19th day. Despite the administration of antibiotics and percutaneous transhepatic drainage, neither the volume of drainage nor the size of the biloma decreased. Biliary reconstruction was performed using a metallic stent, which decreased the size of the biloma.

Key words: necrotizing cholecystitis, hepatic infarction, liver abscess

Introduction

Transcatheter oily chemoembolization using an emulsion of an oil-soluble anti-cancer agent (styrenemaleic acid neocarzinostatin) and iodized oil (lipiodol) is frequently employed as a treatment for hepatocellular carcinoma in Japan. However, reports of complications have been increasing: hepatic failure, necrotizing cholecystitis, acute gastric mucosal lesions, liver abscesses, hepatic infarction, and bilomas are among the more serious complications (1-3). The cause of most of these complications is failure of the hepatic circulation after the transcatheter oily chemoembolization.

A biloma is a localized intrahepatic cystic space filled with bile extravasated from injured bile ducts. Bilomas can be secondary to iatrogenic injury, hepatic trauma, or tumors. Recently, bilomas of iatrogenic origin after transcatheter arterial embolization have been reported (2, 3). The small-diameter embolic material sometimes used in transcatheter arterial embolization may cause destruction of the wall of the bile duct by obstructing the peribiliary arterial plexus of the duct, resulting in leakage and subsequent pooling of the bile (4-7). This is frequently preceded by hepatic infarction.

We treated a patient who developed necrotizing cholecystitis, hepatic infarction, a giant biloma, and a liver abscess following transcatheter oily chemoembolization performed for hepatic metastases from malignant pheochromocytoma.

Case Report

A 48-year-old woman underwent a thyroidectomy for a medullary carcinoma of the thyroid in 1978. Ten years later, in December 1988, an ectopic pheochromocytoma was resected, and the patient was diagnosed with the multiple endocrine neoplasia syndrome, type 2. Her younger brother also had undergone excision of a pheochromocytoma. In October 1995, multiple liver tumors were seen on computed tomography, and the patient was referred to our hospital. At that time, no malignancy was found either by angiography or tumor biopsy. However, in October 1996, computed tomography revealed that the tumors had increased both in size and number. Moreover, the serum concentrations of catecholamines were elevated. On January 23, 1997, an ultrasonography-guided tumor biopsy was performed and a specimen was taken from a tumor in the posterior segment of the liver. Pathohistologic examination revealed basophilic tumor cells similar to the ectopic pheochromocytoma excised in 1988, and the patient was diagnosed with...
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hepatic metastases from malignant pheochromocytoma. Angiography on February 5 revealed multiple tumor stains in the liver. Accordingly, transcatheter oily chemoembolization employing styrenemaleic acid neocarzionostatin and lipiodol was carried out. On February 19, a computed tomography demonstrated good accumulation of lipiodol in the anterior segment. On April 28, 1997, the patient was hospitalized for further treatment. Hematologic examination on admission revealed elevated serum catecholamines. The epinephrine concentration was 0.21 ng/ml (normal range, <0.17 ng/ml), and norepinephrine was 1.1 ng/ml (normal range, 0.15–0.57 ng/ml). No other biochemical abnormality was found.

Angiography was performed using alpha-receptor blockade (doxazosin mesilate) and beta-receptor blockade (bisoprolol fumarate) on April 30. Multiple tumor stains were observed in the liver (Fig. 1A), although the number had decreased in comparison with the previous examination. The patient’s systolic blood pressure increased to 200 mmHg when 2 ml of an emulsion of styrenemaleic acid neocarzionostatin (4 mg) and lipiodol (6 ml) was infused into the right hepatic artery and 1 ml was infused into the left hepatic artery. A calcium antagonist, nicardipine hydrochloride was injected. After reducing her blood pressure, 0.5 ml of the emulsion was infused into the left hepatic artery. Celiac angiography performed immediately after injection did not visualize the hepatic artery (Fig. 1B). The catecholamines concentrations increased markedly: epinephrine, 2.0 ng/ml, and norepinephrine, 6.7 ng/ml. Just after the infusion, the patient complained of severe pain in the right upper quadrant. On the second day following angiography the serum asparate aminotransferase concentration was 670 U/l (normal range, 6–32 U/l), the alanine aminotransferase concentration was 625 U/l (normal range, 5–31 U/l), the alkaline phosphatase concentration was 144 U/l (normal range, 40–121 U/l), the lactate dehydrogenase concentration was 809 U/l (normal range, 95–243 U/l), the amylase concentration was 2,540 U/l (normal range, 115–360 U/l), and the white blood cell count was 25,300/mm³ (normal range, 4,000–8,000/mm³). A fever of 38.4°C developed on the third day. On May 4, wall thickening and swelling of the gallbladder were observed on ultrasonography. A course of broad spectrum antibiotics was initiated based on a diagnosis of cholecystitis. However, a fever of over 40°C persisted. On May 10, the ultrasonography revealed that the thickening of the gallbladder wall had increased (over 20 mm), suggesting severe cholecystitis. Emergency computed tomography performed on the same day revealed a markedly thickened gallbladder wall of low density. Retention of lipiodol was found in the wall, which, moreover, did not enhance with contrast medium. On the basis of these findings, we diagnosed necrotizing cholecystitis. A cholecystectomy was performed on May 12, and the diagnosis of necrotizing cholecystitis was confirmed.

The fever remained around 39°C. A computed tomography on May 19 demonstrated an extensive low density area in the right hepatic lobe. Magnetic resonance imaging on May 30 revealed air and fluid within the low density region seen on computed tomography (Fig. 2A, B). An abdominal radiograph confirmed air in this region. On the basis of these findings, we diagnosed a liver abscess involving gas-producing bacteria in a biloma. On June 5, ultrasonography-guided percutaneous transhepatic drainage was carried out (Fig. 3). Klebsiella pneumoniae was cultured from this material. On June 24, the fever decreased to 37°C, and bile culture was negative. However, the volume of the drainage did not decrease. Examination with contrast medium revealed extremely low flow to the bile duct. A metallic stent was inserted from the biloma up to the common hepatic duct (Fig. 4), as the drainage tube frequently became clogged even though the drainage volume did not diminish. Subsequently, the size of the biloma in the right hepatic lobe decreased markedly (Fig. 5A, B). However, the bile duct of the left hepatic lobe remained slightly enlarged.

Figure 1. A) Celiac arteriography demonstrates multiple hypervascular tumors (arrowheads) in the liver. B) A common hepatic artery after transarterial oily chemoembolization is completely occluded (arrow).
Figure 2. Magnetic resonance imaging of the abdomen 30 days after transarterial oily chemoembolization. A) Sagittal T1-weighted image demonstrated a large irregular shaped low intensity area in the right lobe of liver (arrowheads). B) Axial T1-weighted image shows heterogeneous hyperintensity region (arrowheads) with black signal intensity area (arrows) indicating exists of gas.

Figure 3. Percutaneous cystography and drainage demonstrates large irregular shaped cavity and leakage of contrast medium to abdominal cavity.

Figure 4. A metallic stent was inserted from cavity of biloma up to common hepatic duct.

Discussion

Severe ischemic injury to the liver should not occur secondary to occlusion of the hepatic artery, because the liver is supplied by both the hepatic artery and the portal vein. However, clinical experience has shown that hepatic infarction does occur with some of the embolic materials used in transcatheter arterial embolization. Portal blood flow is maintained during embolization of the hepatic artery with Gelfoam, and normally, serious complications due to ischemia do not develop, because collateral vessels are formed at an early stage (8). However, it should be clearly understood that the infusion of embolic materials consisting of smaller particles, such as Gelfoam powder, silicone, or iodized oil may fill the sinusoids, and then reflux into the portal vein, possibly inducing severe ischemia (6–8). This is especially likely to happen when the catheter is wedged into the hepatic artery, or transcatheter arterial embolization is carried out repeatedly within a short period of time (3).
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Some limited success using combination chemotherapy, consisting of cyclophosphamide, vincristine and dacarbazine, to treat advanced malignant pheochromocytoma has been reported (9). However, the management of this tumor remains disappointing. Recently, transcatheter oily chemoembolization using an emulsion of styrenemaleic acid necocarzinostatin and iodized oil has been used to treat some types of liver tumors, including hepatocellular carcinoma (10). Since hepatic metastases from this patient’s malignant pheochromocytoma demonstrated a hypervascular pattern, we felt a trial of transcatheter oily chemoembolization was justified.

In the present case, celiac angiography performed immediately following transcatheter oily chemoembolization did not outline the hepatic artery, implying that embolization had completely occluded this vessel. In transcatheter oily chemoembolization, the percentage of the branches of the portal vein visualized with the dye increases as the volume of the lipiodol increases; e.g. 28% will appear with a volume of 10 ml or more, and as many as 84.8% will be seen with a volume of 15 ml or more (11). In fact, the therapeutic effect is directly proportional to the percent of branches visualized. At the same time, however, disturbances of the hepatic blood flow lead to an increase in serious complications.

In the present case, a small amount, about 3.5 ml, of an emulsion of an oil-soluble anti-cancer agent and iodized oil was infused. However, during the angiography, the patient suffered a sudden, severe rise in her systolic blood pressure, with simultaneous narrowing of the hepatic artery. We therefore speculate that even this small dose completely obstructed the hepatic artery. The clinical course in this case demonstrates that angiography for pheochromocytoma carries a previously undocumented risk of abdominal vascular complications. The extreme hypertension and narrowing of the hepatic artery might have been akin to a hypertensive stroke such as occurs, when the postoperative concentrations of catecholamines increase markedly.

As long as it is small, the prognosis of a biloma is good, and conservative treatment usually is sufficient. However, a large biloma can be associated with a bacterial infection, requiring percutaneous transhepatic drainage and antibiotic administration; when internal drainage is not reestablished spontaneously, additional intervention is needed. In the present case, biliary reconstruction with a metallic stent was successful, and decreased the size of the biloma.

References
