Pancreas divisum : an unusual cause of recurrent acute pancreatitis in a child

Khalsi.F [1], BenIsmail.T [1], Trabelsi.I [1], Brini.I [1], Louati.H [2], Hamouda.S [1], Boussetta.K [1]

[1] Pediatrics Department B, Children's Hospital of Tunis
[2] Radiolgy Department, Children's Hospital of Tunis
Medecine Faculty of Tunis, University Tunis El Manar

ABSTRACT

The prevalence of Pancreas Divisum ranges from 5-14% in the general population. Divisum is considered a potential cause of recurrent acute pancreatitis (RAP) due to decreased flow of secretions through a stenotic minor papilla. Therapy includes different endoscopic and surgical procedures. Patients with this condition are usually asymptomatic, however, 25-38% of these patients experience recurrent pancreatitis that may further progress to chronic pancreatitis. This case is of a 10-year-old child presenting with abdominal pain in the left and right upper quadrants of the abdomen with a significant history of recurrent pancreatitis since the age of nine. The patient was examined with computed tomography (CT), which identified pancreatitis. Further magnetic resonance cholangiopancreatography (MRCP) assisted in the diagnosis of a type III pancreatic divisum, given the remnant of short communication between the dorsal and ventral duct..

INTRODUCTION & DEFINITIONS :

Acute pancreatitis (AP) was diagnosed when at least two of three criteria were fulfilled; (1) abdominal pain suggestive of AP, (2) serum amylase and/or lipase activity at least 3 times greater than the upper limit of normal and (3) imaging findings characteristic of, or compatible with AP. [1] RAP was defined as two or more distinct episodes of acute pancreatitis (AP) along with complete resolution of pain (≥1-month pain free interval between the diagnosis of AP) or complete normalization of serum pancreatic enzyme levels along with complete resolution of pain irrespective of specific time interval between AP episodes. [1] Approximately 10% to 20% of RAP occurs in pediatrics with idiopathic and structural etiologies in most of the cases [2,3]. Through a case of a 10-year-old girl who presented RAP secondary to pancreas divisum we discuss diagnostic, treatment and management of this pathology.

CASE REPORT:

A 10-year-old girl presented with **abdominal pain** and **vomiting** to the Pediatrics B Department B of Children's Hospital of Tunis. She underwent surgery for acute appendicitis at the age of seven. The pathological examination of the appendix was normal. She was admitted to the surgery department with acute abdominal pain.

She had no history of trauma, drug intake, infection or systemic disease. Family history was also unremarkable.

She described the pain as sharp, stabbing of 9/10 on severity scale. It was radiating to the back, to the left inferior angle of the scapula. She mentioned that she has experienced this type of pain before, but it has been 12 months since her last episode. Her vitals were as follow: blood pressure of 102/70 mmHg, heart rate of 81 bpm, 96% oxygen saturation, and a temperature of 37.2°C .

Auteur correspondant :
Fatma Khalsi,
E-mail : Khalsif@gmail.com

Patient weighed 29 kg with a BMI of 17. On abdominal examination, her abdomen was soft, and non-distended. She had a negative Murphy sign. Her labs were consistent with elevated lipase and amylase. DeBanto score was zero. Serology for pancreatitis-associated viruses (the mumps virus, EBV, CMV, mycoplasma pneumonia), cystic fibrosis sweat test and antinuclear antibodies were negative.

Screening for CFTR, PRSS1 and SPINK1 mutations was also negative. Ultrasound examinations revealed a swollen pancreas; a moniliform dilation of Wirsung and visualization of a dilated duct with anechoic content, which gets into the Wirsung shortly after its origin with densification of peripancreatic cephalic fat and a small fluid collection, measuring 19 mm in maximum diameter of the lesser omental sac.

Computed tomography examination showed a moderately swollen pancreas with dense peripancreatic fat with necrosis of the lesser omental sac, the root of the mesentery and surrounding the tail of the pancreas; a dilated Wirsung and Santorini duct. Acute pancreatitis stage E of Balthazar (score of 4) without parenchymal necrosis.

We suggested magnetic resonance cholangiopancreatography (MRCP) radiological analysis for the patient which displayed a dilated pancreatic head with a maximal diameter of 6-mm. The MRCP findings demonstrated a small amount of fluid between the pancreatic head and proximal descending duodenum, as well as the posterior border of the liver and diaphragm consistent with pancreatitis. The MRCP also showed evidence of a small remnant communication between the dorsal duct (which becomes the main source of drainage in pancreatic divisum) and the ventral duct leading to the crossing duct sign .

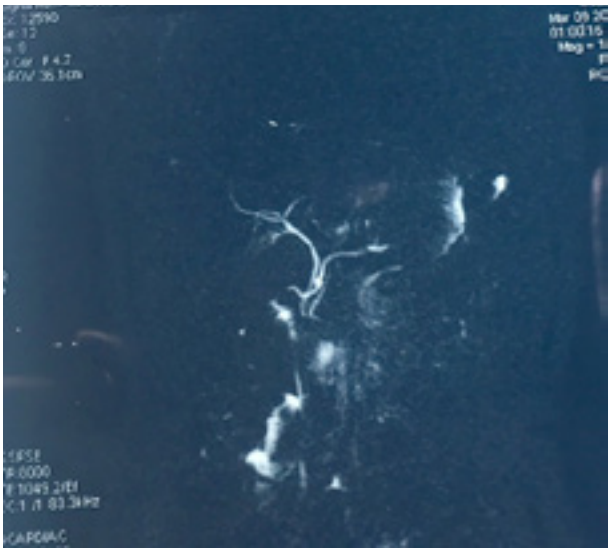

FIGURE 1 : MRCP (magnetic resonance cholangiopancreatography) showing the crossing duct sign

The patient was restricted for oral feeding and put under continuous intravenous infusion and analgesic treatment; then progressive feeding with a fat-free diet. The outcome was favorable, and the patient was discharged within 10 days of hospital

DISCUSSION:

Anatomy and epidemiology:

Pancreas divisum is the most common congenital ductal anomaly of the pancreas [4]. It was first described by Joseph Hyrtl in 1866. [5] its prevalence is estimated at 2.7% to 22%. [6-8]. The frequency of PD is approximately 5% to 10% in autopsy series [9] and 2,9% (range 0.5% to 17,6 %) in ERCP studies [8].

The dorsal and ventral pancreatic buds of the foregut fail to fuse during the 7th week of intrauterine life and results in pancreas divisum, in which the duct of Wirsung drains the minor part of the pancreas, that is, ventral pancreas through the major papilla, whereas the dominant duct of Santorini drains the major part of the pancreas, that is, the dorsal pancreas, through the minor papilla.

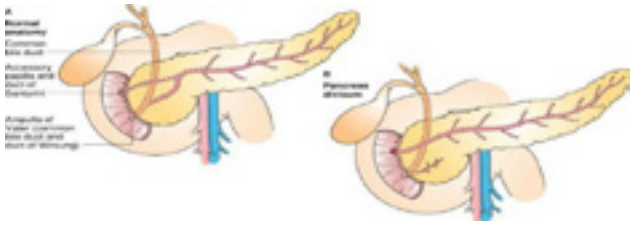

FIGURE 2 : **A** : normal pancreas;

B : Pancreas Divisum

Only a minority (<5%) of patients with PD become symptomatic with RAP. [4, 12] The clinical significance of PD remains controversial.

Clinical presentation of AP :

In pediatric studies of AP, 80% to 95% of patients presented with abdominal pain. the epigastric region is the most common location of pain. But diffuse abdominal pain is possible (12% to 20% of patients). [13] Our case corroborates this finding since she was admitted for diffuse abdominal pain and she underwent wrongly surgery (appendectomy with normal pathological examination). The second most common symptom was nausea or vomiting (40% to 80% of patients). Other symptoms included fever, jaundice, ascites, and pleural effusion. [13]

Diagnosis of severity of AP :

Severity scores are used to predict the outcome of acute pancreatitis (AP). Several scores are used in adult patients. In pediatrics, DeBanto et al [14] created the pediatric acute pancreatitis severity (PAPS) scoring system for use in children in 2002.

Then, several literature studies have followed and demonstrated the low sensitivity of clinical scores (the Ranson, modified Glasgow, and DeBanto scores) (approximately 50%) [15-18] the modified Ministry of Health, Labour and Welfare of Japan (JPN) scoring system was validated in 2017 and had advantages over the other clinical scoring systems for risk stratifying these children (sensitivity: 83,3% vs 50%; specificity: 98,4%). Other studies have demonstrated the superiority of the Balthazar computed tomography severity index CTSI to clinical scoring systems for identifying children with acute pancreatitis at risk for developing serious complications. [15, 19]

Imputability of PD in RAP :

The involvement of pancreas divisum in the occurrence of AP or CP has been a subject of controversy for many years. Some studies have shown an association between PD and RAP [20-24] while others do not. The physiopathological hypothesis is that the size of the minor papilla is too small to properly drain the secretions of the entire pancreatic gland, and that this could be causing a functional stenosis [23]. Other authors have emphasized the role of an additional organic stenosis of the accessory papilla as responsible for the pathogenic effects [20,25-27]. Our clinical case is in agreement with these last studies since ERCP showed an accessory papilla with an eccentric orifice impossible to catheterize.On the other hand, several studies in the literature have suggested an association between mutations of major genes involved in pancreatitis and the occurrence of pancreatitis in patients with PD. [23, 28-31]. In our case, mutations of PRSS1, SPINK1 and CFTR genes were searched and were negative. In practice, retain the diagnosis of pancreas divisum only after eliminating other etiologies (Biliary Disease, trauma, drugs, multisystem disease, infections, Metabolic, Hereditary).

Radiological explorations of PD :

Pancreas divisum is best diagnosed by ERCP, magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasonography [32]. MRCP is the noninvasive test of choice to diagnose the condition. T2-weighted sequences show a dilated dorsal pancreatic duct crossing the main bile duct with which he has a separate inflow (through accessory papilla); it's the crossing sign. [33] However, despite the recent advances in MRCP and endoscopic ultrasound, pancreas divisum may not be detected using these techniques, and ERCP remains the test of choice "the gold standard" to diagnose or manage pancreas divisum for most patients [10,32].

Management of PD :

the management of RAP has two components: Symptomatic & curative. Symptomatic treatment includes hemodynamic stabilization, parenteral analgesia, temporary withholding of oral foods and liquids or enteral feedings with free-fat diet. Curative treatment, in this case PD, is based on: surgical sphincteroplasty [26, 27, 34] or endoscopic therapies such as endoscopic sphincterotomy of the accessory papilla [10, 35-37] and insertion of dorsal duct stents [10, 37].Bradley et al [34] have shown that surgical sphincteroplasty provides superior long-term results compared to endoscopic sphincterotomy. in the same way, liao et al [8] have shown in a meta-analysis that the response rate in symptomatic patients with pancreas divisum who underwent endoscopic therapy was found to be slightly but insignificantly lower than those with surgery (69.4% vs 74.9%, P = 0.106). However, other studies argue in favor of endoscopic treatment with regard to short-term [10, 37] and long-term [36] improvement. In conclusion, given the risk of surgery-related morbidity and mortality, it is more reasonable to choose first-line endoscopic treatment.

Prognosis & Evolution of RAP and PD :

Poddar et al [38] have conducted a retrospective study over a period of 13 years, including 373 cases of pancreatitis. 93 (25%) of them were ARP. Etiology included biliary in 14 (15%), pancreas divisum in 6 (7%), others in 3 (3.5%) and idiopathic in the remaining 70 (75%). They have concluded that ARP is a precursor of CP and progression is associated with idiopathic etiology ($p < 0.03$) and presence of SPINK1 mutation (p=0,01). Biliopancreatic structural lesions such as PD is a correctable cause of ARP.

CONCLUSION :

Pancreas divisum is a potentially treatable cause of RAP. Pancreas divisum cases are unique requiring clinical experience, rational approach, and complex multimodal management. MRCP is a valuable diagnostic method however, ERCP remains the modality of choice for interventional management

Conflict of interest : the authors declare no conflict of interest.

RÉFÉRENCES :

[1] Mornville VD, Husain SZ, Bai H, Barth B, Alhosh R, Durie P R et al. Definition of pediatric pancreatitis and survey of present clinical practices. J Pediatr Gastroenterol Nutr. 2012;55(3):261–265.

[2] Benifla M, Weizman Z. Acute pancreatitis in childhood: analysis of literature data. J Clin Gastroenterol. 2003; 37:169-172.

[3] Pezzilli R, Morselli-Labate AM, Castellano E, et al. Acute pancreatitis in children. An Italian multicentre study. Dig Liver Dis. 2002;34(5):343-348.

[4] Klein SD, Affronti JP. Pancreas divisum, an evidence-based review: Part I, pathophysiology. Gastrointest Endosc. 2004; 60:419-24.

[5] Stern CD. A historical perspective on the discovery of the accessory duct of the pancreas, the ampulla 'of Vater' and pancreas divisum. Gut. 1986; 27:203–12.

[6] Kin T, Shapiro AM, Lakey JR. Pancreas divisum: a study of the cadaveric donor pancreas for islet isolation. Pancreas. 2005; 30:325–7.

[7] Alempijevic T, Stimec B, Kovacevic N. Anatomical features of the minor duodenal papilla in pancreas divisum. Surg Radiol Anat. 2006; 28:620–4.

[8] Liao Z, Gao R, Wang W et al. A systematic review on endoscopic detection rate, endotherapy, and surgery for pancreas divisum. Endoscopy. 2009; 41:439–44.

[9] Stimec B, Bulajic M, Tatic S, et al. Unusual variants of the tributaries of the main pancreatic duct revealed by postmortem and¬¬ endoscopic pancreatography. Ann Anat. 1996; 178:169-71.

[10] Rustagi T & Golioto M. Diagnosis and therapy of pancreas divisum by ERCP: A single center experience. J Dig Dis. 2013;14(2):93-9.

[11] Mulholland MW, Lillemoe KD, Doherty GM, Maier RV, Upchurch GR, eds. Greenfield's Surgery. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

[12] Khalid A, Slivka A. Approach to idiopathic recurrent pancreatitis. Gastrointest Endosc Clin N Am. 2003; 13(4):695-716.

[13] Bai HX, Lowe ME, Husain SZ. What Have We Learned About Acute Pancreatitis in Children? J Pediatr Gastroenterol Nutr. 2011; 52(3):262–270.

[14] DeBanto JR, Goday PS, Pedroso MR, Iftikhar R, Fazel A, Nayyar S et al. Acute pancreatitis in children. Am J Gastroenterol. 2002; 97:1726–31.

[15] Fabre A, Petit P, Gaudart J, Mas E, Vial J, Olives J P et al. Severity Scores in Children With Acute Pancreatitis. J Pediatr Gastroenterol Nutr. 2012 ;55(3):266-7.

[16] Lautz TB, Chin AC, Radhakrishnan J. Acute pancreatitis in children: spectrum of disease and predictors of severity. J Pediatr Surg. 2011;46:1144–9.

[17] Suzuki M, Fujii T, Takahiro K, et al. Scoring system for the severity of acute pancreatitis in children. Pancreas. 2008;37:222–3.

[18] Suzuki M, Saito N, Minowa K, Kagimoto S, Shimizu T. Validation of severity assessment for acute pancreatitis in children. Pediatr Int. 2017;59(10):1127-1128.

[19] Lautz T B, Turkel G, Radhakrishnan J, Wyers M, Chin A C. Utility of the computed tomography severity index (Balthazar score) in children with acute pancreatitis. J Pediatr Surg. 2012;47(6):1185-91.

[20] Cotton PB. Congenital anomaly of pancreas divisum as cause of obstructive pain and pancreatitis. Gut. 1980;21:105e14.

[21] Buhler H, Seefeld U, Deyhle P, et al. [Clinical significance of pancreas divisum]. Schweiz MedWochenschr.1983;113:320e4

[22] Reshef R, Shtamler B, Novis BH. Recurrent acute pancreatitis associated with pancreas divisum. Am J Gastroenterol.1988;83:86e8.

[23] Frédérique M. Pancréas divisum et pancréatite: la controverse continue ! Hépato Gastro. 2011 ; 18 : 442-445.

[24] Gonoi W, Akai H, Hagiwara K, Akahane M, Hayashi N, Maeda E et al. Pancreas divisum as a predisposing factor for chronic and recurrent idiopathic pancreatitis: initial in vivo survey. Gut. 2011;60:1103e1108.

[25] Hayakaw T, Kondo T, Shibato T, Sugimoto Y, Kitagawa M, Suzuki T et al. Pancreas Divisum : A predisposing factor to pancreatitis. Int J Pancreatol. 1989;5(4):317-26.

[26] Warschaw AL, Richter JM, Schapiro RH. The cause and treatment of pancreatitis associated with pancreas divisum. Ann Surg. 1983;198(4):443-52.

[27] Warschaw AL, Simeone J F, Schapiro RH, Flavin Warshaw B. Evaluation and treatment of the dominant dorsal duct syndrome (pancreas divisum redefined). Am J Surg. 1990;159(1):59-66.

[28] Dray X, Fajac I, Bienvenu T, et al. Association of pancreas divisum and recurrent acute pancreatitis with the IVS8-5T-12TG allele of the CFTR gene and CFTR dysfunction. Pancreas. 2007 ; 35 : 90-3.

[29] Garg PK, Khajuria R, Kabra M, Shastri SS. Association of SPINK1 gene mutation and CFTR gene polymorphisms in patients with pancreas divisum presenting with idiopathic pancreatitis. J Clin Gastroentero. 2009 ; 43 : 848-52.

[30] Gelrud A, Sheth S, Banerjee S, et al. Analysis of cystic fibrosis gene product (CFTR) function in patients with pancreas divisum and recurrent acute pancreatitis. Am J Gastroenterol. 2004 ; 99 : 1557-62.

[31] Montagnani M, Cazzato S, Mutignani M, Cevenin M, Guidetti E, Ben Zvi I et al. A Patient With Pancreas Divisum, Recurrent Acute Pancreatitis, and Homozygosity for the Cystic

Fibrosis Transmembrane Regulator–Associated Protein 5T Allele. Clin Gastroenterol Hepatol. 2013;11(5):579-81.

[32] Wendy K, Tarabain O. Pancreas divisum: a cause of idiopathic acute pancreatitis. CMAJ. 2009.28; 180(9): 949–951.

[33] Agostini S, Garçon S, Durieux O, Guénat R, Peretti P. Aspects du pancréas normal. Variantes et malformations. J Radiol. 2005 ;86(6) :719-732.

[34] Bradley 3rd EL, Stephan RN. Accessory duct sphincteroplasty is preferred for long term prevention of recurrent acute pancreatitis in patients with pancreas divisum. J Am Coll Surg. 1996;183(1):65-70.

[35] Heyries L, Barthet M, Delvasto C, Zamora C, Bernard JP, Sahel J. Long-term results of endoscopic management of pancreas divisum with recurrent acute pancreatitis. Gastrointest Endosc. 2002; 55: 376–81.

[36] Borak GD, Romagnuolo J, Alsolaiman M, Holt EW, Cotton PB. Long-term clinical outcomes after endoscopic minor papilla therapy in symptomatic patients with pancreas divisum. Pancreas. 2009; 38: 903–6.

[37] Michailidis L, Aslam B, Grigorian A, Mardini H. The efficacy of endoscopic therapy for pancreas divisum: a meta-analysis. Ann Gastroenterol. 2017; 30(5): 550–558.

[38] Poddar U, Yachha SK, Borkar V, Srivastava A. Is acute recurrent pancreatitis in children a precursor of chronic pancreatitis? A long-term follow-up study of 93 cases. Dig Liver Dis. 2017;49(7):796-801.