

Prevalence of viral hepatitis in hemodialysis patients in Tehran, Iran

To the Editor,

Chronic hemodialysis (HD) in end-stage renal failure patients is a life saving procedure [1]. Patients undergoing chronic hemodialysis potentially have an increased risk of exposure to infections with viruses, such as hepatitis B (HBV) and hepatitis C (HCV) viruses [2]. After cardiovascular diseases and bacterial infections, viral hepatitis is the most frequent disease resulting in a complication of hemodialysis treatment [1]. The prevalence of parenterally transmitted viral hepatitis in the population of hemodialyzed patients is far higher than the prevalence of these diseases in the general population. Different preventive protocols have changed the incidence of viral hepatitis. HBV infection has been effectively controlled by screening of blood donors, erythropoietin therapy, isolation of HBV positive patients, use of dedicated dialysis machines, improved disinfectant procedures, regular surveillance for HBV infection and active HBV vaccination before entering dialysis program [2, 3].

Even with the increase in the safety of blood products and the decrease in the need for transfusions in hemodialysis patients, several prophylactic measures have been suggested for the prevention of infection by HCV in the hemodialysis environment. These can be from isolating the patients carriers of HCV to adopting a series of biosafety measures specific for hemodialysis, such as preparing medications in a separated area, cleaning and disinfecting dialysis station surfaces, washing hands and changing gloves between patient contacts, and items dedicated for use only with a single patient [4].

We assessed the seroprevalence and risk-related factors of hepatitis B and C in patients of hemodialysis (HD) units of two university-affiliated hospitals in Tehran. The prevalence of anti-HCV positivity was found to be 8.5%. Different

prevalence of anti-HCV was reported by similar studies on Iranian hemodialysis patients in Guilan (24.8%) and Semnan (10.5%). In other countries such as those in Persian Gulf area, in Bahrain and Saudi Arabia it was reported to be 9.24% [5]. The difference in the prevalence rate for anti-HCV positivity in hemodialysis patients reported in various studies might be due to different lengths of time on hemodialysis of the different populations. Another possibility could be the hemodialysis unit environment condition as a way of transmission of HCV.

The aminotransferase levels did not differ significantly in our anti-HCV positive and negative patients, suggesting that ALT or AST level alone are not sufficient to monitor hepatitis C infection.

In our study, the prevalence of HbsAg was 4.6%. It was reported to be 3.7% in Semnan, 1.7% in Kashan, and 5.88 % in countries in Persian Gulf area, Bahrain and Saudi Arabia [5]. Our data, similarly to previous studies [2], show a positive relationship between duration of dialysis and positivity of anti-HCV (not of HbsAg), which confirms the hemodialysis environment as a source of transmission ($p=0.000$).

Even though there was a decreased seroprevalence rate of antibodies to HCV in the hemodialysis unit, correlation of duration of hemodialysis with the presence of antibodies to HCV strongly supports the hemodialysis environment as a source of transmission of this disease. Adherence to strict universal precautions within the hemodialysis units might possibly control the spread of HCV infection. There is also a high prevalence rate of HbsAg positivity in hemodialysis units. Closer observation and even more restricted rules for immunization with HBV before starting hemodialysis will reduce HBV infection. Health care providers should evaluate every hemodialysis patient for viral hepatitis markers and refer them for HBV vaccination if they are not immune for HBV infection.

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Acute pancreatitis after early termination of brucellosis antibiotic therapy

To the Editor,

Brucellosis is a zoonosis caused by Gram negative bacteria belonging to the *Brucella* genus. It has a worldwide diffusion, particularly in the Mediterranean countries. In our region, Calabria, (Southern Italy), the prevalence of this infection among the general population is 3.8% [1]. The disease is transmitted from domestic animals to humans through ingestion of fresh milk and its by-products and more rarely through a dermic or an inhalatory passage. Once it has penetrated into the system, the *Brucellas* pass into the lymphatic system and, consequently, into the circulatory system. During this phase of bacteriemia, the microorganisms can potentially reach every other organ. This explains the clinical polymorphism of brucellosis. The gastrointestinal symptoms in brucellosis are nonspecific: abdominal pain, dyspepsia, emesis, diarrhoea (2), and mild hepatic involvement. Pancreatic involvement is extremely rare and there are very few references in the literature [3-6].

A 29-year-old man was admitted in our hospital for fever, vomiting, and abdominal pain which developed five days after early termination of antibiotic therapy (12 days of doxycycline and rifampin) prescribed by his GP for brucellosis. The diagnosis had been based on a 1/1200 agglutinin titre. The patient's body temperature was 38.6°C with profuse perspiration. The physical examination revealed pain in the epigastrium and moderate hepatomegaly. The most significant lab test results were: WBC 4,800, without alterations of the leukocyte formula; creatinine 60.9 µmol/l, glycemia 5.4 mmol/l, total bilirubin 50.2 µmol/l (conjugated 22.5 µmol/l), AST 106 U/L, ALT 180 U/L, γglutamyl transpeptidase 40 U/L, amylase 334 U/L (normal values 28 – 100 U/L), lipase 455 U/L (normal values 13

– 60 U/L), triglycerides 1.9 mmol/l, calcemia 2.4 mmol/l. Anti-viral screening for HAV, HBV, HCV, EBV, CMV, ECHO, HIV, type 1 and 2 HSV (Herpes Simplex Virus) were negative, as were the serologic tests for toxoplasma, typhoid and paratyphoid A and B. The agglutinin titre for brucella was 1/1200. The hemoculture was positive for *Brucella melitensis*. The abdominal ultrasonography showed hepatomegaly, gallbladder without stones, the choledochus of normal calibre, and a hypoechogenic pancreas. The patient denied any intake of alcohol or medicine. It was decided that the patient should start doxycycline 200 mg/day of and streptomycin 1 g/day. After three days of therapy there was complete remission of pain in the abdomen and, upon discharge, after 13 days, amylase and lipase levels were normal. Sixty days after discharge, a check-up proved that the patient was in good health and that amylase, lipase and aminotransferase levels were normal and the agglutinin titre for brucellosis was 1/80.

In each of the previously reported cases, pancreatitis was mild, with a quick resolution of the symptoms and of biochemical changes in a few days after antibiotic treatment started. In the course of brucellosis, pancreatitis would occur due to a hematogenous passage of bacteria, or to a reflux of the infected bile through the Wirsung's duct [3]. What makes this case of particular interest is the rarity of this association and the later development of acute pancreatitis, once the initial antibiotherapy was suspended. Acute pancreatitis is a potentially serious illness, with over a 10% death rate. Therefore, although this association is infrequent, it is important to check the amylase and lipase serum levels in case of brucellosis infection. In addition, it is necessary to ensure the patients compliance with the antibiotic therapy.

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Shoulder pain as the first sign of a hepatic fibrolamellar carcinoma in a young man

To the Editor,

A 19 year old male patient was admitted for severe right shoulder pain and also light abdominal pain located in the right upper quadrant. His symptoms started 1 week before admission. The patient reported a history of flu-like symptoms, nausea and vomiting in the past week. He received Cefixime as medication. He did not have any significant past medical history or previous medication.

No history of jaundice or hepatitis was found in his family. Reviewing his history, the patient also reported right shoulder pain that aggravated with breathing. The physical examination showed normal blood pressure, heart and respiratory rates, and temperature. The liver and spleen were normal at palpation. A shoulder X ray was normal. Chest X ray was also normal.

The laboratory tests were normal except: ALT – 590 IU/L, AST – 310 IU/L, ALP – 308 IU/L, ESR- 60, positive C reactive protein.

Ultrasonography showed a 99 x 67 mm heterogeneous lesion in the right hepatic lobe with irregular contour. Abdominal CT scan was done and a solid 11x 8 cm tumor with irregular borders and hypodense zones with fine calcification was seen in the right liver lobe (Fig. 1). Other organs were normal and no enlarged lymphnodes were found.

These features did not differentiate the lesion from a complicated hemangioma or hydatid cyst, that is endemic in Iran.

Additional lab tests were performed : tumor markers - α FP was 0.6 (NL<10), CEA - 1.3(NL<5), CA-19-9 - 3.5 (NL<35), as well as the Hydatid antibody - 3 (NL<8).

An RBC liver scan was not concordant with hemangioma and showed an area of decreased radiotracer uptake in the posterior part of the right lobe, without change in delayed image. This indicated a solid primary neoplasm, probably malignant, in the liver. We decided to perform a liver biopsy.

In optic microscopy, neoplastic changes consisting of cellular bundles with abundant eosinophilic and hyaline cytoplasm surrounded by lamellar fibrotic bundles were seen, which allowed the diagnosis of fibrolamellar hepatocellular carcinoma.



Fig 1. Fibrolamellar carcinoma: axial cut of liver show a large tumor with hypodense and calcified parts.

Complete surgical resection by lobectomy was performed in our patient.

In macroscopy the tumor was 12 x 11 x 7 cm, well circumscribed. On the section, central fibrosis was detected, as well as green to yellowish and cream colored nodules showing green areas of bile production. The microscopical evaluation confirmed the diagnosis of fibrolamellar carcinoma; hepatocytes with abundant eosinophilic hyaline cytoplasm that fenced by lamellated fibrous septa with considerable bile production and areas of necrosis.

The patient was discharged in good condition. He is symptom free and tumor free at 7 months after surgery.

Fibrolamellar carcinoma, such as any type of hepatic solid or cystic lesion, may present with right shoulder pain as in this patient [2]. Etiology is unknown. It is not associated with chronic hepatitis B or C infection, and almost always arises in a noncirrhotic liver [1]. It does not secrete α -fetoprotein [3]. At ultrasonography the tumor is often large, hypoechoic or mixed, focal calcification and a central scar are frequently seen. The CT scan usually shows a well-circumscribed large single tumor, which may have visible calcification or central scare [3].

In microscopic survey it shows well differentiated, polygonal, deeply eosinophilic cells growing in cords and surrounded by abundant fibrous stroma composed of thin, parallel lamellar fibrous bands that separate the cells into

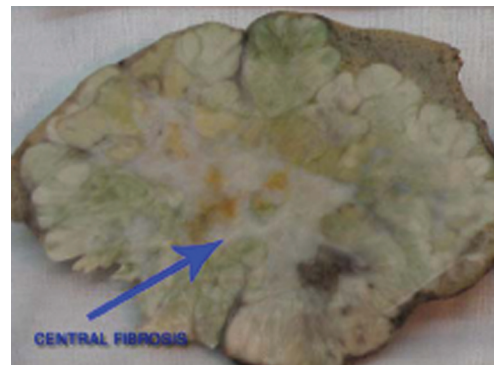


Fig 2. Fibrolamellar carcinoma : yellowish and cream nodules separated by fibrous bans and a central fibrous pat.

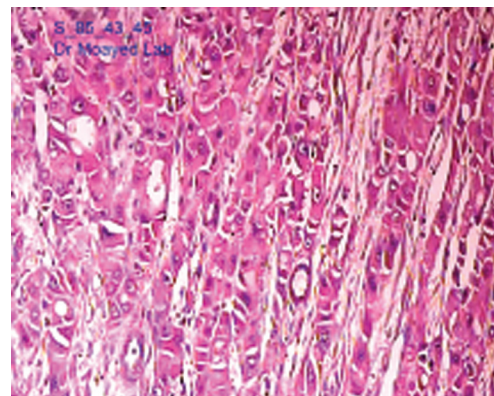


Fig 3. Fibrolamellar carcinoma: polygonal large tumoral cells separated by fibrous bundles (H-E).

trabeculae or nodules. The cytoplasm is packed with swollen mitochondria and, approximately half of the tumors contain pale or hyaline bodies. Nuclei are prominent, and mitoses are rare [4]. Rarely, fibrolamellar carcinoma shows areas of glandular type with mucin production [5].

The fibrolamellar carcinoma is more often treatable by surgery and has a better prognosis than hepatocellular carcinoma, especially at an age younger than 23 years [6]. It is a slow growing tumor and late recurrence is common [1]. Better prognosis is related to absence of cirrhosis and younger age of the patients rather than to its nature [5].

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Prophylactic endoscopic band ligation of esophageal varices during pregnancy

To the Editor,

Pregnancy associated with cirrhotic or non-cirrhotic portal hypertension and esophageal varices (EV) is rare [1]. Patients with cirrhosis are not likely to become pregnant due to endocrine and metabolic imbalances. On the other hand, women with non-cirrhotic portal hypertension have normal fertility rates [2, 3]. The incidence of variceal bleeding during pregnancy may reach up to 45% with a mortality rate of 18-50% [4]. Various treatment modalities, either prophylactic or urgent, such as endoscopic injective sclerotherapy (EIS), endoscopic band ligation (EBL) as well as transjugular intrahepatic portosystemic shunt (TIPS) have been reported as possible management procedures

of this medical dilemma [1-5]. Since there are only a few case reports published, regarding the treatment options for this clinical condition, the management of EV and their major life-threatening complication – hemorrhage during pregnancy is still under evaluation [2, 6]. To the best of our knowledge, until now only one case report regarding prophylactic EBL during pregnancy has been published [4]. We report an additional case of successful prophylactic EV banding during pregnancy.

A 27-year-old (para 0, gravida 1) female with a history of idiopathic portal hypertension (according to the Japan Idiopathic Portal Hypertension Study Committee criteria) [7], presented for routine examination at our surgical department in the 22nd week of pregnancy. Significant medical history included a modified Hassab-Paquet surgical procedure with splenectomy due to EV and hypersplenism, performed three years previously (2004) in our unit [8]. Regular upper gastrointestinal (GI) endoscopy demonstrated complete (F0 RCS-) postoperative EV eradication. Taking into account the possibility of EV recurrence during pregnancy, upper GI endoscopy was performed, which demonstrated recurrent EV (F2, Li, RCS++). In order to prevent variceal bleeding in the last two trimesters of pregnancy, prophylactic EBL with a MBL-10-F device (Wilson Cook® Medical, Winston-Salem, NC, USA) was performed. Four bands were applied and complete EV eradication (F0 RCS-) was obtained. Repeated upper GI endoscopy at 35 weeks of pregnancy demonstrated no EV recurrence. The patient underwent delivery by Cesarean section at 40 weeks of gestation. The new-born was a 3485 g healthy male, appropriate for his gestational age. The postoperative period was uneventful.

In the early 80's, EIS was generally accepted as the first-line treatment procedure for bleeding EV. Despite this fact, only few cases of EIS with conventional sclerosants (polidocanol, absolute alcohol, sodium tetradecyl sulfate) were reported during pregnancy [1, 6]. There are no studies regarding the effect of the conventional sclerosants on the fetus published in the literature, although the procedure is considered safe and effective to control active variceal bleeding [1, 6]. Vasoactive drugs used to achieve hemostasis are contraindicated during pregnancy, since these (vasopressin and terlipressin) may induce labor or fetal malformations [2]. TIPS was reported as another possible management option for bleeding EV refractory to endoscopic treatment during pregnancy [5]. Recently, EBL was reported as an effective treatment option for active variceal hemorrhage as well as prophylaxis of this severe complication during pregnancy [2-4].

Since EBL is free of the potential adverse effects related to EIS with conventional sclerosants or pharmacological treatment, we support the opinion that variceal ligation could be the most appropriate endoscopic procedure to prevent and to control bleeding EV during pregnancy [2-4]. Despite the fact that the evolution was uneventful in our case, additional experience with this group of patients must be gained before the final conclusions regarding the most appropriate treatment modality may be established.

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Prevalence of the metabolic syndrome in patients with prostate cancer

To the Editor,

Metabolic syndrome (MS) is a cluster of the most dangerous risk factors for cardiovascular disease: diabetes and increased fasting plasma glucose, abdominal obesity, high cholesterol level and high blood pressure. It is also a risk factor for neoplastic diseases, especially for the hormonal ones such as prostate cancer.

While MS pathogenesis is complex and not entirely elucidated, central obesity and insulin resistance are acknowledged as important causative factors. Central obesity, independently associated with each of the other MS components including insulin resistance, is a prerequisite for the diagnosis of MS in the new definition.

We evaluated the prevalence of MS and its components (as number and type of associations: waist circumference, hypertriglyceridemia, reduced HDL cholesterol level, high blood pressure, increased fasting plasma glucose) in 82 patients who were actively diagnosed with prostate cancer in a screening program at the Urology Department of the Municipal Clinical Hospital in Cluj-Napoca. The diagnosis of prostate cancer was established by prostate biopsy in

patients in whom neoplasia was suspected based on clinical data and elevated prostatic specific antigen (PSA) level. Statistical analysis included mean \pm SD for the quantitative variables, chi square test, Pearson coefficient, with the limit value for statistical significance at 0.05.

Prevalence of MS in the patients with prostate cancer was 68.29% (56 out of 82 patients). The most important associated risk factors were abdominal obesity (in 69.51%), reduced HDL-cholesterol (58.53%) and increased fasting plasma glucose levels (57.31%). We found in these patients a predominance of T3-T4 stages (53.65%) and of a mean Gleason score (between 5 and 7) (79.26%).

Raised fasting plasma glucose and low levels of HDL-cholesterol were strongly related to the presence of prostate cancer: O.R. was 7.31 for hyperglycemia and 9.93 for low HDL-cholesterol.

Subjects with T3-T4 tumor stage had hyperglycemia ($p=0.005$), hypertriglyceridemia ($p=0.001$), low HDL, hypertension, as well as fatty liver disease ($p=0.001$) more frequently than those in the early disease stages.

Our findings are in agreement with previous studies. In a prospective cohort of 16,209 men aged 40-49 years an association between insulin resistance and the incidence of prostate cancer was found [1]. Another study went further and concluded that efforts to curb the epidemic of overweight and sedentary lifestyle and the accompanying MS might decrease the risk for prostate cancer [2].

Many studies have linked larger abdominal waist circumference and obesity to the increased risk of several malignancies, including cancer of the colon, gallbladder, kidney and pancreas. This was explained by the association between obesity and a state of inflammation, expressed through markers such as leptin, IL-6, TNF, which were shown to enhance tumor growth [3]. Similar to other studies [4], we also showed that hypertriglyceridemia could be a possible risk factor for prostate cancer.

Another study performed on 299 subjects with prostate cancer concluded that patients in T3 stage were more obese (BMI, waist and hip circumference) and had a higher systolic blood pressure than subjects in the T2 stage of disease. It was also observed that subjects in T3 had more often high triglyceride, low HDL cholesterol and high plasma insulin levels. The authors concluded that prostate cancer was a component of MS and that insulin resistance was a promoter of prostate cancer [5].

In **conclusion**, our results have demonstrated an association between T3 stage and hyperglycemia, low HDL-cholesterol, hypertriglyceridemia, hypertension and especially increased waist circumference, supporting the view that features of MS could represent risk factors for prostate carcinogenesis.

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Ectopic openings of the bilio-pancreatic ducts in the stomach in an elderly case presenting with choledocholithiasis and acute cholangitis

To the Editor,

A 74-year-old female presented in February 2007, with severe right upper quadrant abdominal pain, chills, elevated body temperature (39.5 °C) and mild jaundice. Her past medical history was uneventful.

On admission, physical examination revealed only mild tenderness in the upper abdomen and mild scleral jaundice. Routine laboratory tests revealed elevated alkaline phosphatase 771 U/L (normal range: 40-150 U/L), gamma glutamyl transpeptidase 1249 U/L (normal range 0-50 U/L), total and direct bilirubin levels 5.6 mg/dl and 3.8 mg/dl respectively. Alanine aminotransferase 48 U/L (normal range: 10-35 U/L) and aspartate aminotransferase 81 U/L (normal range 10- 40 U/L) were slightly elevated also. The white blood cell count was 12,800 per ml with normal hemoglobin (14 g per dl) and thrombocyte count (175,000 per ml). An abdominal ultrasonography revealed the gall bladder with few small stones and dilatation of the choledochus of more than 10 mm with multiple stones in the lumen. During endoscopic procedure, we could not find the papilla in the second part of the duodenum by using a standard duodenoscope. Reexamination with a forward viewing gastroscope showed two slit-like orifices just before the pylorus and a large benign appearing gastric ulcer in the prepyloric region (Figs. 1, 2). The cannulation of the common bile duct through the slit like orifice (Fig. 2a) showed marked dilatation of whole biliary tree. There were multiple stones in the choledochus (Fig. 2b). The main pancreatic duct which was visualized via the second orifice (Fig. 3a) was normal (Fig. 3b).

We dilated the biliary orifice with a 12 mm pyloric

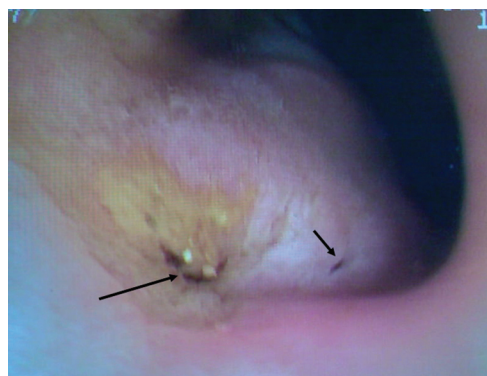


Fig 1. Biliary orifice indicated by taller arrow. The pancreatic duct orifice indicated by smaller arrow.

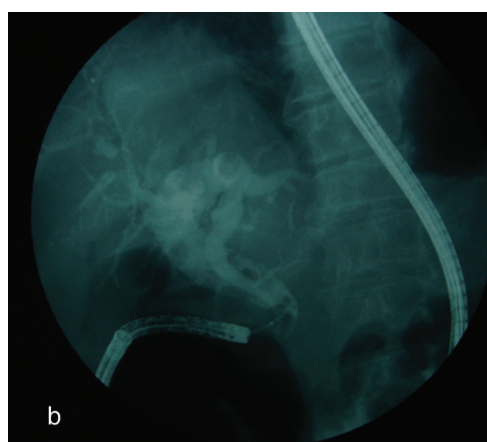
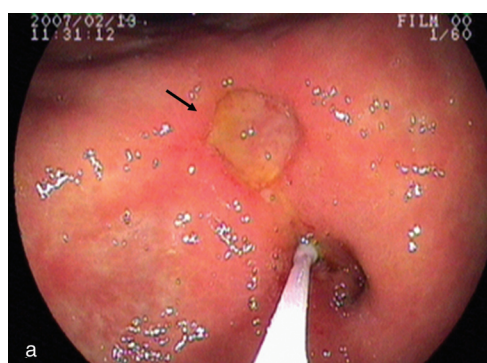


Fig 2. Large antral ulcer indicated by the arrow (a). The dilated biliary tree and choledocholithiasis seen on scopic examination (b).

dilatation balloon and extracted many stones and sludge into the stomach. After the procedure, the patient was free of previous complaints and his laboratory tests returned to normal.

Probably the rarest of the congenital anomalies of the excretory ducts of the liver is the ectopic opening of the common bile duct at anomalous sites. Potential sites include the third or fourth portion of the duodenum, duodenal bulb, pyloric channel, and stomach [1-5]. In the present case, both the common bile duct and Wirsung duct ended up in the stomach.

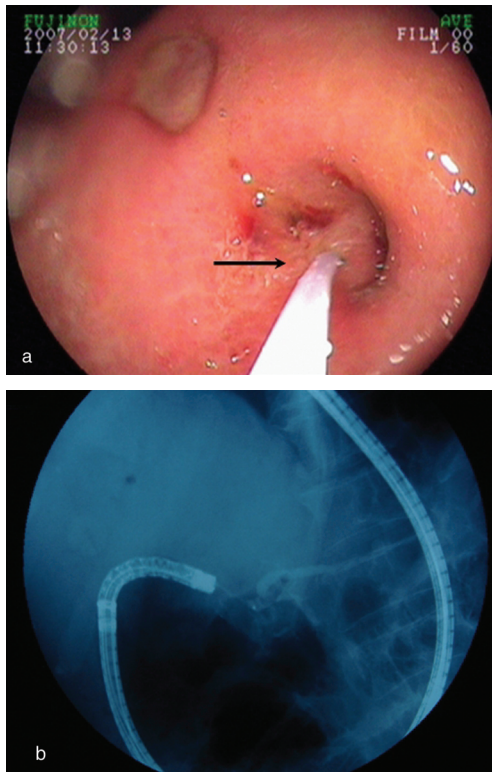


Fig 3. Endoscopic image: the cannulation of the pancreatic duct orifice (a). The contrast injection delineates the main pancreatic duct (b).

This kind of combined anomalous termination of the biliary-pancreatic ductal system in the stomach has not been reported previously. We can also rule out any other possible diagnoses such as fistula secondary to ulcer disease or choledocholithiasis, spontaneous or iatrogenic surgical fistula, and surgical choledochoenteric diversions in the present

case. The clinical implication of this anomaly is debatable. Although its association with prepyloric antral ulcer in this case is not clear, cholangitis and choledocholithiasis can be obviously related with this anomalous condition. Ectopic opening of the common bile duct in the stomach may not be a benign and incidental condition. Nevertheless, it could be a benign condition as was in our patient, who did not have any previous history compatible with pancreatitis or other pancreatic pathology. To prevent hazardous lesion of the biliary and pancreatic ducts during ulcer surgery and or bile duct explorations, we consider that awareness of these conditions should be important.

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