

Living donor liver transplantation as treatment for diffuse Caroli's disease

To the Editor,

Caroli's disease (CD) is a rare autosomal recessive disorder characterized by intrahepatic cystic dilatation of the bile ducts. When progressive, it leads to recurrent cholangitis, jaundice, intrahepatic stones accumulation, portal hypertension, cirrhosis and liver failure [1]. Additionally, patients with CD have another life threatening problem: the risk of developing cholangiocellular carcinoma is 100 times greater than in the general population [2]. Patients with bilobar disease with recurrent cholangitis or complications related to portal hypertension and cirrhosis may require orthotopic liver transplantation (OLT).

Iancu et al [3] described a case of diffuse CD in a 49-year-old female, with acute cholangitis associated with intrahepatic lithiasis and important fibrosis of the left hepatic lobe. She was submitted to a left lobectomy, lavage of the bile ducts and a cholangio-jejunal Roux-en-Y anastomosis. Even though the optimal treatment for this patient was OLT, the author's choice was based on two facts: the emergency status of the patient and the shortage of liver donors in Romania.

At our unit, between March 2002 and February 2009, we performed 416 OLT, 142 with living donors. Among these 142, two patients were transplanted due to diffuse CD. The diagnosis was based on clinical presentation, magnetic resonance image (Fig. 1) and pathological findings.

Patient 1: a 2-year-old girl, who was diagnosed with CD associated with cirrhosis when she was 6 months old due to symptomatic hepatomegaly. Her PELD score was 6 and she received a left lobe graft from her father, corresponding to 1.96% GRWR (graft weight/recipient's body weight ratio).

Patient 2: a 19-year-old girl, diagnosed with bilobar CD since she was 13 years old, was suffering from repeated cholangitis events. She received a right liver graft from her father. Her MELD score was 15. The weight of the graft

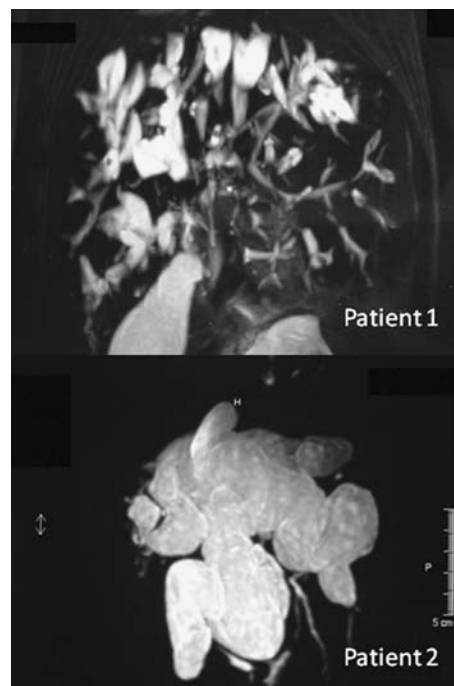


Fig 1. Preoperative magnetic resonance in patients 1 and 2, showing the intrahepatic cystic dilatation of the bile ducts.

was 706g, corresponding to 1.21% GRWR. Liver specimen confirmed intrahepatic cystic dilatation of the bile ducts (Fig. 2).

Both patients are alive after 83 and 30 months post-transplantation, respectively.

In Brazil, as in Romania, there is a crucial shortage of potential liver grafts – 7.0 donors/million habitants/year [4]. In this situation, patients with a low MELD score, such as CD, have little chance to receive a graft from a deceased donor. Thus, LDLT has become the ultimate option for patients with complicated CD.

Long term outcomes for patients with CD submitted to OLT are encouraging and show a 5-year survival up to 77% [5], which is comparable with those who undergo OLT for other etiologies of chronic liver disease [6]. There is no large



Fig 2. Inspection of liver specimen of patient 2 confirming intrahepatic bile ducts' cystic dilatation.

series regarding LDLT for CD, but isolated reports show similar results [5].

In **conclusion**, LDLT is a feasible option in the treatment of diffuse CD, even when complicated by recurrent cholangitis or carried out in an early age patient. Moreover, for regions where there is a lack of deceased donor grafts, LDLT may be the only option for transplant in patients with CD.

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Ecstasy induced fatal hepatic failure

To the Editor,

In recent years, parallel to the increase in the usage of narcotic and psychotropic drugs, complications related to these substances have occurred more often. One of these substances, a synthetic amphetamine derivative, 3,4-methylene dioxy-metamphetamine (MDMA), known as "ecstasy", is a psychostimulant and hallucinogen drug. This

substance has the potential of leading to severe psychological and physical side effects. Hyperthermia, cerebral edema, hepatotoxicity and nephrotoxicity have been reported as related complications [1]. These side effects occasionally may be fatal. In this letter, we are reporting a case resulting in death because of acute fulminant hepatitis after MDMA usage.

A 19-year old male admitted to our clinic with symptoms of nausea, emesis, and abdominal pain. At the initial evaluation, there was no history of usage of any (medical, narcotic) drug or herbal consumption. The laboratory examination revealed, leukocyte 27,000/mm³, neutrophils 20,000/mm³, hemoglobin 19 g/dl, AST 257 U/l, ALT 375 U/l, LDH 1,023 U/l, total bilirubin 7.8 mg/dl (direct bilirubin 4.9 mg/ml, indirect bilirubin 2.9 mg/dl); PT and PTT was infinite. Serologic markers for acute hepatitis A, B, C, and E were negative as were those for HIV, CMV, EBV, Herpes simplex 1 and 2, and Varicella-zoster virus. Autoantibodies (antinuclear antibody, antimitochondrial antibody, anti-smooth muscle antibody, and anti-liver-kidney microsomal type 1) were negative. Alpha-1 antitrypsin, serum and urine copper, ceruloplasmin, p-ANCA, creatinine kinase, and immunoglobulins were normal or negative. In clinical follow-up blurred consciousness, increase in jaundice, gradual increase in transaminases and bilirubin levels (AST 3,233 U/l, ALT 4,555 U/l, total bilirubin 26 mg/dl) were seen. Persistent questioning about drug use revealed that the patient had used MDMA a week ago. His follow up in intensive care unit was unsuccessful and resulted in death despite supportive medical treatment and liver transplantation efforts.

One of the most serious side effects of MDMA is hepatotoxicity. This toxicity can range from asymptomatic liver injury to acute hepatic failure [2]. This hepatotoxicity does not rely on dosage and even with a single dose, fulminant hepatitis may occur [3-5]. The interval from exposure to the first signs of toxicity in most cases amounts to a few days, although it can extend even to two or three weeks [6]. In conclusion, especially in young patients, ecstasy and other psychotropic drugs have to be considered as causes of non-viral hepatitis and patients should be questioned carefully during anamnesis.

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EUS-FNA using a forward-view echoendoscope in difficult cases

To the Editor,

Endoscopic ultrasound-fine needle aspiration (EUS-FNA) was introduced at the beginning of the 90's thanks to the linear echoendoscopes allowing real time visualization of aspiration needles [1]. A prototype forward view (FV) echoendoscope (XGF-UCT160JAL5, Olympus Medical Systems Europe GmbH, Hamburg, Germany) was recently developed with an ultrasound field of view almost coaxial to the exit path of the working channel, allowing the use of needles and other devices in a straight position similarly to a gastroscope. The FV echoendoscope was originally designed for therapeutic procedures [2-4]; however, it has been reported that it can be very useful for standard EUS-FNA too [5, 6].

This is a report regarding a group of patients in whom we used the FV echoendoscope with a 22-Gauge needle after failure with standard EUS-FNA.

The reasons for the unsuccessful standard EUS-FNA were: (group 1) inability to reach the desired position with the linear echoendoscope (n=3); (group 2) inability to puncture adequately the target lesions (n=10) (Table I).

With regard to group 1, it had been impossible in the colon cases to advance the linear echoendoscope to the level of the lesions because of the oblique endoscopic view and the long tip. In the duodenal case the linear echoendoscope was too angulated in the second portion and could not be advanced to the third portion. In group 2, it had been possible to visualize the target lesions but not to adequately perform EUS-FNA with the linear echoendoscope in 10 patients (in 7/10 the lesions could not be punctured due to anatomic obstacles, and in 3/10 the lesions could be punctured only marginally).

On the other hand, it was possible to perform FV EUS-FNA in all these patients by being able to reach the site where the lesions were (group 1) and/or positioning the needle tract under different angulations (group 2). No complications occurred with the FV EUS-FNA. The scope maneuverability and the ease of performing FNA were satisfactory.

The forward endoscopic view allowed the reaching of portions of the gastrointestinal tract that are not easily accessible with a linear echoendoscope, such as the colon proximal to the rectum, the third and the fourth portion of the duodenum. Another relevant improvement consisted of the EUS field almost parallel to the endoscopic view, which allowed a great penetration force and a precise orientation of the needle, just by up/down deflections of the tip. Moreover, the needle could be advanced through the working channel also in the retroflexed position in a patient with a gastric submucosal lesion in the fundus (Fig. 1).

The major limitation of the FV echoendoscope consisted of its narrow EUS field, compared to the linear echoendoscope. This characteristic might prove a limitation

Table I. Patients characteristics

Sex/Age	Site of lesion	Diameter (mm)	Reasons for failure with standard EUS-FNA	FV EUS-FNA cytology	Surgery
M/82	Sigmoid colon	36	Inability to reach the lesion	Adenocarcinoma	Yes
F/73	Pancreas, head	35	Marginal puncture	Inadequate	Yes
F/79	Descending colon	29	Inability to reach the lesion	GIST	No
M/55	Duodenum, upper genu	23	Failure to puncture the lesion (interposition of the pylorus)	GIST	Yes
M/66	Pancreas, genu	22	Failure to puncture the lesion (tangential approach)	Absence of neoplastic cells *	No
M/59	Pancreas, head	12	Failure to puncture the lesion (tangential approach)	NET	No
M/66	Duodenum, third portion	25	Inability to reach the lesion	GIST	Yes
F/49	Gastric fundus, greater curvature	38	Failure to puncture the lesion (too much retroflexion needed)	GIST	Yes
F/73	Pancreas, tail	35	Failure to puncture the lesion (interposition of splenic artery)	Absence of neoplastic cells, +ve mucin staining **	Yes
M/75	Pancreas, uncinate	28	Marginal puncture	Adenocarcinoma	Yes
F/74	Pancreas, head	20	Failure to puncture the lesion (tangential approach)	Adenocarcinoma	Yes
M/48	Pancreas, tail	45	Failure to puncture the lesion (interposition of splenic vein collaterals)	Adenocarcinoma	No
F/41	Pancreas, head	25	Marginal puncture	NET	Yes

GIST: gastrointestinal stromal tumor; NET: neuroendocrine tumor; * Biochemical markers: low amylase (133 U/L) and low CEA (4.1 ng/ml); ** Biochemical markers: low amylase (250 U/L), high CEA (414 ng/ml)

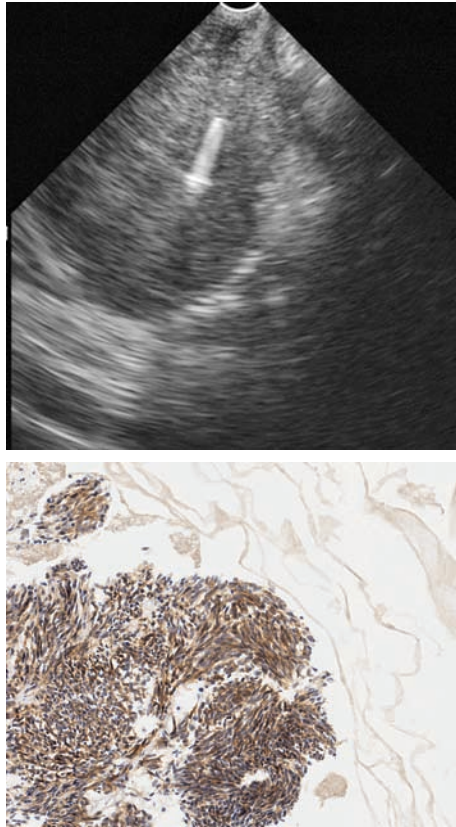


Fig 1. (A) A large hypoechoic lesion in the gastric fundus, originating from the 4th layer, is punctured with the FV echoendoscope in retroflexion; (B) Cellblock: spindle cells positive for CD117 immunostaining (100X). The findings are compatible with a gastrointestinal stromal tumor (GIST).

of its diagnostic abilities. However, with increasing experience, it is possible to visualize satisfactorily all the organs that are commonly explored with EUS. We believe

that FV EUS-FNA could become a valid complement to standard EUS-FNA particularly in tertiary centers.

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