CASE REPORT
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A Case of Klatskin Tumor Showing Slow Progression

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A 64-year-old man was admitted due to jaundice for 2 weeks. Radiologic findings revealed biliary stricture at the hepatic hilum with intrahepatic duct dilation suggesting Bismuth type IV Klatskin tumor. Jaundice improved spontaneously several days after hospitalization. Surgical treatment was considered but he only wanted to observe without specific treatment. Ten months later, he was re-admitted due to the recurrence of jaundice. Computed tomography (CT) showed no significant difference compared to previous results. Serum cancer antigen 19-9 and Immunoglobulin G4 were normal. Endoscopic forcep biopsy during endoscopic retrograde cholagiopancreatography (ERCP) revealed chronic inflammation. After steroid use under possible diagnosis of IgG4 related cholangiopathy, biliary stricture improved slightly. Four years later, he was hospitalized with the occurrence of acute cholangitis. Endoscopic retrograde biliary drainage was performed following endobiliary forcep biopsy. Pathology revealed well-differentiated adenocarcinoma at this time. Combined chemotherapy based on gemcitabine and cisplatin was performed. Six months later, CT revealed partial response.

Key Words: Klatskin tumor, Immunoglobulin G4, Gemcitabine, Cisplatin

INTRODUCTION

Cholangiocarcinoma (CCC) is an aggressive malignancy with late onset manifestation including obstructive jaundice and low response to chemotherapy or radiotherapy, which is 47% operable at the time of diagnosis.[1,2] Klatskin tumor, which occurs at the confluence site of the intrahepatic bile duct, accounts for 40-60% of the CCC.[3,4] Radical complete resection of the tumor is the most effective and maybe curative therapeutic modality. However, the 5-year survival rate after surgery varies from 8-47% in patients with negative resection margins, and is generally less than 20%.[5-7] Classically, the Bismuth type 4, which involves both right and left hepatic ducts in the classification of Klatskin tumor, has been known to be a contraindication to surgery.[8]

We reported a case of Bismuth type 4 Klatskin tumor showing slow progression over a period of 5 years.

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CASE REPORT

A 64-year-old man was admitted due to jaundice, intermittent abdominal pain and reddish urine for 2 weeks. He had no familial history of liver or biliary disease, alcohol consumption, and herbal medication except hypertension. Physical examination showed mild right upper quadrant tenderness and icteric sclera. Initial laboratory analysis revealed the following values: white blood cells, 7,430/μL; hemoglobin, 12.8 g/dL; platelets, 338×103/μL; serum bilirubin, 12.74 mg/dL; direct bilirubin, 9.46 mg/dL; serum aspartate aminotransferase, 34 IU/L; serum alanine aminotransferase, 39 IU/L; alkaline phosphatase, 463 IU/L; gamma-glutamyl transpeptidase, 155 IU/L; amylase, 127 IU/L; lipase, 33 IU/L and serum cancer antigen 19-9 (CA 19-9), 33.23 U/mL (0-37 U/mL). Abdominal CT and magnetic resonance cholangiopancreato-

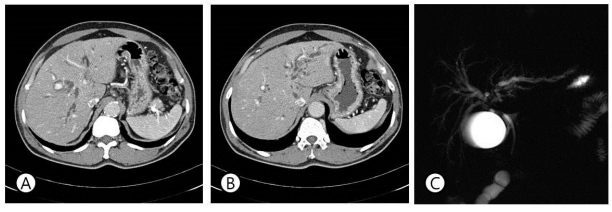

Fig. 1. (**A**), (**B**) Abdominal CT reveals prominent both intrahepatic ductal dilatation. (**C**) Magnetic resonance cholangiopancreatography shows common hepatic ductal luminal narrowing with both intrahepatic ductal irregular dilatation.

graphy revealed biliary stricture at the hepatic hilum with intrahepatic duct dilation suggesting Bismuth type IV Klatskin tumor (Fig. 1). His symptoms and blood tests were improved spontaneously, and he wanted to observe without specific treatment.

Ten months later, he was re-admitted due to the recurrence of jaundice. Serum total bilirubin and direct bilirubin were 5.43 mg/dL and 4.7 mg/dL, respectively. CT scan showed no significant difference compared to previous results. Serum CA 19-9 and immunoglobulin G4 (IgG4) were normal. Tissue diagnosis using ERCP revealed chronic inflammation and endoscopic nasobiliary drainage was performed for biliary decompression (Fig. 2). There was a partial improvement in biliary stricture using corticosteroid (prednisolone 40 mg qd) under possible diagnosis of inflammatory cholangiopathy. Afterwards, he did not have any problems and no significant change was noted in follow-up imaging studies.

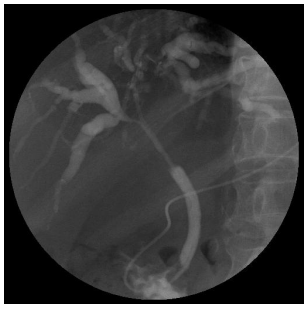

Fig. 2. Endoscopic retrograde cholangiopancreatography reveals proximal common hepatic duct stricture and both intrahepatic ductal dilatation at hilum and biliary decompression was performed with endoscopic nasobiliary drainage.

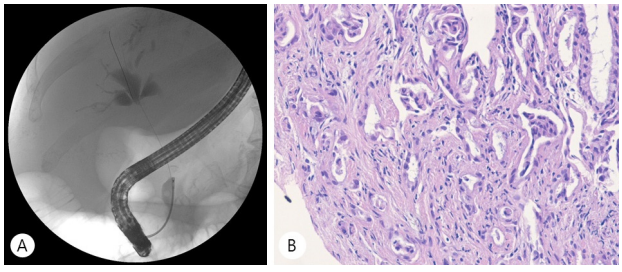

Fig. 3. (**A**) Endoscopic retrograde cholangiopancreatography shows diffuse long stricture from distal common bile duct to hilum, endobilliary forcep biopsy was performed. (**B**) Microscopic examination reveals well-differentiated adenocarcinoma (H&E stain, ×200).

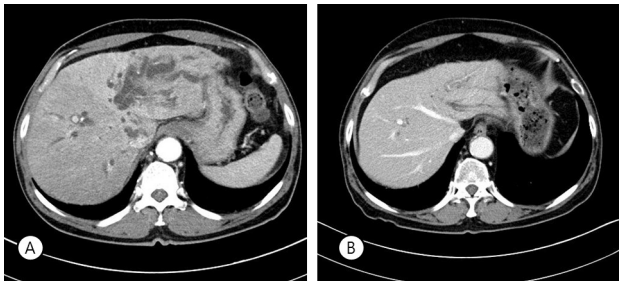

Fig. 4. Partial response after 7th cycle of chemotherapy. (**A**) Computed tomography scan at the time of histologic cancer diagnosis. (**B**) Follow up computed tomography scan after 7th cycle of therapy.

Four years later, he was hospitalized with the occurrence of acute cholangitis. Abdominal CT scan revealed diffuse dilatation of both intrahepatic ducts. Serum CA 19-9 level was elevated to 961 U/mL. ERCP showed long stricture from distal CBD to the hilar area with both intrahepatic ductal dilatation. Endoscopic retrograde biliary drainage was performed following endobiliary forcep biopsy and pathology revealed well-differentiated adenocarcinoma at this time (Fig. 3). Combined chemotherapy based on gemcitabine plus cisplatin (gemcitabine of 1,000 mg/m^2 for day 1, 8 and cisplatin of 60 mg/m^2 for day 1) was administrated. After 7th chemotherapy, partial remission of Klatskin tumor was observed in follow-up CT scan (Fig. 4). He did not want to receive further chemotherapy due to side effect. Biliary stent could be removed without any development of biliary obstruction and he remained well for 13 months after chemotherapy.

DISCUSSION

Cholangiocarcinoma is characterized by silent and aggressive nature, which is usually diagnosed at advanced stage without any specific symptoms in elderly patients.[1] According to the anatomical location of the cancer, the pattern of Klatskin tumor invading perihilar accounts for 60% of the total CCC.[8] Because of the anatomical characteristics of the hepatic hilum, which collects the bile duct, hepatic artery and portal vein, the cancer easily invades surrounding blood vessels and lymph nodes and proceeds through the submucosal layer of the bile duct.[3]

The curative resection of the tumor can prolong the survival period of patients with CCC. However, surgery is often impossible due to the fact that 75% of patients at the time of diagnosis are older than 65 years of age, the presence of various underlying diseases and the characteristics of invasive cancer.[9] The 5-year overall survival rate is less than 20% including resected patents.[8] Almost all patients who have not undergone surgery die within 1 year from cancer cachexia and a sudden drop in performance status.1 The mean survival time for unresectable CCC is 3 months without drainage and 6 months with drainage procedure.[8,10] Our case is an unusual example of a Klastkin tumor showing slow progression over 5 years follow-up without specific treatment after initial ra-

diological diagnosis of Bismuth type 4 Klatskin tumor.

In the differential diagnosis of CCC, there are benign inflammatory biliary tract diseases such as primary sclerosing cholangitis, IgG4-related cholangiopathy as well as malignant tumor including invasion of the biliary tract of pancreatic cancer, gallbladder cancer, other metastatic lesion and intraductal papillary neoplasm.[4] If infectious conditions including parasitic infection are excluded, steroids can be used in these inflammatory biliary diseases.[4]

Endoscopic biopsy and brush cytology with ERCP can detect Klatskin tumor, but it is difficult to diagnose Klatskin tumors with a low sensitivity of 50%.[2] In our case, the first histological examination was chronic inflammation, but the second histological diagnosis was cancer.

The evaluation of benign diseases which should be differentiated from Klatskin tumor was also carried out with the characteristics of growing slowly. The results of autoimmune tests and serum IgG4 levels were normal. However, there was no change in the follow-up test including CA 19-9 and CT, and as a result of ERCP-induced histological examination, chronic inflammation was regarded as inflammatory cholangiopathy and 40 mg of prednisolone was administered per day for a month. After using steroids, symptoms and biliary stricture improved and prednisone was maintained at 5 mg daily for six months. Afterwards, he did not have any problems and no significant change was noted in follow-up imaging studies. Four years later, sudden jaundiced occurred and multiple paraaortic lymph nodes were observed on CT and a well differentiated Klatskin tumor was confirmed by endobiliary forcep biopsy.

In advanced CCC patients, combined chemotherapy based on gemcitabine and cisplatin is a standard treatment.[11] Our patient is well maintained with partial response status on follow-up CT after 7th combined chemotherapy and is being followed up without any special symptoms for 13 months after initiation of chemotherapy.

CONCLUSION

Klatskin tumor is a very poor prognosis with a characteristic of silent and aggressive involvement, and is diagnosed in elderly patients with a predominantly comorbid disease. The survival time after diagnosis is less than 1 year, curative resection of the tumor is the only curative treatment method, and less than half of the cases are possible. The 5 - year survival rate including the patients who underwent surgery is 20%.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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