

# Endoscopic therapy for gastro-oesophageal varices of Caroli's syndrome: a case report

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Song Wang , Mei Xiao, Liqun Hua, Yong Jia,  
Si Chen and Kaiguang Zhang

## Abstract

Caroli's disease (CD) is a very rare congenital disorder that is characterized by non-obstructive, segmental and cystic dilatation of intrahepatic ducts. Most patients with CD are asymptomatic, but some patients may suffer from hepatic fibrosis, liver cirrhosis or/and portal hypertension. In complex CD, cystic dilatations of the intrahepatic bile ducts can be present with congenital hepatic fibrosis, liver cirrhosis, portal hypertension, oesophageal varices and autosomal recessive polycystic kidney disease; a condition known as Caroli's syndrome. This report describes the case of a 28-year-old woman that had gastro-oesophageal varices that were caused by hepatic fibrosis and portal hypertension as part of Caroli's syndrome. The patient underwent successful treatment with endoscopic injection sclerotherapy with lauromacrogol and endoscopic variceal obturation using tissue adhesive. There were no immediate complications and the patient remained free of complications at 1-year follow-up. There are no current reports in the published literature describing Caroli's syndrome induced by gastro-oesophageal varices that were treated by a combination of endoscopic injection sclerotherapy and endoscopic variceal obturation. Endoscopic therapy was an effective technique for the treatment of gastro-oesophageal varices in a patient with Caroli's syndrome awaiting a liver transplant.

## Keywords

Caroli's syndrome, gastro-oesophageal varices, endoscopy

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Department of Gastroenterology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui Province, China

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## Corresponding author:

Kaiguang Zhang, Department of Gastroenterology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, 17 Lujiang Road, Hefei 230001, Anhui Province, China.

Email: [zhangkaiguang0097@163.com](mailto:zhangkaiguang0097@163.com)



## Introduction

Caroli's disease (CD) is a very rare congenital disorder of the intrahepatic bile ducts characterized by duct dilation.<sup>1</sup> The disease is characterized by multifocal congenital segmental dilatation of the intrahepatic bile ducts, which may involve a segment, a lobe or the entire liver.<sup>1</sup> It is currently included in group V of the Todani classification of biliary tract cystic diseases and was first described by the French gastroenterologist J Caroli in 1958.<sup>2-4</sup> Two forms of CD have been described: a simple form and a complex form.<sup>4</sup> The simple form of CD is limited to cystic dilatations of the intrahepatic bile ducts, while the complex form is associated with congenital hepatic fibrosis, liver cirrhosis, portal hypertension, oesophageal varices and autosomal recessive polycystic kidney disease, which are in combination described as Caroli's syndrome.<sup>5-7</sup> CD has no specific symptoms or clinical signs, so the diagnosis is usually based on magnetic resonance imaging (MRI), computed tomography (CT) and ultrasound evidence. This current report describes a case of complex CD with upper gastrointestinal haemorrhage caused by gastro-oesophageal varices and hepatic fibrosis. The varices were treated successfully using endoscopic therapies.

## Case presentation

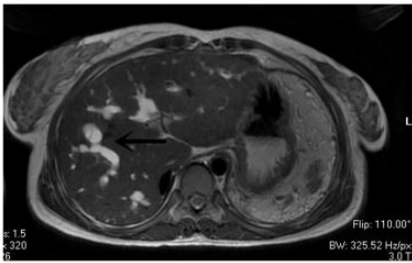
In February 2018, a 28-year-old woman was admitted to the Department of Gastroenterology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui Province, China with upper gastrointestinal haemorrhage. She had a 10-year history of cryptogenic liver cirrhosis and a 7-year history of upper gastrointestinal haemorrhage caused by gastro-oesophageal varices. She had undergone a splenectomy

and a splenorenal shunt in 2009. The patient had undergone endoscopic injection sclerotherapy (EIS) for upper gastrointestinal haemorrhage in another hospital in 2011 and 2014. A starting dose of 10 mg propranolol orally three times a day was used in 2011. However, the patient refused to continue because of hypotension. A dose of 250 µg/h somatostatin administered by continuous infusion was used when she was admitted to our hospital and when the endoscopic therapy was performed; and the bleeding was inactive. The size of the oesophageal varices was grade II and the gastric varices of the patient were classified as GOV1.<sup>8</sup> Physical examination showed that the patient's skin had a pale anaemic appearance (haemoglobin 86.6 g/l), without other abnormalities. The vital sign measurements were as follows: body temperature, 36.5°C; blood pressure, 120/78 mmHg; respiratory rate, 18 breaths/min; and pulse rate, 78 beats/min. The patient was 160 cm tall and her body weight were 56 kg. She reported no history of alcohol and tobacco consumption and her family history was unremarkable. Laboratory test results showed slightly increased alkaline phosphatase (116 IU/l) and gamma-glutamyl transferase (57 IU/l) levels but other parameters were normal. The model for end-stage liver disease score of the patient was 8 and the Child-Pugh score was 5. The level of serum  $\alpha$ -fetoprotein was 1.91 ng/ml. Serological examinations for hepatitis B surface antigen and anti-hepatitis C virus were negative. The results of other tests, including the measurement of serum iron and ceruloplasmin concentrations, iron saturation, anti-mitochondrial antibodies, smooth muscle antibodies and antinuclear antibodies, were unremarkable.

Abdominal CT (Figure 1) and MRI (Figure 2) scans revealed multiple saccular dilated intrahepatic bile ducts and hypertrophy of the left and caudate lobes.



**Figure 1.** Abdominal computed tomography scan of a 28-year-old woman that presented with upper gastrointestinal haemorrhage showed multiple saccular dilated intrahepatic bile ducts and hypertrophy of the left and caudate lobes.



**Figure 2.** Multiple saccular dilated intrahepatic bile ducts and hypertrophy of the left and caudate lobes presented as a high signal intensity in T2-weighted abdominal magnetic resonance imaging of a 28-year-old woman that presented with upper gastrointestinal haemorrhage.

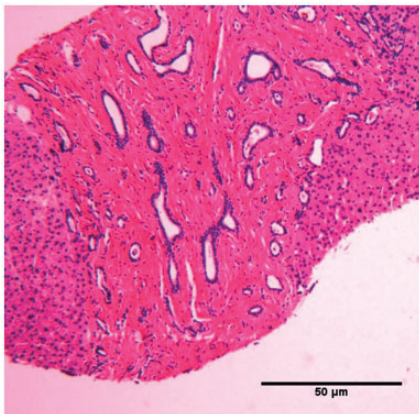
Abdominal CT and MRI also showed polycystic kidney disease (Figure 3). Histopathological findings showed congenital dilations of the intrahepatic bile ducts

and hepatic fibrosis (Figure 4). Gastroscopy showed gastro-oesophageal varices (Figure 5). EIS with lauromacrogol and methylthionine chloride and endoscopic variceal obturation (EVO) with tissue adhesive were used to treat the varices (Figure 5). A modified ‘sandwich’ method was used. The injection order was 3.0 ml of lauromacrogol, 0.5 ml of undiluted tissue adhesive and 3.0 ml of 50% glucose. The symptoms subsided and the patient was discharged from the hospital with no complications. After 1 year, the patient was rechecked during clinical follow-up and had no complications.

Ethical approval was not required for this case report and the Medical Ethics Committee of The First Affiliated Hospital of University of Science and Technology of China provided an ethical



**Figure 3.** Abdominal T1- and T2-weighted magnetic resonance imaging (a, b) and computed tomography (c) scans of a 28-year-old woman that presented with upper gastrointestinal haemorrhage showed concomitant polycystic kidney disease.



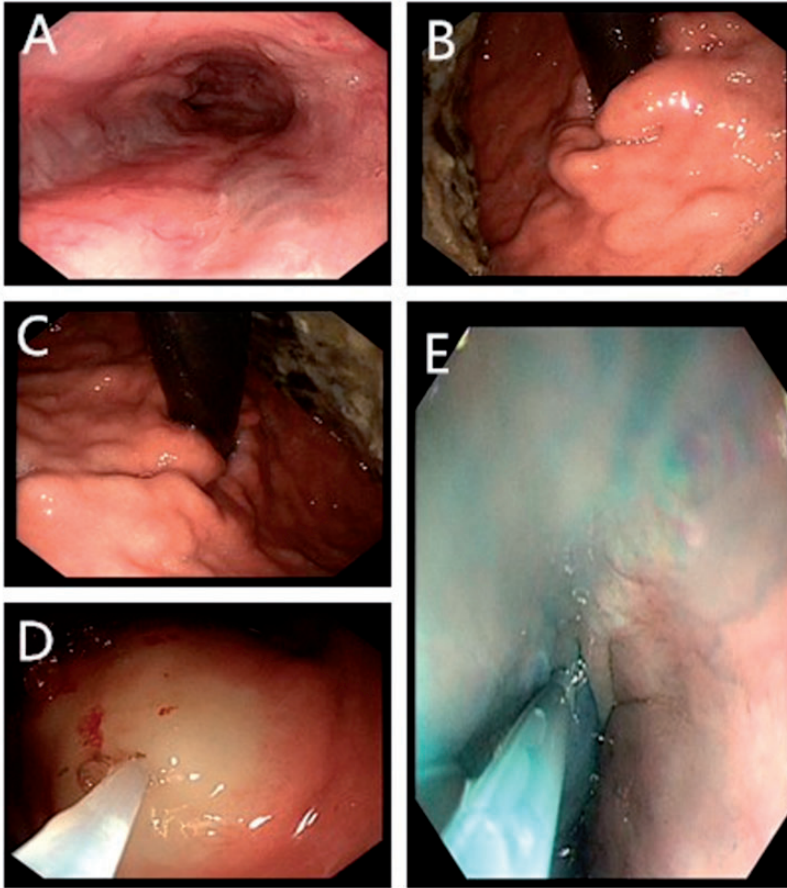
**Figure 4.** Histological findings of a liver biopsy specimen from a 28-year-old woman that presented with upper gastrointestinal haemorrhage. Intrahepatic bile ducts were dilated and there was evidence of hepatic fibrosis (haematoxylin and eosin stain). The colour version of this figure is available at: <http://imr.sagepub.com>. Scale bar 50  $\mu$ m.

exemption statement in support. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## Discussion

Caroli's disease is a rare congenital cystic dilatation of the intrahepatic ducts, which

was first reported in 1958.<sup>2</sup> The incidence of CD is one case per million worldwide and most patients are diagnosed before the age of 30 years.<sup>9–11</sup> A previous study reported that an unbalanced translocation between chromosomes 3 and 8 suggests that loss of distal 3p and/or a gain of 8q is of pathogenetic importance in CD.<sup>12</sup> CD is divided into two forms: a simple form and a complex form.<sup>4</sup> The complex form of CD, also called Caroli's syndrome, is associated with liver fibrosis, hepatic cirrhosis and portal hypertension.<sup>5,7,13</sup> Caroli's syndrome is mostly comorbid with cystic kidney diseases such as polycystic kidney disease and medullary cystic kidney disease.<sup>10,14</sup> CD, especially the complex form, usually involves the entire liver.<sup>15</sup> However, the simple form is often limited to one lobe, which is usually localized in the left liver lobe.<sup>15,16</sup> The treatment of CD depends on the symptoms and range of cystic dilatations. Potential curative treatment of the simple form of CD is surgery, because the lesion size of the bile duct dilatation is small.<sup>10,16</sup> However, the complex form of CD or patients with end-stage liver disease are usually treated conservatively with antimicrobial and ursodeoxycholic acid administration, stone removal, bile duct drainage with endoscopic retrograde cholangiopancreatography or liver transplantation.<sup>15,17</sup>



**Figure 5.** Treatment of the gastro-oesophageal varices of a 28-year-old woman involved endoscopic injection sclerotherapy with lauromacrogol and endoscopic variceal obturation using tissue adhesive. The following endoscopic images are presented: oesophageal varices (a); gastric varices (b and c); endoscopic variceal obturation with tissue adhesive (d); endoscopic injection sclerotherapy with lauromacrogol (e). The colour version of this figure is available at: <http://imr.sagepub.com>.

Liver transplantation may be the optimal management option in CD patients.<sup>18</sup> However, survival after liver transplantation was found to be poor in congenital hepatic fibrosis patients.<sup>19</sup> Early diagnosis is important to the survival of CD patients.<sup>7</sup> The clinical presentation in this current case lead to a diagnosis of complex CD (i.e. Caroli's syndrome) with concomitant hepatic fibrosis, gastro-oesophageal varices caused by portal hypertension and polycystic kidney disease.

There are no specific symptoms or signs of CD, which makes diagnosis difficult. The diagnosis mainly depends on imaging (e.g. ultrasound, CT, MRI and magnetic resonance cholangiopancreatography) and pathological examinations. Hepatomegaly is usually present in CD and laboratory tests typically show elevated levels of alkaline phosphatase and gamma-glutamyl transferase.<sup>16</sup> In this current case, the patient did not experience febrile episodes caused by cholangitis, jaundice or



abdominal pain. Abdominal CT and MRI in this current case showed multiple saccular dilated intrahepatic bile ducts and hypertrophy of the left and caudate lobes.

Gastro-oesophageal variceal haemorrhage is a medical emergency and bleeding from ruptured gastro-oesophageal varices is the cause of death in one-third of patients; and it can be rapidly fatal unless quickly controlled.<sup>20</sup> There are two categories of treatment of gastro-oesophageal varices: (i) methods that decrease portal pressure (including medication, transjugular intrahepatic portosystemic shunt and surgery); and (ii) methods that obstruct the gastro-oesophageal varices (including endoscopic variceal ligation, EIS and endoscopic variceal obturation with tissue adhesive).<sup>21–24</sup> In the current case, the initial symptom was variceal bleeding. The current patient received EIS with lauromacrogol combined with EVO using tissue adhesive for their gastro-oesophageal varices, which showed a good short-term effect with no complications after 1-year of follow-up. However, these endoscopic therapies were palliative and surgical resection would be a potentially curative treatment, especially for localized disease. For complex forms of Caroli's syndrome, as in this current case, liver transplantation should be recommended.

In conclusion, this current patient had a complex form of CD with hepatic fibrosis, portal hypertension and upper gastrointestinal haemorrhage caused by gastro-oesophageal varices. The use of endoscopic therapies is widespread in gastro-oesophageal variceal bleeding due to portal hypertension induced by different aetiologies, but their use is rarely reported in Caroli's syndrome. This current case showed that endoscopic therapies can be used efficiently for the treatment of patients with Caroli's syndrome who are awaiting a liver transplant.

## Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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## ORCID iD

Song Wang  <https://orcid.org/0000-0001-7122-013X>

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