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Helicobacter pylori infection and gastroesophageal reflux disease - Barrett's esophagus sequence "dilemma"

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Regarding Zullo *et al*'s Hamletic dilemma [1], the authors claimed that the reasons why *Helicobacter pylori* (*Hp*) does not prevent gastroesophageal reflux disease (GERD) symptoms, though appears to prevent Barrett's esophagus (BE), remain unclear.

Concerning this conflicting scenario, upper gastrointestinal microbiota appear to be involved in GERD and BE pathophysiology; the occurrence of nitrate-reducing *Campylobacter* species in the esophagus of BE patients compared with controls without BE, may imply that there is a link with BE initiation, maintenance, or exacerbation [2,3]. *Hp* infection (*Hp*-I) may also be involved in GERD pathogenesis, at least in some ethnic populations, thereby predisposing for BE development, a long-standing GERD complication and well-recognized premalignant condition involved in gastroesophageal junction cancer, also mentioned by the authors [1], and esophageal adenocarcinoma development [2]. In this respect, contrary to expectations, ethnic Malays who have a long history of low *Hp*-I prevalence, GERD, BE and distal esophageal cancers are all of low incidence, suggesting that *Hp*-I is not protective against the aforementioned diseases; its absence is more likely to be beneficial [3]. Our data show that *Hp*-I is frequent in Greek GERD patients and its eradication leads to better control of GERD symptoms [4,5]; consistent associations are also reported by others [4]. The interplay between Hp and host factors holds an important role in GERD and BE pathogenesis; *Hp* could contribute to GERD and BE pathogenesis via several mechanisms including induction of several mediators, oncogenes and metabolic parameters (i.e., obesity, insulin resistance) mentioned previously [2-4]; for instance, *Hp*-induced gastrin is an oncogenic growth factor contributing to esophageal, gastric, and colon carcinogenesis [6,7]. Recent data indicate that both *Hp*-I and BE are associated with an increased risk of colorectal adenoma (CRA) and colorectal cancer (CRC) development, reflecting real relationship [8-10]; *Hp*-I seems to be involved in GERD-BE-EA and CRA-CRC sequences, at least in some subpopulations, and its eradication might inhibit these oncogenic properties [8-10].

References

1. Zullo A, Hassan C, De Francesco V, Manta R, Romiti A, Gatta L. *Helicobacter pylori* infection and gastroesophageal cancer: unveiling a Hamletic dilemma. *Ann Gastroenterol* 2014;**27:**291-293.
2. Kountouras J, Chatzopoulos D, Zavos C, et al. *Helicobacter pylori* infection might contribute to esophageal adenocarcinoma progress in subpopulations with gastroesophageal reflux disease and Barrett's esophagus. *Helicobacter* 2012;**17**:402-403.
3. Kountouras J, Stergiopoulos C, Zavos C. Obstructive sleep apnea and environmental contributors for Barrett's Esophagus. *Clin Gastroenterol Hepatol* 2014;**12:**1055-1056.
4. Kountouras J, Zavos C, Chatzopoulos D, Katsinelos P. *Helicobacter pylori* and gastro-oesophageal reflux disease. *Lancet* 2006;**368**:986.
5. Kountouras J, Chatzopoulos D, Zavos C. Eradication of *Helicobacter pylori* might halt the progress to oesophageal adenocarcinoma in patients with gastro-oesophageal reflux disease and Barrett's oesophagus. *Med Hypotheses* 2007;**68**:1174-1175.
6. Kyrgidis A, Kountouras J, Zavos C, Chatzopoulos D. New molecular concepts of Barrett's esophagus: clinical implications and biomarkers. *J Surg Res* 2005;**125**:189-212.
7. Kountouras J, Zavos C, Chatzopoulos D, Katsinelos P. New aspects of *Helicobacter pylori* infection involvement in gastric oncogenesis. *J Surg Res* 2008;**146**:149-158.
8. Kountouras J, Zavos C, Chatzopoulos D, et al. Letter: is *Helicobacter pylori* behind Barrett's oesophagus and colorectal neoplasms? *Aliment Pharmacol Ther* 2013;**37**:837.
9. Kapetanakis N, Kountouras J, Zavos C, et al. Association of *Helicobacter pylori* infection with colorectal cancer. *Immunogastroenterology* 2013;**2**:47-56.
10. Kountouras J, Kapetanakis N, Zavos C, Polyzos SA, Romiopoulos I. Active *Helicobacter pylori* infection on colorectal mucosa-adenomatous polyp-adenocarcinoma sequence. *Eur J Gastroenterol Hepatol* 2014;**26**:243-244.

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Desmoplastic small-round-cell rectal tumor

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A 22-year-old male presented with abdominal and back pain and significant weight loss. On examination he was cachectic with a large palpable mass arising from the pelvis. A digital rectal exam revealed an obstructed rectal mass 5 cms from the anal verge. A contrast-enhanced computed tomography (CT) scan of the abdomen revealed a rectal mass with peritoneal metastasis in the form of extensive pelvic deposits with surface liver deposits (Fig. 1 A-D). Rectal biopsy revealed nests of small round cells with

scanty cytoplasm, round to oval nuclei and visible mitotic figures, embedded in a desmoplastic stroma seen in the lamina propria and muscularis mucosa of the rectum. On immunohistochemistry, these cells were immunopositive for cytokeratins AE1/AE3 (focally positive) and desmin (strongly positive), while they were negative for leukocyte common antigen (LCA), synaptophysin, Wilm's tumour-1 protein (WT-1) and neuron-specific enolase (NSE). MIC2 protein showed dot-like positivity (Fig. 2 A-D). A diagnosis of desmoplastic small-round-cell rectal tumor was made. No cytogenetic analysis was performed. The patient had a poor general condition and did not opt for further treatment.

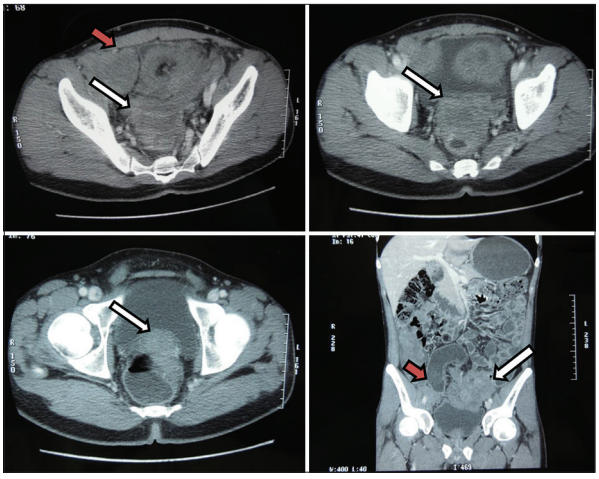

Figure 1 Pelvic sections of contrast-enhanced computed tomography scan of the abdomen and pelvis showing a low attenuation rectosigmoid upper rectal growth (white arrow) with peritoneal metastasis in the form of multiple, low attenuation soft tissue masses in the pelvis (red arrow) with surface liver deposits (section not shown)

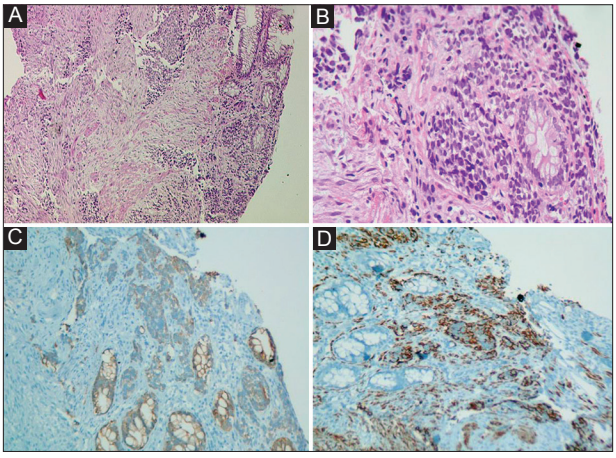

Figure 2 Histopathological examination of rectal biopsy showed malignant round cell tumor nests of small round cells with scanty cytoplasm, round to oval nuclei and visible mitotic figures, embedded in a desmoplastic stroma seen involving the lamina propria and muscularis mucosa of the rectum [A; H&E (40X) & B; H&E (200X)], intervening colonic mucosal glands are unremarkable. The tumor cells revealed weak and focal immune-positivity for cytokeratin [C; DAB (100X)] and strong immune-positivity for desmin [D;DAB (100X)]

Desmoplastic round-cell-tumor was first described as a pathological entity by Gerald and Rosai in 1989 [1]. It is a rare, highly aggressive tumor associated with poor prognosis, predominantly affecting young males. It is a sarcoma belonging to the family of "small round blue cell tumors" of the pediatric population [2]. It is associated with a unique chromosomal translocation t (11:22) (p 13; q 12) that involves the *EWSR1* and *WT1* genes.

This tumor is usually large and widespread at presentation and it is impossible to identify the organ of origin in many instances. Hence it is speculated that the tumor most probably arises from mesothelial cells explaining its occurrence in the peritoneum and occasionally in the pleura, lung, tunica vaginalis, sinus cavity and the posterior cranial fossa [5,6]. However, it has also been reported to arise from organs like the stomach, ovary, liver, pancreas, kidneys, bone etc. One report described a localized origin from the sigmoid [3]. In our reported case, the rectum was the organ of origin with metastasis to the peritoneal cavity.

CT scan aids in the diagnosis of these tumors by demonstrating multiple, bulky low attenuation soft tissue masses in the omentum or mesentery or peritoneum mostly without a distinct organ of origin. Histological analysis typically shows small round blue cells in nests separated by an abundant desmoplastic stroma. Immunohistochemistry demonstrates a polyphenotypic antigen expression profile and is positive for desmin, vimentin, smooth muscle actin, neuron specific enolase, cytokeratin and epithelial membrane antigen. Diagnosis can be confirmed by cytogenetic studies.

The combination of Ewing-sarcoma-based induction chemotherapy followed by aggressive surgical debulking and external beam radiotherapy has been recommended for the treatment of these tumors. The impact of intensive chemotherapy regimens and new techniques such as HIPEC or IMRT needs to be clearly defined [4,5].

This report highlights a rare pathological diagnosis of desmoplastic small-round-cell tumour of the rectum, never reported previously.

References

1. Gerald WL, Rosai J. Desmoplastic small cell tumour with divergent differentiation. *Paediatr Pathol* 1989;**9**:177-183.
2. Dorsey BV, Benjamin LE, Rauscher F, et al. Intraabdominal desmoplastic small round cell tumour: expansion of the pathologic profile. *Mod Pathol* 1996;**9**:703-709.
3. Kim K, Kim J, Kim I. Desmoplastic small round cell tumor of the sigmoid colon. *Korean J Pathology* 2001;**35**:451-454.
4. Schwarz RE, Gerald WL, Kushner BH, Coit DG, Brennan MF, La Quaglia MP. Desmoplastic small round cell tumors: prognostic indicators and results of surgical management. *Ann Surg Oncol* 1998;**5**:416-422.
5. Kushner BH, La Quaglia MP, Wollner N, et al. Desmoplastic small round-cell tumor: prolonged progression-free survival with aggressive multimodality therapy. *J Clin Oncol* 1996;**14**:1526-1531.

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Endoscopic variceal ligation in children with extrahepatic portal vein thrombosis: long-term follow up of 2 cases

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Endoscopic methods such as sclerotherapy and endoscopic variceal ligation (EVL) are considered highly effective in the treatment and prophylaxis of recurrent esophageal variceal bleeding. EVL is a treatment of option for preventing a first bleeding episode and for the treatment of acute and recurrent variceal bleeding in adult patients [1,2]. Limited data are available regarding this treatment option in children, although it is considered highly effective and is recommended by most pediatric experts [3]. We report our experience regarding two pediatric patients who suffered from extrahepatic portal vein obstruction (EHPVO).

The first case is a 3-year-old boy referred to our department for evaluation of hepatosplenomegaly noticed at the age of 7 months. The patient's physical examination was normal, while the laboratory investigation revealed thrombocytopenia and normal blood clotting tests. Portal vein catheterization confirmed the diagnosis of portal vein thrombosis (PVT). Due to esophageal varices grade I revealed by upper gastrointestinal (GI) endoscopy propranolol was commenced, and was discontinued one month later because of its adverse effects. All the esophageal varices (EV) were eradicated by EVL and no recurrence was observed upon repeated endoscopies over an 8-year follow-up period. The patient, now 11 years old, has not experienced episodes of GI bleeding but his liver function deteriorated. A recent magnetic resonance venogram (MRV) indicated cirrhosis.

The second case is a 6-year-old boy presented at our emergency department with hematemesis and hypovolemic shock. On clinical examination the child's spleen was palpable 3 cm below the left costal margin. After resuscitation, the patient underwent an upper GI endoscopy revealing grade II gastroesophageal varices. PVT was confirmed by MRV, with normal blood clotting tests. The patient underwent 3 successive EVL sessions until variceal obliteration was achieved. In ultrasonography 7 years later the liver appeared cirrhotic. The liver synthetic function has been well preserved and the endoscopy of the gastroesophageal junction revealed normal findings during the follow up.

Pharmacologic therapy, endoscopic methods and surgical portosystemic shunting have been used to treat EV in patients with PVT. Data on long-term efficacy and safety of these methods in children are scarce deriving mainly from case series [4,5]. β-Adrenergic blockers in adults are not routinely used in children because of unproven efficacy and significant adverse effects [6]. The main advantages of EVL over sclerotherapy are the need for fewer endoscopic sessions and lower complication and relapse rates [7]. Zargar *et al* showed that in children treated for bleeding EV, bleeding and major complication rates in the sclerotherapy group were significantly higher [8]. There is currently insufficient evidence to support a role of EVL for primary prevention in children [9].

In conclusion, our two cases indicate that EVL for primary or secondary prophylaxis of variceal bleeding in children with EHPVO is well tolerated, effective, reduces morbidity, and improves quality of life in the long-term follow up. A concern in children with EHPVO is the development of cirrhosis long-term, as in our cases, thus future studies are warranted to establish prognosis after EVL application in these patients.

References

1. Sarin SK, Agarwal SR. Extrahepatic portal vein obstruction. *Semin Liver Dis* 2002;**22**:43-58.
2. Sarin SK, Sollano JD, Chawla YK, et al. Consensus on extra-hepatic portal vein obstruction. *Liver Int* 2006;**26**:512-519.
3. Giouleme O, Theocharidou E. Management of portal hypertension in children with portal vein thrombosis. *JPGN* 2013;**57**:419-425.
4. Celińska-Cedro D, Teisseyre M, Woynarowski M, Socha P, Socha J, Ryzko J. Endoscopic ligation of esophageal varices for prophylaxis of first bleeding in children and adolescents with portalhypertension: preliminary results of a prospective study. *J Pediatr Surg* 2003;**38**:1008-1011.
5. Gürakan F, Eren M, Koçak N, et al. Extrahepatic portal vein thrombosis in children: etiology and long-term follow-up. *J Clin Gastroenterol* 2004;**38**:368-372.
6. Ling SC. Should children with esophageal varices receive beta-blockers for the primary prevention of variceal hemorrhage? *Can J Gastroenterol* 2005;**19**:661-666.
7. Abd El-Hamid N, Taylor RM, et al. Aetiology and management of extrahepatic portal vein obstruction in children: King's College Hospital experience. *J Pediatr Gastroenterol Nutr* 2008;**47**:630-634.
8. Zargar SA, Javid G, Khan BA, et al. Endoscopic ligation compared with sclerotherapy for bleeding esophageal varices in children with extrahepatic portal venous obstruction. *Hepatology* 2002;**36**:666-672.
9. Shneider BL, Bosch J, de Franchis R, et al. Portal hypertension in children: expert pediatric opinion on the report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *Pediatr Transplant* 2012;**16**:426-437.

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Unexpected drainage of pancreatic pseudocyst through the common bile duct

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We herein report the unexpected spontaneous communication of a pancreatic pseudocyst (PP) with the common bile duct (CBD) detected during endoscopic retrograde cholangiopancreatography (ERCP) in a 56-year-old female patient. Complete cyst drainage was achieved after endoscopic sphincterotomy and CBD stent placement.

A 56-year-old woman hospitalized elsewhere with a 4-week history of acute gallstone pancreatitis was transferred to our hospital due to fever, worsening abdominal pain, progressive jaundice, nausea, and vomiting. Physical examination revealed fever, tachycardia, and signs of peritoneal irritation.

Abnormal laboratory findings included hemoglobin of 7.9 g/dL, leukocyte count of 11.5 K/μL (78% neutrophils), C-reactive protein of 115 mg/L, alkaline phosphatase of 435 U/L, γ-glutamyl transferase of 457.0 U/L, total bilirubin of 4.66 mg/dL (90% direct), and amylase of 252 U/L.

Abdominal computed tomography (CT) showed a pseudocyst sized 11 cm x 7 cm x 8.6 cm along the proximal pancreatic body and a dilated to 12 mm CBD containing a 6 mm stone.

Following initial conservative management, an ERCP was performed 7 days after admission and CBD opacification revealed a leak between the CBD and a neighboring cavity. Sphicterotomy was performed, followed by stone extraction and placement of a plastic CBD stent sized 10 Fr x 7 cm. Whitish semitransparent liquid came out from the ampulla of Vater, indicating transpapillary PP drainage.

Following ERCP, patient's symptoms subsided and laboratory tests improved significantly. Abdominal CT scan 5 weeks postoperatively revealed a markedly shrunk pseudocyst.

One month later the patient was asymptomatic and had no laboratory abnormalities. Stent removal with ERCP was performed and subsequent opacification of the CBD disclosed no contrast leak.

We herein present for the first time the spontaneous drainage of a PP in the CBD that was evident during ERCP, without previous imaging documentation of PP leak to the CBD. Our hypothesis is that the close contact of the CBD with the large PP led to the erosion of the former, due to an inflammatory process triggered by the rich in proteolytic enzymes pseudocyst fluid. This resulted in the acute rupture of the PP into the CBD. An alternative hypothesis is that maneuvering during ERCP might have caused the acute rupture of the PP into the CBD.

Literature reveals only 21 cases of PP with fistula to the CBD. Sixteen have been reviewed by Ali *et al* [1], while there are also 2 published in Japanese and 1 in French with inaccessible content [2-4]. Regarding the 18 cases published in English [1,5], all but one patient suffered from either acute or chronic alcoholic pancreatitis. Management is reported in 17 patients (15 male) [1,5]. In detail, 9 patients were treated surgically, 3 with percutaneous external drainage, 1 with expectant observation, while 4 patients underwent endoscopic biliary stenting similar to our case.

In conclusion, we report the first case of PP rupture in the CBD in a woman with non-alcoholic acute pancreatitis. Diagnosis and treatment were accomplished during ERCP, since previous imaging was of no diagnostic value and no further intervention was warranted.

References

1. Al Ali JA, Chung H, Munk PL, Byrne MF. Pancreatic pseudocyst with fistula to the common bile duct resolved by combined biliary and pancreatic stenting - a case report and literature review. *Can J Gastroenterol* 2009;**23**:557-559.
2. Doi T, Wakabayashi N, Iwai N, et al. Pancreatic pseudocyst with fistula to the common bile duct and the duodenum. *Nihon Shokakibyo Gakkai Zasshi* 2013;**110:**1288-1295.
3. Miyanishi K, Watanabe H, Hayashi S, et al. Spontaneous internal drainage of pancreatic pseudocyst with fistula to the common bile duct. *Nihon Shokakibyo Gakkai Zasshi* 2000;**97**:213-217.
4. Chapuis Y, Liguory C, Bonnette P, Rossat-Mignod JC, Launois B. Cure of an external biliary fistula complicating pancreatic pseudocyst by an endocholedochal prosthesis. *J Chir (Paris)*1986;**123**:35-38.
5. Rickes S, Monkemuller K, Peitz U, et al. Sonographic diagnosis and endoscopic therapy of a biliopancreatic fistula complicating a pancreatic pseudocyst. *Scand J Gastroenterol* 2006;**41**:989-992.

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