

Case report of intestinal non-rotation, heterotaxy, and polysplenia in a patient with pancreatic cancer

Spyridon Pagkratis, MD^a, Sara Kryeziu, MD^a, Miranda Lin, BS^a, Samah Hoque, BA^a, Juan Carlos Bucobo, MD^b, Jonathan M. Buscaglia, MD^b, Georgios V. Georgakis, MD, PhD^a, Aaron R. Sasson, MD^a, Joseph Kim, MD^{a,*}

Abstract

Rationale: Heterotaxy with polysplenia is an extremely rare congenital condition resulting from abnormal arrangement of organs in the abdominal and thoracic cavities during embryologic development. When a malignancy such as pancreatic cancer develops under these conditions, surgical resection becomes particularly complex. This case report demonstrates successful pancreatic cancer resection despite the patient's complicated anatomy.

Patient concerns: An 82-year-old female presented to our institution with complaints of mild right upper quadrant pain radiating to the mid-epigastric region.

Diagnoses: Physical examination revealed jaundice with scleral icterus consistent with obstructive jaundice. Radiographic imaging revealed hepatic duct dilation with several anatomic anomalies including small bowel location in the right upper abdomen, cecum, and appendix in the left lower quadrant, reversed superior mesenteric artery and superior mesenteric vein positions, and right-sided duodenal-jejunal flexure as well as an entirely right-sided pancreas, and left lower pelvis with ≥ 6 separate splenules. These findings resulted in a diagnosis of heterotaxy syndrome with polysplenia.

Interventions: Careful preoperative planning and total pancreatectomy was performed without complication.

Outcomes: The patient recovered well. Pathologic examination of the pancreatic mass revealed moderately/poorly differentiated invasive pancreatic duct adenocarcinoma. The patient remains alive and well without signs of recurrent disease at the 2-year follow-up.

Lessons: Given the wide range of anatomical variants observed in patients with heterotaxy syndrome, a thorough radiologic assessment is necessary before engaging in any surgical procedure. In our case, preoperative identification of the various anatomic anomalies, such as the short and vertically oriented pancreas, the porta hepatis position anterior to the duodenum, the nonrotation of the intestines and the anomalous origin of the right hepatic artery allowed us to perform a safe and uncomplicated total pancreatectomy.

Abbreviations: CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatogram, IVC = inferior vena cava, POD = post-operative day, SMA = superior mesenteric artery, SMV = superior mesenteric vein.

Keywords: heterotaxy, pancreatic cancer, polysplenia

Editor: Hisashi Oshiro.

SP and JK contributed to the conception/design of the work; SP, and SK contributed to the acquisition of data; SP, SK, JCB, JMB, GG, and AS contributed to the analysis/interpretation of data; SP, ML, and SH drafted the manuscript; all authors critically revised the manuscript for intellectual content; all authors approved the final version submitted and agree to be accountable for all aspects of the work.

Informed consent was obtained from the patient and publication.

All data were available for editorial review.

The authors report no conflicts of interest.

^a Department of Surgery, ^b Department of Gastroenterology, SUNY Stony Brook, Stony Brook, NY.

* Correspondence: Joseph Kim, MD, Associate Professor of Surgery, Stony Brook University Hospital, HSC, Level 18 Rm065, Stony Brook, NY 11794 (e-mail: joseph.kim1@stonybrookmedicine.edu).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

Medicine (2017) 96:49(e8599)

Received: 26 July 2017 / Received in final form: 13 October 2017 / Accepted: 16 October 2017

<http://dx.doi.org/10.1097/MD.0000000000008599>

1. Introduction

During normal embryologic development, the midgut rearranges into the umbilical stalk and then reenters the abdominal cavity. In rare cases, the intestines fail to return to the abdominal cavity, resulting in abnormal arrangement of the abdominal and thoracic organs. This condition is called intestinal nonrotation and presents a challenge when treating malignancies such as pancreatic adenocarcinoma. In our case, detailed radiologic assessment of the anatomic anomalies before surgery allowed for successful total pancreatectomy.

2. Case presentation

An 82-year-old female with medical history significant for major depressive disorder, gastroesophageal reflux disease, and thalassemia minor presented to our institution with complaints of mild right upper quadrant pain radiating to the mid-epigastric region for 1 week. She had noticed for several days that her urine was dark, stool pale, and skin yellow. Her family members noted during the past 3 months she had decreased appetite with 20-pound weight loss. Laboratory tests revealed total bilirubin of 9.2, alkaline phosphatase of 152, aspartate aminotransferase

of 33, alanine aminotransferase of 42, and lipase of 2000. As her symptoms and bloodwork were consistent with obstructive jaundice and suggestive of acute pancreatitis, she was admitted for further work-up and treatment.

Physical examination revealed jaundice with scleral icterus and right upper quadrant discomfort on palpation. An abdominal ultrasound was performed demonstrating dilated intra- and extrahepatic ducts, distended gallbladder, and absence of cholelithiasis. Computed tomography (CT) scan was then performed showing several noteworthy findings (Figs. 1–4), including small bowel location in the right upper abdomen, cecum and appendix in the left lower quadrant, superior mesenteric artery (SMA) to the right of the superior mesenteric vein (SMV), and right-sided duodenal-jejunal flexure (i.e., ligament of Treitz). These findings were consistent with nonrotation of the midgut structures during embryologic development, where only 90 degrees of the innate 270-degree counterclockwise rotation occurs. In addition to these nonrotation anomalies, CT scan demonstrated extrahepatic biliary dilation with abrupt termination in the vertically oriented, entirely right-sided pancreas, which harbored a 2.7×2.1 cm mass that constricted the adjacent duodenum. CT scan also showed the inferior vena cava (IVC) had azygos-type configuration with interruption above the renal veins in an intrahepatic location and polysplenia from the left hemi-diaphragm to the left lower pelvis with ≥ 6 separate splenules. Altogether, the combination of nonrotation of the small intestine and colon, abnormal orientation and position of the pancreas, anomalous configuration of the IVC, and polysplenia resulted in a diagnosis of heterotaxy syndrome with polysplenia, an extremely rare congenital condition resulting from abnormal arrangement of organs in abdominal and thoracic cavities during embryologic development. These anatomic anomalies were discussed with the

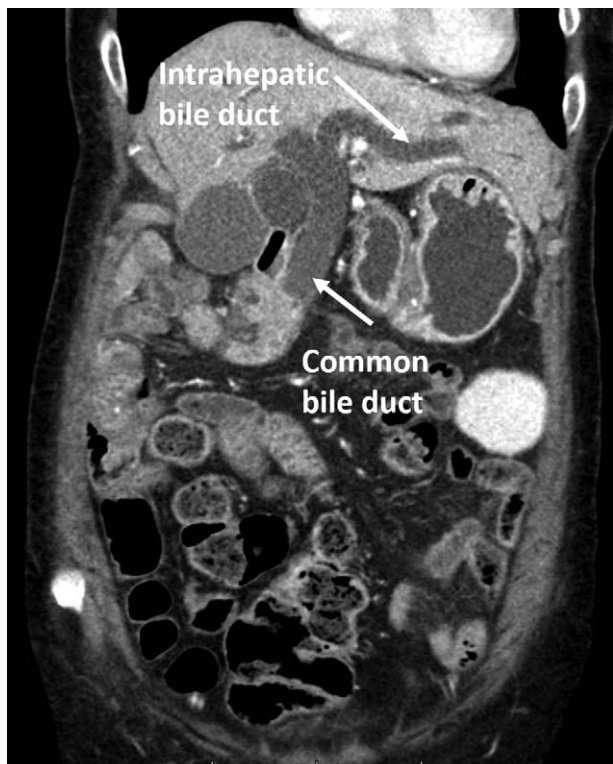


Figure 1. CT in coronal view with dilated intra and extra hepatic bile ducts.

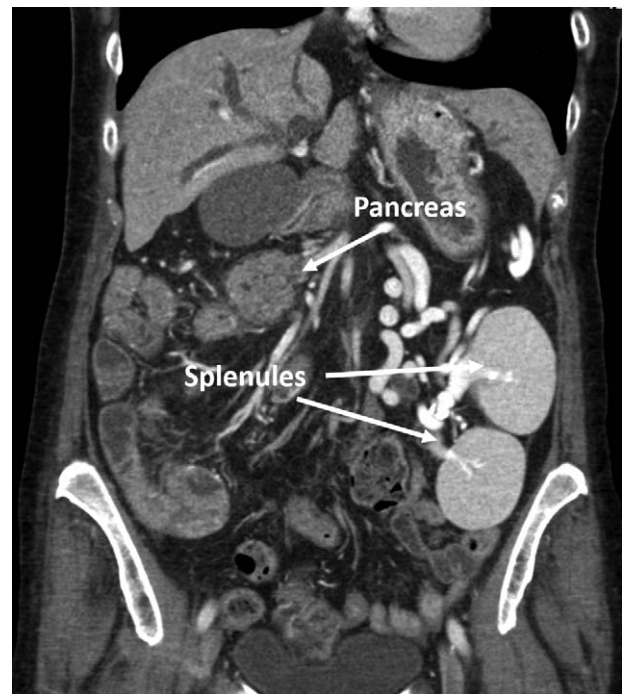


Figure 2. Pancreatic mass (arrow) and 2 of the splenules in the left side of the abdomen.

patient, who indicated knowledge of having “many spleens,” but she was unaware of the other findings.

The gastroenterology service was consulted, and endoscopic ultrasound and endoscopic retrograde cholangiopancreatogram (ERCP) were attempted. Abnormal anatomy did not permit safe cannulation of the ampulla of Vater, which was located on the right half of the duodenum. Furthermore, because of the anomalous location of the gastric antrum and duodenum (i.e., posterior to the porta hepatis) and malrotated pancreas, a fine-needle aspiration could not be performed. Therefore, percutaneous transhepatic cholangi catheter was placed for biliary decompression and fluoroscopic mapping of the biliary tree did not reveal gross anatomic aberrancies. The patient was then referred to the surgical oncology service for consideration of

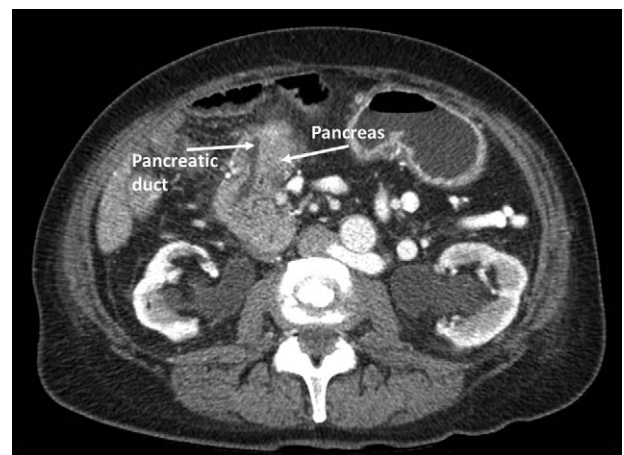


Figure 3. Short and vertically oriented pancreas with dilated pancreatic duct.

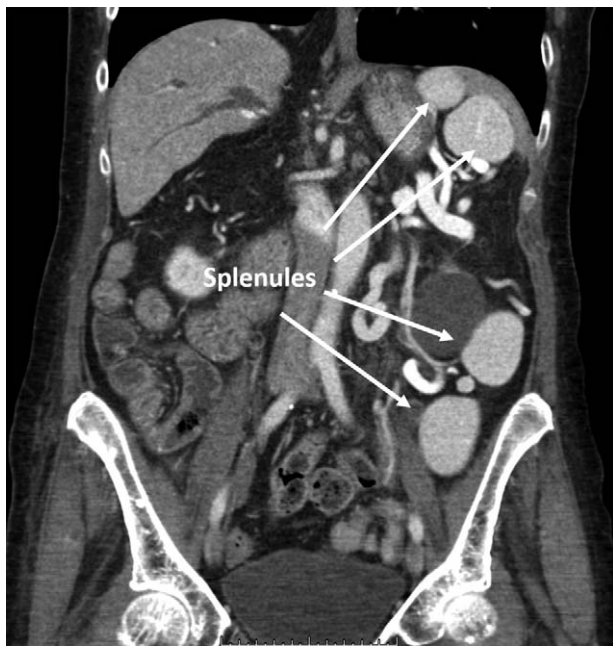


Figure 4. Multiple splenules (arrows) identified in the left side of the abdomen.

resection. As the radiographic imaging studies did not reveal evidence of metastatic disease, the patient was considered a candidate for curative intent resection of the pancreatic mass.

As heterotaxy syndrome can occur with various congenital cardiac anomalies (e.g., dextrocardia, single atrium or ventricle, atrial and ventricular septal defects, transposition of the great vessels, among others), an echocardiogram was obtained but did not reveal pathologic or anomalous findings. Secondary to the complex anatomic findings, the potential need for total pancreatectomy was discussed with the patient and preoperative endocrine consultation was obtained. Following medical clearance and resolution of the mild acute pancreatitis, the patient was taken to the operating room.

Surgical exploration confirmed that the SMA was to the right of the SMV, the duodenum was posterior to the porta hepatis, and the appendix was in the left lower quadrant (Figs. 5–8). The

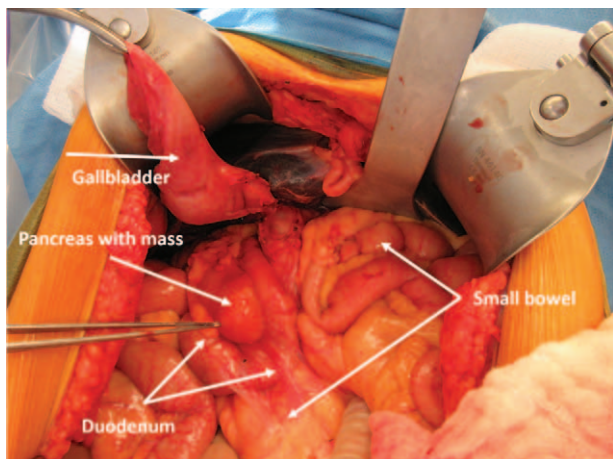


Figure 5. Intraoperative picture with pancreatic mass, duodenum, gallbladder, and small bowel identified.

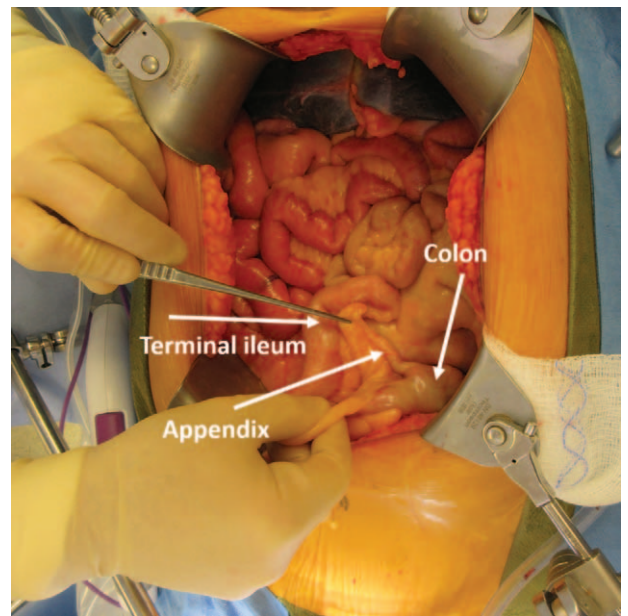


Figure 6. Intraoperative picture identifying the appendix in the left lower quadrant and the colon in the pelvis.

pancreatic mass was palpable in the most superior (i.e., cephalad) portion of the pancreatic gland and pancreatic parenchyma was not preserved because of small future remnant size and suboptimal reconstruction options. As such, after appendectomy and cholecystectomy, portal lymph node dissection was undertaken to fully delineate portal structures, followed by antrectomy, duodenectomy, and total pancreatectomy. For reconstruction, single-layer hepaticojejunostomy and double-layered gastrojejunostomy were performed. The procedure was without complication and the patient recovered in the surgical intensive care unit with continuous intravenous insulin administration. The postoperative course was unremarkable with return of bowel function on the fourth postoperative day (POD) and resumption of solid diet on POD#5. Final pathologic examination revealed a 2.7 × 2.0 × 1.5 cm, moderately/poorly differentiated invasive pancreatic duct adenocarcinoma with 4 of 13 lymph nodes harboring metastatic disease for final pathologic stage of pT3N1M0.

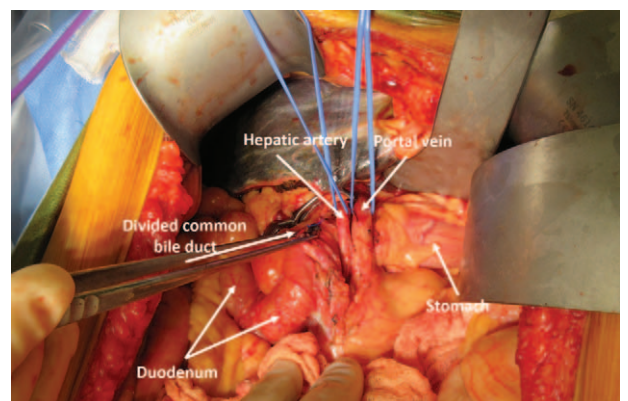


Figure 7. Intraoperative picture with portal vein, hepatic artery, bile duct, stomach, and duodenum identified.

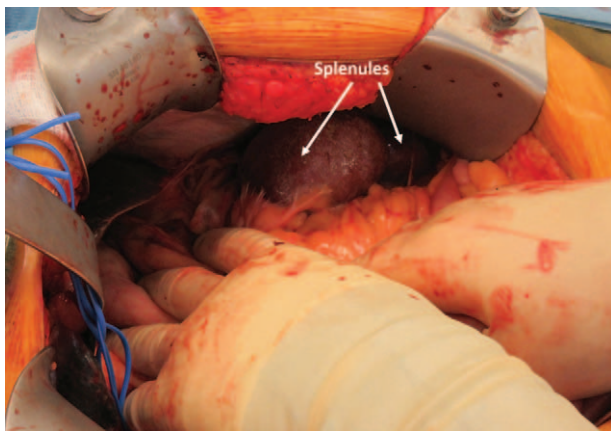


Figure 8. Intraoperative picture with 2 of the splenules.

3. Discussion

Surgery for cancers of the pancreatic gland is technically challenging, requiring a carefully coordinated sequence of steps around major vascular structures. For conventional cancers of the pancreatic head, the authors follow a clockwise series of steps. However, this routine could not be followed in this patient because of the numerous anatomic anomalies. To perform safe pancreatic resection, we used a carefully scripted series of steps that was specifically designed for this patient to avoid major vascular injury and to safely remove the pancreatic tumor. The complexity of total pancreatectomy was magnified by the presence of a short, right-sided and vertically oriented pancreas, reversed SMA and SMV positions, and portal hepatis located anterior to the duodenum. Although previous cases of pancreaticoduodenectomy with intestinal malrotation have been reported,^[1–4] there is no report of pancreatectomy in patients with intestinal nonrotation and heterotaxy syndrome.

During the 6th week of fetal life in normal embryologic development, the midgut herniates into the umbilical stalk and also undergoes a 90-degree counterclockwise rotation around the SMA. During the 10th week, the midgut returns to the abdomen and completes an additional 180-degree counterclockwise rotation. Malrotation refers to the failure of the midgut to complete the 270-degree counterclockwise rotation around the SMA, a process that can be halted at any stage, with nonrotation being one of the possible outcomes. In nonrotation, the first 90-degree counterclockwise rotation is completed; however, there is no further rotation once the midgut returns to the abdominal cavity, resulting in small bowel on the right and colon to the left of the midline.^[5]

In addition to nonrotation, our patient had findings consistent with heterotaxy, which in Greek literally translates to different arrangement in space. It is a congenital condition that occurs from failure of the intra-abdominal and intrathoracic organs to rotate correctly during embryologic development, resulting in abnormal arrangement of the organs across the left-right axis of the body. The incidence of heterotaxy may be underestimated as individuals can be asymptomatic throughout their lifetime, but it is estimated that 1 in 2500 people may have heterotaxy with polysplenia syndrome.^[6] The exact cause of heterotaxy is unknown, but its etiology may be related to multiple gene mutations. Some of these genes are responsible for transcription factors that regulate development (e.g., FOXA2)

and metalloproteinases that are required for normal left-right asymmetry (i.e., MMP21).^[7,8]

The presence and severity of the anomalies observed in patients with heterotaxy depend on the presence of either left or right isomerism. Right isomerism is consistent with asplenia, bilateral trilobed lungs, and occasionally severe cardiovascular anomalies, whereas left isomerism is associated with polysplenia, bilateral bilobed lungs, pancreatic anomalies, and mild heart disease.^[9] The cardiac anomalies in right-sided isomerism are more common and more severe than with left-sided isomerism.^[9] Furthermore, the presence of cardiac lesions makes the patient susceptible to the development of congestive heart failure, so patients with right isomerism and asplenia have decreased survival compared to patients with left isomerism and polysplenia. For our patient, the presence of multiple spleens and echocardiogram showing no cardiac lesions of congestive heart failure indicated left isomerism.

Many patients with left isomerism suffer from gastrointestinal complications including gallstones and pancreatitis related to abnormal bowel rotation and dorsal agenesis of the pancreas.^[5] Dorsal pancreatic agenesis may lead to the development of pancreatitis as there is poor drainage from the remnant ventral duct. It can be distinguished from a short pancreas, a finding that is caused by fat replacement of the distal pancreas typically diagnosed with ERCP or magnetic resonance cholangiopancreatography.^[10] Our patient was unable to be cannulated during ERCP so it was not possible to differentiate between dorsal agenesis and a short pancreas. However, the patient's pancreas was short and vertically oriented, requiring total pancreatectomy. In previous reports of pancreaticoduodenectomy in a patient with nonrotation, total pancreatectomy was not required because of normal pancreatic anatomy.^[11] Additional pancreatic anomalies may include pancreatic malrotation, annular pancreas, and pancreas divisum.^[9]

Before engaging in a major or complex operative procedure, it is critical to understand that heterotaxy and intestinal nonrotation syndromes are also associated with various vascular and venous anomalies, aside from variations in the positioning of the organs across the left-right axis of the body. The most common vascular variants found in nonrotation involve the inversion of the mesenteric artery and vein, in which case the artery is positioned to the right of the vein.^[11] Additionally, the hepatic artery originating from the SMA has been reported in multiple cases.^[4,12,13] Suprarenal IVC interruption with azygos continuation, as observed in our patient, is also a common abnormality.^[14] The presence of a preduodenal portal vein is associated with polysplenia. This anomaly involves the portal vein coursing anterior to the duodenum and occurs when the vitelline veins lose their cranial and middle anastomoses as opposed to their caudal and cranial anastomoses during normal development.^[7] These vascular and venous anomalies should be identified during preoperative imaging as they may lead to intraoperative complications if they are left undetected and unintentionally injured.

4. Conclusion

Heterotaxy syndromes may involve numerous anatomical abnormalities encompassing multiple organ systems and may complicate any surgical intervention. Therefore, understanding and cataloguing the anatomic aberrancies was paramount to undergoing successful resection of pancreatic adenocarcinoma in our patient. Preoperative preparation and medical clearance

should entail a thorough cardiopulmonary evaluation as there can be cardiac and pulmonary complications. Congenital pancreatic anomalies in heterotaxic syndromes may pose difficulties during standard evaluation of a pancreatic adenocarcinoma and dorsal pancreatic agenesis or a short pancreas may require a total pancreatectomy instead of a pancreaticoduodenectomy. Given the wide range of anatomical variants that may be observed in patients with heterotaxy syndrome, a thorough radiologic assessment is warranted to ensure familiarity with the anatomical landmarks and vasculature before engaging in any surgical procedure. In our case, pre-operative identification of the various anatomic anomalies, such as the short and vertically oriented pancreas, the porta hepatis position anterior to the duodenum, the nonrotation of the intestines and the anomalous origin of the right hepatic artery allowed us to perform a safe and uncomplicated total pancreatectomy.

References

- [1] Jagannath P, Albuquerque K, de Souza LJ, et al. Reversed rotation of midgut which caused problems during Whipple's procedure. *Eur J Surg* 1995;161:765–6.
- [2] Daniels BT, Clader DN, Luter PW, et al. Pancreatico-duodenectomy in incomplete bowel rotation, anatomical peculiarities. *Rocky Mt Med J* 1957;54:445–7.
- [3] Meyer J, Rossetti A, Scheffler M, et al. Ampullectomy for an unexpected ampullary hamartoma in a heterotaxic patient. *Int J Surg Case Rep* 2013;4:544–6.
- [4] Hayashi T, Takano S, Kimura F, et al. [A case of cholangiocarcinoma with hepatomesenteric trunk and intestinal malrotation treated with pancreaticoduodenectomy]. *Gan To Kagaku Ryoho* 2010;37:2723–5.
- [5] Gupta AC, Herts B. Heterotaxia with Polysplenia. *J Urol* 2015;194:801–2.
- [6] Low JP, Williams D, Chaganti JR. Polysplenia syndrome with agenesis of the dorsal pancreas and preduodenal portal vein presenting with obstructive jaundice—a case report and literature review. *Br J Radiol* 2011;841007:e217–220.
- [7] Perles Z, Moon S, Ta-Shma A, et al. A human laterality disorder caused by a homozygous deleterious mutation in MMP21. *J Med Genet* 2015;52:840–7.
- [8] Li Y, Yagi H, Onuoha EO, et al. DNAH6 and Its Interactions with PCD Genes in Heterotaxy and Primary Ciliary Dyskinesia. *PLoS Genet* 2016;12:e1005821.
- [9] Rameshbabu CS, Gupta KK, Qasim M, et al. Heterotaxy polysplenia syndrome in an adult with unique vascular anomalies: case report with review of literature. *J Radiol Case Rep* 2015;9:22–37.
- [10] Kapa S, Gleeson FC, Vege SS. Dorsal pancreas agenesis and polysplenia/heterotaxy syndrome: a novel association with aortic coarctation and a review of the literature. *JOP* 2007;8:433–7.
- [11] Plackett TP, Takamori R, Izawa M. Pancreaticoduodenectomy in the setting of intestinal malrotation. *Hawaii Med J* 2011;70:237–8.
- [12] Mateo R, Stapfer M, Singh G, et al. Pancreaticoduodenectomy in adults with congenital intestinal rotation disorders. *Pancreas* 2005;31:413–5.
- [13] Nakano H, Kikuchi K, Seta S, et al. A patient undergoing pancreaticoduodenectomy in whom involved common hepatic artery anomalously arising from the superior mesenteric artery was removed and reconstructed. *Hepatogastroenterology* 2005;52:1883–5.
- [14] Tawfik AM, Batouty NM, Zaky MM, et al. Polysplenia syndrome: a review of the relationship with viscerotaxial situs and the spectrum of extra-cardiac anomalies. *Surg Radiol Anat* 2013;35:647–53.