Major hepatectomy for peripheral papillary cholangiocarcinoma with hilar extension in a patient with situs ambiguous

Mircea CHIRICA (1), Marie-Pierre VULLIERME (2), Annie SIBERT (2), Dominique CAZALS-HATEM (3), Bruno GAUDIN (4), Jacques BELGHITI (1), Alain SAUVANET (1)

(1) Service de Chirurgie Digestive, (2) Service d’Imagerie Médicale, (3) Service d’Anatomopathologie, Hôpital Beaujon, AP-HP, University Paris VII, 92110 Clichy ; (4) Service de Médecine, Hôpital de Meulan, 1 rue du Fort, 78250 Meulan.

SUMMARY

Situs ambiguous is a rare anomaly, which includes various abnormalities of position and development of trunk organs and results in diagnostic and therapeutic problems during major abdominal intervention. We report the case of a woman with peripheral papillary cholangiocarcinoma and hilar extension, developed on situs ambiguous associated with the following abnormalities: agenesis of the retrohepatic vena cava, preduodenal portal vein, a variant of the hepatic arteries, truncated pancreas, polysplenia, and mesenteric malrotation. After complete anatomical assessment, resection of segments 4 to 8 extended to the common bile duct with lymphadenectomy and reconstruction by hepaticojjunostomy was performed with no surgical complications. The patient was alive with no signs of recurrence at 18 month follow-up. The specificities of situs ambiguous must be identified by anatomical assessment but do not prevent complex abdominal surgery.

Hépatectomie majeure pour cholangiocarcinome papillaire périphérique avec extension hilare chez un malade ayant un situs ambigu

Mircea CHIRICA, Marie-Pierre VULLIERME, Annie SIBERT, Dominique CAZALS-HATEM, Bruno GAUDIN, Jacques BELGHITI, Alain SAUVANET

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Le situs ambigu est une anomalie rare, associant à des degrés variables des anomalies positionnelles et de développement des organes du tronc. Il pose des problèmes diagnostiques et tactiques lors d’interventions chirurgicales abdominales majeures. Nous rapportons ici l’observation d’une femme ayant un cholangiocarcinome périphérique de type papillaire, à extension hilare et développé sur situs ambigu qui comporte comme anomalies associées une agénésie de la veine cave rétrohépatique, une veine porte préduodénale, une variante artérielle hépatique, un pancréas tranqué, une polysplénie, et un mésentère commun. Après un bilan anatomique complet, une résection des segments 4 à 8 étendue à la voie biliaire principale avec curage ganglionnaire pédiculaire et reconstruction par anastomose hépatico-jejunale a été réalisée sans complication chirurgicale. La malade était vivante sans signes de récidive 18 mois après l’intervention. Les particularités du situs ambigu doivent être identifiées par un bilan anatomique mais n’empêchent pas la réalisation d’interventions abdominales complexes.

Case report

A 57-year-old woman was referred for jaundice. In her past medical history, situs inversus was diagnosed at birth on a chest roentgenogram performed for respiratory failure and was confirmed during childhood after appendicectomy. Intermittent pruritus with epigastric pain began four months ago, and was associated with a progressive 6 kg weight loss. At physical examination, the liver was enlarged and palpated in the epigastrium. Her serum biological profile was as follows: bilirubine level = 73 µmol/L, alkaline phosphatase = 1277 IU/L (upper normal limit [N] < 100 IU/L), gamma-glutamyltransferase = 2380 IU/L (N < 40 IU/L), aspartate aminotransferase = 176 IU/L (N < 40 IU/L), alanine aminotransferase = 248 IU/L (N < 40 IU/L), prothrombine index = 104%, carcinoembryonic antigen = 2.3 ng/ml (N < 5 ng/ml), CA 19-9 = 700 UI/ml (N < 37 IU/ml). Serum hepatitis B and C antibodies were absent.

Abdominal ultrasound revealed intrahepatic bile duct dilatation and a normal diameter common bile duct, with a 25 mm tumor on the left side of the hepatic hilum. Abdominal CT scan showed right-sided stomach, polysplenia, a truncated pancreas, a “reversed” liver across the midline with marked atrophy of segments 5-8 (situated on the left) and significant hypertrophy of segments 2-3 (situated on the right), while size of segment 4 was normal. The liver tumor was hypodense, heterogeneous, located in segments 5-6, and separated from the gallbladder (figures 1a and 1b). Other anomalies included a pre-duodenal portal vein, absence of retro-hepatic vena cava, hepatic veins converging to a thin supra-hepatic vena cava draining into the right atrium, and a dilated left azigos vein (figure 1c). Cholangio-MRI confirmed stenosis of the hilar biliary confluence. At endoscopic ultrasound, the retro-pancreatic
Peripheral cholangiocarcinoma in situs ambiguous

common bile duct was not shown and there were no metastatic lymph nodes in the hepatic pedicle.

Because of an onset of cholangitis during in-hospital stay, percutaneous transhepatic biliary drainage was performed. Opacification through segment 8 revealed multiple filling defects in both hilar confluence and upper common bile duct (figure 2) suggesting the papillary pattern of the tumor. Biliary external drainage was inserted through segment 3.

“Right” hepatic resection was planned. To obtain precise vascular assessment, arteriography was performed and revealed both common hepatic artery emerging from superior mesenteric artery, taking a retropancreatic course and irrigating the whole liver (figure 3a) and an accessory “right” hepatic artery emerging from the “right” gastric artery and irrigating segments 2 to 4 (figure 3b). Both hepatic arteries seemed fully anastomosed together at the hilar level.

Surgery was performed two weeks after percutaneous transhepatic biliary drainage, once serum bilirubin level has decreased to 30 µmol/L. A left subcostal incision was done and the surgeon was positioned on the left side of the patient. Exploration confirmed situs inversus, prepancreatic course of both portal vein and common bile duct, and absence of both retro-hepatic vena cava and segment I. The whole liver had a firm consistency. Furthermore, there was a complete intestinal malrotation with the whole colon on the right side of the abdominal cavity, the whole small intestine on the left side, and absence of retro-mesenteric duodenal segment (figure 4). The tumor was located between the hilum and the left side of the gallbladder fossa (figure 5). Upper common bile duct was slightly enlarged. There were neither metastases nor vascular encasement. Mobilization of the “left” liver from the left hemidiaphragm was easy due to liver atrophy and absence of vascular attachments. En-bloc resection of segments 4 to 8 extended to hilar plate and extra-hepatic common bile duct was performed. Elements of portal pedicle were meticulously skeletonized for safe lymph node dissection without injuring pedicles of segments II and III. The distal common bile duct was divided anteriorly to the pancreatic head, after complete lymph node clearance exposing its penetration into pancreatic parenchyma. Frozen section revealed no tumoral

Fig. 1 – Abdominal CT scan with intravenous contrast: 1a) hypodense tumor (arrow) in atrophic segments 5-6. Bile ducts are dilated in hypertrophic segments 2-3 and normal-size segment 4. Polysplenia (PS) is present in the right hypochondrium; 1b) the tumor is separated from the gallbladder. Portal vein (arrow) is prepancreatic and preduodenal. At this level, the common hepatic artery (dotted arrow) (originating from superior mesenteric artery) has a retropancreatic course and the pancreas (P) is truncated; 1c) Absence of retrohepatic vena cava with marked dilatation of left azygos vein (arrow).

Scannographie abdominale avec contraste intraveineux : 1a) tumeur hypodense (flèche) localisée dans les segments 5-6 qui sont atrophiques. Les voies biliaires sont dilatées dans les segments 2-3 qui sont hypertrophiques et le segment 4 qui est de taille normale. Il existe une polysplénie (PS) dans l’hypochondre droit ; 1b) la tumeur est distincte de la vésicule biliaire. La veine porte (flèche) est pré-pancréatique et pré-duodénale. A ce niveau, l’artère hépatique commune (flèche pointillée) (naissant de l’artère mésentérique supérieure) a un trajet rétropancréatique et le pancréas (P) est tronqué ; 1c) Absence de veine cave rétro-hépatique avec dilatation marquée de l’hémi-azygos gauche (flèche).

Fig. 2 – Percutaneous cholangiography: opacification through segment 8 showing multiple filling defects obstructing the hilar confluence and the upper part of common bile duct. The distal part of ducts draining segments 2-4 is dilated without tumoral feature.

Cholangiographie per-cutanée : opacification par le segment 8 montrant de multiples lacunes obstruant la convergence biliaire supérieure et la partie haute de la voie biliaire principale. La partie terminale des canaux des segments 2 à 4 est dilatée, sans aspect tumoral.
involvement on both distal and proximal biliary sections. The “left” hepatic vein was controlled extrahepatically and a Pringle maneuver was necessary for 22 minutes during parenchymal transsection. Biliary drainage was re-established with a Roux-en-Y hepaticojejunostomy. The operating time was 6 hours 30 minutes and total blood loss was 1000 ml without need for transfusion.

Pathological examination showed a 3-cm well differentiated intrahepatic cholangiocarcinoma with papillary pattern and intraductal growth. Resection margins and lymph nodes were free of tumor. No vascular invasion was noted. The biliary tree upstream and downstream from the tumor was normal with a non-dysplastic mucosa. Non-tumoral hepatic parenchyma showed patterns of secondary biliary cirrhosis.
Postoperatively, the patient developed prolonged ascites with left pleural effusion. There was no hepatic failure (prothrombin index = 75% and serum bilirubine level = 32 micromoles/l on postoperative day 5). She was treated by diuretics and chest drainage, and was discharged on postoperative day 32. No adjuvant therapy was given, due to presumed good prognosis of the disease and lack of proven efficacy of adjuvant chemotherapy after radical resection of cholangiocarcinoma. Twelve months after operation, the patient was in good general condition with normal liver function tests and no signs of recurrence on CT scan.

**Discussion**

The present observation shows that a complex surgical procedure can be performed safely in patients with situs ambiguous, if complete anatomical assessment is done preoperatively. Our patient had an anatomical variant different from situs inversus totalis, with special features (predisduodenal portal vein and common bile duct, retropancreatic hepatic artery, and agenesis of retrohepatic vena cava) which can interfere with major hepatobiliary-pancreatic resections. Furthermore, the tumor was a cholangiocarcinoma with papillary pattern and intraductal growth, a rare and good-prognosis variant of intrahepatic cholangiocarcinoma. To our best knowledge, this is the first case in the literature of papillary cholangiocarcinoma in a patient with situs ambiguous and polysplenia.

Situs anomalies are rare and generally incidental findings in adults in contrast with children in whom they are usually diagnosed early because of associated malformations [6]. Situs inversus totalis is the most frequent variant and is observed approximately 1:5000 to 1:10000 adults [1]. Whatever complete (with dextrocardia) or not (with levocardia), situs inversus totalis includes a complete mirror-image location of the abdominal viscera [2]. Situs ambiguous, or heterotaxia, is defined as the abnormal arrangement of organs and vessels as opposed to the typical arrangement of situs inversus, and is rarer than situs inversus totalis [6]. Although it is frequently mixed up with situs inversus in the literature, it can be easily recognized since it is frequently associated with spleen anomalies. Situs ambiguous with asplenia includes ambiguous location of abdominal organs and absence of the spleen, but is associated with lethal congenital heart disease in almost cases [6]. Situs ambiguous with polysplenia — as observed in our patient - is more common in females and associated with congenital heart disease in 50-80% of cases [2, 6]. Patients without or with mild heart disease can reach adult age. The two most consistent findings in patients with situs ambiguous and polysplenia are absence of retrohepatic vena cava withazygos or hemiazygos continuation, and a single polysegmented or multiple spleens of variable size and number that can be located either in the left side or the right side of the abdomen with the stomach always on the same side as the spleens [2, 6]. Other abdominal anomalies include truncated pancreas, predisduodenal portal vein, “bridging” or “reversed” midline liver, biliary atresia, and intestinal malrotation [2, 3, 5, 6].

Our patient showed many of these anomalies but had no heart disease and experienced a normal life until discovery of the biliary tumour. Situs ambiguous with polysplenia is linked to a gene mutation [7]. Although situs anomalies are not considered as premalignant syndrome, there are several reports in the literature of tumors associated with these conditions [3, 8-11].

Major upper abdominal procedures have been described in patients with situs ambiguous, including total gastrectomy [3], pancreaticoduodenectomy [4], and orthotopic liver transplantation [5]. In these procedures, and in major hepatectomy with common bile duct resection as performed in our patient, special care must be taken to avoid inadvertent major vascular or biliary damages. In our patient, both retropancreatic course of common hepatic artery and prepancreatic course of common bile duct could have predisposed to either inappropriate dissection or interruption of the main hepatic artery with possible ischemic damages of intrahepatic biliary tree; on the opposite, agenesis of retrohepatic vena cava and segment I, associated with the presence of an extrhepatic segment of hepatic veins facilitated retrohepatic mobilization. During pancreaticoduodenectomy in patients with situs ambiguous and polysplenia, dissection is made more difficult by a pre-duodenal portal vein [4] and can result in damage of the main hepatic artery, which was retropancreatic in our patient and in others cases, due to its origin on superior mesenteric artery or abdominal aorta [5]. Total gastrectomy with lymphadenectomy in the same condition can probably result in splenic or hepatic devascularization. Orthotopic liver transplantation is characterized by variability of techniques used for caval and arterial reconstructions [5]. Extensive preoperative anatomical assessment does not suppress the need for meticulous dissection since, in our patient, precise course of the lower common bile duct was only established at laparotomy.

Biliary carcinomas have been previously described in patients with situs inversus [9, 10] but another particularity of the present observation is the papillary pattern of the peripheral cholangiocarcinoma. Three pathological types of peripheral cholangiocarcinoma have been described: the mass forming type, the periductular infiltrating type characterized by tumor infiltration along the bile duct, and the intraductal growth type characterized by papillary growth within the bile duct lumen [11, 12]. Intraductal growth type represents 15% to 20% of peripheral cholangiocarcinomas [12, 13]. The intraductal growth type appears as a slowly progressive disease. In our patient, parenchymal atrophy without vascular encasement in segments 5 to 8, coexisting with secondary biliary cirrhosis suggests that biliary obstruction was present for several months. Intraductal growth type has a good prognosis with a 80% to 100% 5-year survival rate [12, 13], comparing favorably with the 20% to 40% 3-year survival rates of other types of peripheral cholangiocarcinoma [13, 14]. The usually limited infiltration of biliary duct wall and an uncommon lymph node involvement could explain this better prognosis. However, intrahepatic recurrence is possible despite negative resection margins [12] thus justifying periodical follow-up.

In conclusion, major hepatectomy can be performed safely in patients with situs ambiguous with polysplenia, provided a complete anatomical assessment is done by pre-operative imaging and perioperative dissection is meticulous. Major hepatectomy is not precluded by preduodenal portal vein and its technique should take into account both absence of retrohepatic vena cava and anatomical variants of hepatic artery.

**REFERENCES**


