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Case Report

Intraductal Papillary Mucinous Neoplasm of the Pancreas Associated with Polycystic Liver and Kidney Disease

Norio Yokoigawa Yusai Kawaguchi

Department of Surgery, Kitakawachi Fujii Hospital, Osaka, Japan

Keywords
Intraductal papillary mucinous neoplasm of the pancreas · Polycystic liver · Kidney disease

Abstract
A 77-year-old man was pointed out thrombocytopenia and polycystic liver and kidney disease following hypertension and diabetes mellitus and duodenitis. He consulted to our hospital for further examination. Computed tomography (CT) showed multiple cysts in the liver and kidney and also showed cystic lesions in the pancreatic tail. The size of the tumor of pancreas was 3 cm × 4 cm. FDG-PET CT showed FDG uptake in the tumor of the pancreatic tail. It has not showed metastasis in the other organs. The examinations suggested that the cause of thrombocytopenia was infection of *Helicobacter pylori* or idiopathic thrombocytopenic purpura or drugs. We performed distal pancreatectomy for the tumor of pancreas. Histological findings revealed that the tumor of pancreas was invasive intraductal mucinous carcinoma. He had no recurrence for 3 months after operation. In this case, the patient with autosomal-dominant polycystic kidney disease (ADPKD) and multiple liver cysts developed IPMC. We suggest that some genetic interactions may exist between ADPKD and pancreatic carcinogenesis.

Introduction

Polycystic kidney disease and polycystic liver disease are known to have several manifestations, respectively. In most cases, polycystic liver disease is related to autosomal-dominant polycystic kidney disease (ADPKD). There are two types of ADPKD. The gene of ADPKD-1 is the most common, accounting for 85% of cases, and the main locus responsible for the disease. The gene of ADPKD-2 accounts for 15% of cases. ADPKD is characterized by

Correspondence to:
Norio Yokoigawa, alywk@mx5.canvas.ne.jp

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the multiple renal cysts and cystic tumor of other organs, including liver, pancreas, spleen, uterus, and testis. Furthermore, it is characterized by the dysfunction of valve of heart and intracranial aneurysm.

IPMC associated with ADPKD has been few reported. We report a case of IPMC that occurred in the patient with polycystic liver and kidney disease. The CARE Checklist has been completed by the authors for this case report, provided as supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000528387).

Case Report

A 77-year-old man was pointed out thrombocytopenia and polycystic liver and kidney disease following hypertension and diabetes mellitus and duodenitis. He has no complaints.

In our hospital, laboratory data on the liver, pancreas were within normal ranges. It was suggested renal dysfunction that GFR was 59 mL/min. The serum CEA and CA19-9 levels were 3.7 ng/mL and 42.8U/mL, respectively. CT showed multiple cysts in the liver and bilateral kidney and also showed cystic lesions in the pancreatic tail (Fig. 1). The size of the tumor of pancreas was 3 cm × 4 cm. There was septum in the cystic tumor of pancreas. Magnetic resonance cholangiopancreatography showed the cystic tumor of pancreas and dilatation of main pancreatic duct. Gastrointestinal fiber showed mucinous discharge oozing from the ampulla of Vater. It showed gastritis and *Helicobacter pylori* was detected by biopsy. FDG-PET CT showed FDG uptake in the tumor of pancreas. It has not showed metastasis in the other organs. Then, we diagnosed that the tumor of pancreas was IPMC.

Furthermore, the patient was pointed out thrombocytopenia. Laboratory data showed antiplatelet antibody. The level of the antibody was 79 ng/10^7ce. The cause of thrombocytopenia has suggested infection of *H. pylori* or idiopathic thrombocytopenic purpura or drugs before operation. The patient was not diagnosed with the dysfunction of valve of heart or intracranial aneurysm. We performed distal pancreatectomy (Fig. 2).

Pathological examination of the resected specimens revealed dilatation of main and branched pancreatic duct involving papillary proliferation. The ducts were filled with mucin (Fig. 3a, b). The tumor cells invaded not only in these ducts but also the pancreatic parenchyma (Fig. 3c). Thus, the tumor of pancreas was diagnosed as invasive intraductal mucinous carcinoma. The patient had no recurrence after the operation for 5 years.

Discussion

ADPKD is known to be multisystem disorder characterized by bilateral renal cysts. It is responsible for genetic interactions. The reported incidence of ADPKD is 2.5:1,000 [1]. The two genes mutations which are known to cause ADPKD are PKD1 and PKD2. In 85% of patients with ADPKD, mutations in PKD1 exist and in 15% mutations in PKD2 are causative [2]. It was reported that those with a PKD1 mutation were younger than patients with PKD2 mutation [3]. Renal manifestations include hypertension, renal insufficiency. The diagnosis of ADPKD is often established by abdominal ultrasound sonography, CT, and MRI. Early detection and treatment of hypertension in ADPKD is important because cardiovascular disease is the main cause of death. Approximately 50% of individuals with ADPKD have end-stage renal disease by age 60 years [4].

The patients of ADPKD have been associated with polycystic liver disease [5]. ADPKD is characterized by the multiple renal cysts and cystic tumor of other organs, including pancreas,

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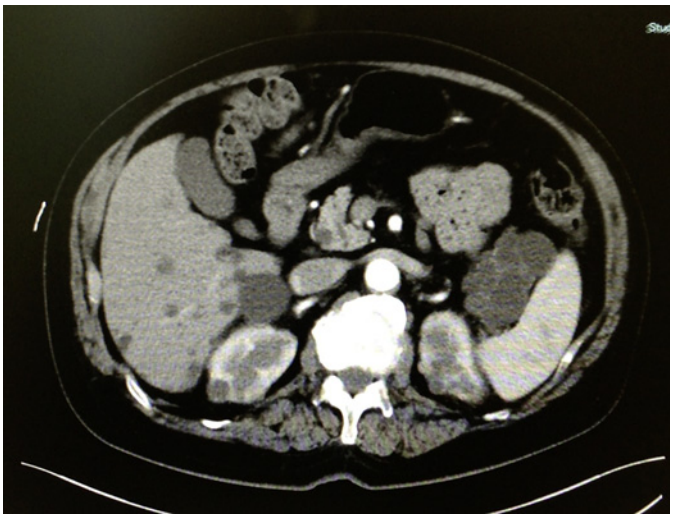

Fig. 1. CT of the abdomen. CT showed multiple cysts in the liver and bilateral kidney and also showed cystic lesions in the pancreatic tail.

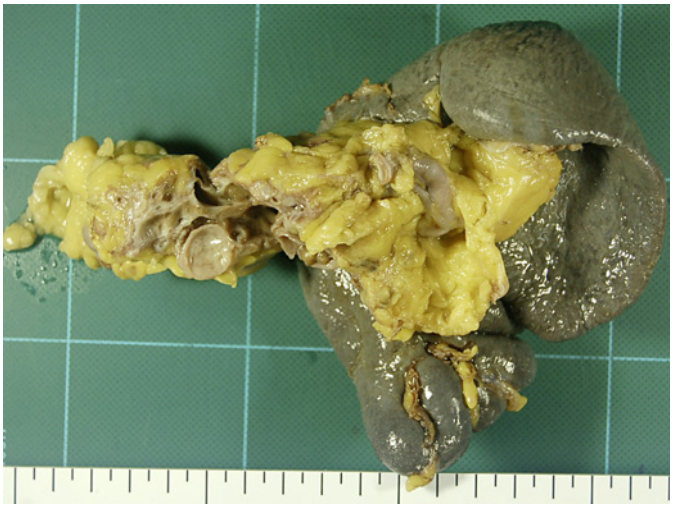

Fig. 2. Specimen finding. The specimen showed multiple cysts in the pancreatic tail.

spleen, uterus, and testis. The frequency of liver cysts increases with age and may have been underestimated by abdominal ultrasound sonography and CT [6]. Multiple liver cysts develop at a younger age in women than men and are more severe in women [7]. It was occasionally associated with congenital hepatic fibrosis. Multiple liver cysts in ADPKD are thought to be due to an abnormality of remodeling of the ductal plate [8]. Furthermore, it was reported that liver cysts in ADPKD originate from biliary epithelium and are the result of progressive dilatation of biliary microhamartoma. Although liver cysts can also cause compression of the inferior vena cava or hepatic veins or bile duct, multiple liver cysts are usually asymptomatic and not causative liver failure. And complications of multiple liver cysts include hemorrhage, infection in the cysts.

Pancreatic cysts occur in approximately 0.7~8% of patients with ADPKD. The reports of IPMC with ADPKD are very rare. IPMN is characterized by intraductal papillary growth,

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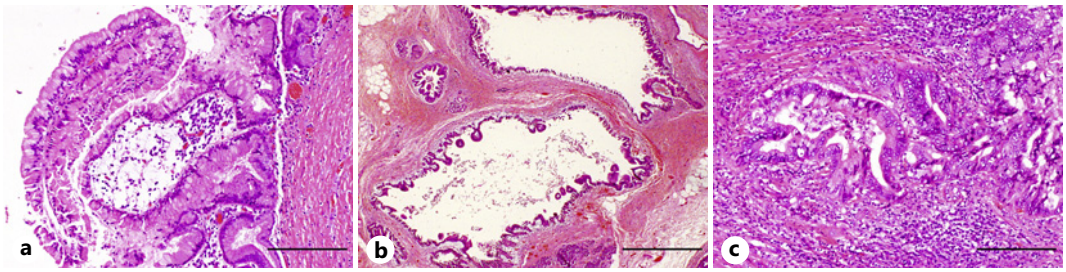

Fig. 3. Pathological findings. **a** Pathological examination of the resected specimens revealed dilatation of main and branched pancreatic duct involving papillary proliferation (bar, 2,000 μm). **b** The ducts were filled with mucin (bar, 2,000 μm). **c** The tumor cells invaded not only in these ducts but also the pancreatic parenchyma (bar, 400 μm).

massive mucin secretion, and dilatation of main pancreatic duct or its branches. It remains uncertain whether ADPKD plays an important role in the development of IPMN. It is suggested that ADPKD may have genetic influence on IPMN. Although IPMN is thought to have malignant potential, it is difficult to diagnose the malignancy preoperatively. We often diagnose the pancreatic tumor as malignant by suggesting the size that exceeds 3 cm, mural nodules, and dilatation of main pancreatic duct.

As in our case, it may be useful to uptake FDG in pancreatic tumor. If the pancreatic tumor is thought to be malignant, a surgical procedure should be made. The prognosis of IPMN is known to be much better than pancreatic carcinoma.

The diagnosis of ADPKD is made by bilateral multiple kidney cysts without other manifestations suggesting renal cystic disease. In our case, he had no family history of polycystic kidney disease. A family history may be absent in 20–40%. The exact mutation of *PKD* gene was examined.

Mitral valve dysfunction and intracranial aneurysm are well-known manifestation of ADPKD. Mitral valve prolapse has been demonstrated by echocardiography in up to 25% of affected individuals. Aortic valve insufficiency may occur in association with dilatation of the aortic root. Although these lesions may progress with time, they rarely require valve replacement. Intracranial aneurysms occur in approximately 10% in patients with ADPKD [9]. The mean age of rupture of intracranial aneurysms is lower in patients with ADPKD. In our case, mitral valve dysfunction and intracranial aneurysms were not shown. Decreased expression of polycystine-1 or -2 produced by PKD-1 or -2 genes may induce endothelial dysfunction and carotid abnormalities and renal cyst formation and renal ischemia [10]. Because of the role of the renin angiotensin system in the pathogenesis of hypertension in ADPKD, angiotensin-converting enzyme inhibitors angiotensin II receptor antagonists may be superior to other agents in patients with ADPKD. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers increase renal blood flow, have a low side effect, and may reduce vascular smooth muscle proliferation and development of atherosclerosis.

In our patient, the examinations suggested that the cause of thrombocytopenia was infection of *H. pylori* or idiopathic thrombocytopenic purpura or drugs. The patient had taken medicines for *H. pylori* before operation. And cilostazol was taken for cerebral infarction. Only this medicine was stopped before operation. Because serum level of platelet was increased gradually after operation, cilostazol was taken by the patient. This case demonstrates that IPMC of the pancreas can occur in patients with polycystic liver and kidney disease.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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There were no funding sources.

Author Contributions

Norio Yokoigawa contributed to and drafted the design of the report. Yusai Kawaguchi has read and approved the final version of the manuscript.

Data Availability Statement

All data generated during this study are included in this article. Further inquiries can be directed to the corresponding author.

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