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Case Report

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The First Case of Caroli Disease Presented as Diabetes and Gastric Perforation

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Abstract

Caroli disease is a rare autosomal recessive disorder with cystic changes in liver, kidney and pancreas. It is a genetic disorder involving PKHD1 gene, encoding fibrocystin, often seen in liver and kidney. This is the first case reported with diabetes and gastric perforation. This 26 years old man presented as diabetes and abdominal pain, which worsened as gastric perforation. He also had enlarged spleen, cystic liver and kidney. His ALT and AST were normal, but GGT and bilirubin were elevated. None of hepatic virus related antigen is positive. No autoimmune hepatitis antibody was found. His blood glucose was high, with the hemoglobinA1c of 12.3% and reduced postprandial C peptide, but negative autoimmune diabetic antibodies. He has an 18 years old sister who was operated at 12 years old due to gastric bleeding and her spleen was removed. She was also diagnosed as Caroli disease. Neither his parents had similar presentation.

As PKHD1 gene encodes fibrocystin, which may present at any conjunction. While fibrocystin tights up tissues, vessels and walls of the hollow organs, it is my belief that the cystic changes due to PKHD1 deletion or mutation can happen in any organ or vessel. This explains why this patient presented as diabetes and gastric perforation.

Caroli disease is a rare autosomal recessive disorder with cystic changes in liver, kidney and pancreas. It is a genetic disorder involving PKHD1 gene (polycystic kidney and hepatic disease 1), encoding fibrocystin, frequently seen in liver and kidney, very rarely seen in pancreas. So far, there is only one report in pancreas with MRI [1]. This is the first case presented as diabetes and gastric perforation.

This 26 years old man presented as diabetes with a history of polydipsia, polyuria for half a year and abdominal pain for couple of days without fever. On physical exam, he had mild jaundice, pain upon percussion at the right upper quadrant with negative Murphy's sign, palpable liver below the ribs, epigastria pain upon pressure without rebound, and enlarged spleen. Work-up (Table 1) showed normal white blood cells and neutrophiles, normal AST and ALT, normal amylase, normal Hepatitis B panel except a positive surface antibody, but elevated GGT, ALP, total, direct and indirect bilirubin. None of hepatic virus related antigen is positive. No autoimmune hepatitis antibody was found. He had high blood glucose, HbA1c, decreased postprandial C peptide, negative diabetic autoimmune antibodies, decreased platelets, normal cretinine, and eGFR and urine micro albumin. On ultrasound, there are cystic changes in liver and both kidneys, significant dilated portal vein, an enlarged spleen with dilated spleen vein. On the second day, the CT confirmed the funding on ultrasound, along with central dot sign in liver and cystic changes in pancreas (Figure 1). On the fifth day, the patient had worsening abdominal pain, was found air around the liver and under the diaphragm, was operated emergently for gastric perforation at the front wall. He had one episode of gastric bleeding when 6 years old, and was diagnosed esophageal gastric varies. He has an 18 years old sister who had cystic liver and kidneys without diabetes. Her spleen was removed, and her esophageal vessel was ligated at 12 years old. Neither his parents had similar presentation.

Table 1: Lab findings

Labs	Value	Reference range
GGT	200	16-60 U/L
Total bilirubin	42	5-21 umol/L
Direct bilirubin	10	0-3.4 umol/L
Fasting C peptide	3.2	1.1-4.4 ng/ml
Postprandial C peptide	4.9	
HbA1c	12.3%	
Platelet	91*10~9/L	125-135*10~9/L

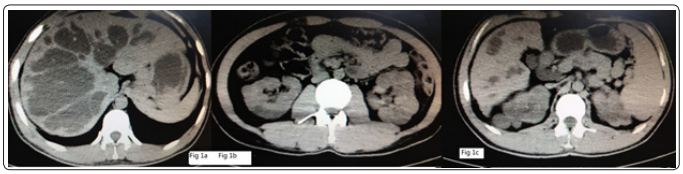

Figure1a: Cystic changes of liver with central dot sign. **Figure 1b:** Cystic changes of kidneys and suspicious pancreas. **Figure 1c:** Cystic changes in liver, kidneys, suspicious changes in pancreas and enlarged spleen.

Caroli disease is a rare inherited disorder commonly seen in conjunction. It is due to the deletion or mutation of PKHD1, similar to ARPKD (auto recessive polycystic kidney disease) gene, on chromosome 6p12. The phenotype depends on the degree of the mutation or deletion. It is usually presented at the early adult with majority onset before 30 years old, more common in Asians.

The deletion or mutation of PKHD1 causes cystic dilation in liver, kidney, and pancreas [2]. The cystic dilatation in liver results in biliary stasis and sludge, thus the patient presents jaundice, right upper quadrant pain and even recurrent cholangitis [3]. This may also explain the lab abnormalities in this patient. This patient had no viral hepatitis or autoimmune hepatitis, further support the possibility of cystic causes. The decreased platelet may be associated with the enlarged spleen. The normal kidney function may suggest that the damage to the kidney is still during the phase of fully compensation. Cystic changes may also happen in the gastric wall, which weakens the wall and finally into gastric perforation [4]. Cystic change in pancreas is very rare. This is the first clinical case presented. This patient presented as poorly controlled type 2 diabetes mellitus. The cystic changes of pancreas decrease its function and thus insufficient insulin. This full-blown case may indicate a gene deletion rather than mutation [5]. The cystic changes may happen at the vessels, which may add better explanation why this patient had dilated portal vein and spleen vein [6-8].

As PKHD1 gene encodes fibrocystin, which may present at any conjunction. While fibrocystin tights up tissues, vessels and walls of the hollow organs, it is my belief that the cystic changes due to PKHD1 deletion or mutation can happen in any organ or vessel. This explains why this patient presented as diabetes and gastric perforation.

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