Primary Pancreatic Malignant Lymphoma Diagnosed from Endoscopic Ultrasound-guided Fine-needle Aspiration Findings

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Abstract

A 60-year-old woman was admitted to our hospital with upper abdominal pain and jaundice. Computed tomography showed a 9-cm mass that was penetrated by the common hepatic artery in the pancreatic head area. Endoscopic retrograde pancreatography revealed no stenosis or obstruction of the main pancreatic duct, and a cytologic examination of the patient’s pancreatic juice was negative. Next, endoscopic ultrasound-guided fine needle aspiration was performed. The immunohistological findings of the specimen revealed a diffuse large B-cell lymphoma. The size of the tumor was significantly reduced after 8 cycles of R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone).

Key words: EUS-FNA, diffuse large B cell lymphoma, pancreas


Introduction

Primary pancreatic lymphoma (PPL) is a rare disease among pancreatic tumors (1). To pathologically diagnose PPL prior to treatment is essential, since the first-line treatment (chemotherapy combined with the administration of rituximab) differs from the therapies for other types of pancreatic tumors. However, it is difficult to diagnose a PPL by a percutaneous biopsy or a cytologic examination of the pancreatic juice. On the other hand, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is reported to be useful for obtaining tissue specimens (2). We herein describe a case of PPL that was immediately diagnosed from a specimen obtained by EUS-FNA, in which a good outcome was obtained by chemotherapy with rituximab.

Case Report

A 60-year-old woman with epigastric pain presented to another clinic with a fever, body weight loss, and drenching night sweats. Jaundice had also developed and ultrasonography showed a hypoechoic lesion measuring 9 cm in diameter in the right upper quadrant. The patient was transferred to our hospital for a more detailed evaluation and treatment. The laboratory results at admission were as follows: leukocyte count (5.17×10³/μL), platelet count (85×10³/L), total bilirubin (8.1 mg/dL), aspartate aminotransferase (91 U/L), alanine aminotransferase (91 U/L), alkaline phosphatase (746 U/L), lactate dehydrogenase (416 U/L), amylase (61 U/L), soluble interleukin-2 (sIL-2) receptor (11,240 U/mL), CEA (0.7 ng/mL), and CA19-9 (147 U/mL). In addition, although an hepatitis C virus (HCV)-RNA qualitative test was negative, the patient’s anti-HCV antibody titer was 80 times above normal. Dynamic enhanced computed tomography
Figure 1. (a) Dynamic enhanced CT revealed a lesion measuring 9.5 cm in diameter. The common hepatic artery had penetrated the mass. (b) The tumor was continuous with the head of the pancreas.

Figure 2. MRCP indicated involvement with the common bile duct (white arrows) and main pancreatic duct (black arrows). The common bile duct was pressed from the left side, narrowing the middle portion.

Figure 3. ERCP showed that the main pancreatic duct was translocated to the inferior side. Disruption and dilatation were not observed. The pancreatic juice cytology was negative.

Figure 4. EUS via the stomach revealed a hypoechoic mass and FNA was performed. Punctures were performed in 3 sessions using a 22-gauge needle and a sufficient amount of tissue was collected.

(CT) revealed a lesion measuring 9.5 cm in diameter that was surrounded by part of the hepatic portal, the head of the pancreas, and the posterior wall of the duodenum (Fig. 1). The mass had a smooth edge and uniform density, and was of lower contrast. Furthermore, the common hepatic artery had penetrated the mass, which was continuous with the head of the pancreas, and there was no lymph node swelling. Magnetic resonance imaging (MRI) showed the mass as a low intensity area in T1-weighted images and a slightly high intensity area in T2-weighted images. There were no findings of necrosis or fluid storage in the mass. Magnetic resonance cholangiopancreatography (MRCP) indicated that the tumor was pressing the common bile duct from the left side, causing the middle part of the common bile duct to narrow (Fig. 2). Fluorodeoxy glucose (FDG) positron emission tomography (PET)-CT showed the accumulation of FDG in the mass (SUV max: 27.65). Endoscopic retrograde cholangiopancreatography (ERCP) indicated that the main pancreatic duct was translocated to the inferior side. Disruption and dilatation were not observed (Fig. 3). A cytologic examination of the patient’s pancreatic juice was performed during ERCP; however, the result was negative.

Following ERCP, we performed endoscopic sphincterotomy and implanted a plastic biliary stent. Thereafter, the patient’s jaundice showed temporary improvement and we at-
tempted to confirm a diagnosis in order to provide the most suitable treatment. The differential diagnoses that were considered included neuroendocrine tumor (NET), gastrointestinal stromal tumor (GIST), serous cyst neoplasm (SCN) microcystic type, invasive ductal carcinoma (IDC), and PPL. NET and GIST were excluded because the artery penetrated the mass. On T2 weighted MRI, there were no findings to indicate fluid storage, which ruled out SCN. IDC is the most common pancreatic neoplasm. However, neither MPD interruption nor an unclear tumor edge, both of which are common observations in IDC, were observed. In addition to the above results, the sIL-2 receptor level was high. As a result, we made a diagnosis of PPL and performed endoscopic ultrasound-guided fine-needle aspiration to obtain a specimen for confirmation (Fig. 4). The procedure was performed under conscious sedation with monitoring of respiratory and circulatory dynamics. Endoscopic ultrasonography revealed a hypoechoic mass with a clear outline and a relatively uniform internal echogenicity through the stomach. We performed 3 puncture sessions with a 22-gauge needle (Expect, Boston Scientific, Natick, USA), each of which included 20 strokes. The amount of specimen tissue was sufficient for the subsequent analyses and there were no complications.

The amount of tissue obtained by EUS-FNA was sufficient to create a number of sections and allow us to complete the pathological diagnosis. A hematoxylin and eosin staining showed that the tumor cells were medium-sized atypical lymphocytes with diffuse proliferation. Follicular structures were not observed (Fig. 5). The immunohistological findings showed atypical lymphocytes that were strongly positive for CD20, CD79a, and Bcl-2, and negative for CD3, CD5, CD10, CD23, CD30, cyclin D1, and Bcl-6. Bone marrow aspiration and biopsy samples demonstrated no infiltration by lymphoma cells. Together, these results supported the diagnosis of diffuse large B-cell lymphoma. Combination chemotherapy was started with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone). After 2 months of R-CHOP therapy, there was a marked reduction in the size of the tumor and ERCP revealed the improvement of the patient’s common bile duct stenosis. After 8 cycles of R-CHOP, a complete response was achieved.

Discussion

PPLs are much less frequently encountered than other pancreatic tumors. Webb et al. reported that PPLs comprised 4.6% of pancreatic neoplasms and 2.2% of non-Hodgkin’s lymphoma cases (3). A literature review by Ji et al. (4) indicated that diffuse large B-cell lymphoma was the most commonly reported histological type of PPL, and that patients were predominantly male. Ji et al. also noted that the tumor
size ranged from 2-15 cm (mean: 8.0 cm) at the longest diameter and that most PPLs (>80%) were located in the pancreatic head, while the body and tail were rarely involved. With the exception of the male predominance, these trends were consistent with the characteristics of the present case. On the other hand, anti-HCV antibody was detected in our patient and she was considered to be in a post-infection state of hepatitis C. There are several reports of patients with malignant lymphoma and a history of HCV infection (5, 6), and the tropism of the lymphoid tissue, which occurs in HCV, has been suggested to be responsible for several immune-mediated disorders such as mixed cryoglobulinemia (7). At the present time, however, there is no accepted evidence to show that HCV induces the carcinogenesis of B-cells. In the present case, an HCV-RNA qualitative test was negative, thus it remains unclear whether the patient’s past history of HCV infection affected the development of the PPL.

Imaging, especially dynamic enhanced CT, is useful for the diagnosis of PPL. A characteristic imaging finding of PPL is an artery penetrating the tumor, the so-called “Sandwich sign” (8). This finding reveals the softness of a lymphoma in comparison to other pancreatic tumors such as NET, GIST, and IDC, which helps to differentiate PPL. In the present case, enhanced CT showed that the common hepatic artery penetrated into the middle of the tumor, which made for a relatively easy diagnosis. On the other hand, it is difficult to distinguish a PPL from a malignant lymphoma of a parapancreatic lymph node. In our patient, the tumor was shown to be continuous with the head of the pancreas and no lymph node swelling was detected around the tumor. Hence, we hypothesized that the tumor was derived from the pancreas head rather than a parapancreatic lymph node. However, since the tumor was too large for its origin to be identified, we could not exclude the possibility that the tumor was derived from a parapancreatic lymph node that had infiltrated the pancreatic head.

A pathological diagnosis is essential for the appropriate treatment of a PPL as well as other malignant neoplasms. Pancreatic juice cytology during ERCP is useful for the pathological diagnosis of pancreatic neoplasms, especially those that are derived from the pancreatic duct, such as IDC (9). On the other hand, it might be difficult to diagnose a pancreatic neoplasm that is not derived from the pancreatic duct, such as a PPL, using pancreatic juice cytology. Rituximab has become available as a first-line therapy for non-Hodgkin’s lymphoma instead of surgery (10), thus it is very important to obtain pathological prior to choosing a treatment. A cytological examination, using EUS-FNA to obtain a specimen of the pancreatic mass, was found to have higher sensitivity and accuracy than ERCP (92.9% and 94.3% vs. 33.3% and 46.7%, respectively) (11). Since Vilmann et al. reported the usefulness of EUS-FNA for pancreatic tumors, it has been used in the diagnosis of abdominal malignant lymphomas (12). Cases that were diagnosed as PPL based on perioperative findings or biopsy findings during laparotomy have also been reported (13, 14). EUS-FNA may help PPL patients to avoid undergoing excessive examinations and unnecessary operations. In the present case, we performed ERCP. Based on the negative findings of the cytologic examination of the pancreatic juice, we hypothesized that the PPL had not infiltrated the pancreatic duct lumen. EUS-FNA may be more appropriate for the diagnosis of patients with suspected PPL than a cytologic examination of the pancreatic juice using ERCP.

In conclusion, we reported a case of PPL that was immediately diagnosed by EUS-FNA findings and treated with R-CHOP. The sandwich sign, which was observed in enhanced CT, was helpful for the diagnosis, even though the pancreatic juice cytology was negative. We therefore consider that EUS-FNA should be immediately performed when findings are obtained that are indicative of a PPL, such as the Sandwich sign.

The authors state that they have no Conflict of Interest (COI).

References


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