Gastrointestinal & Digestive System

Zippi and Quarto, J Gastroint Dig Syst 2014, 4:1
http://dx.doi.org/10.4172/2161-069X.1000171

Short Communication Open Access

Intraductal Papillary Mucinous Neoplasm Associated to Pancreas Divisum

Maddalena Zippi[1]* and Angeloluca De Quarto[2]

[1]Unit of Gastroenterology and Digestive Endoscopy, Sandro Pertini Hospital, 00157 Rome, Italy
[2]Unit of Oncolgy, Sandro Pertini Hospital, 00157 Rome, Italy

Abstract

Pancreas divisum (PD) is one of the embryologic anomalies of the pancreas, in which the dorsal and the ventral pancreatic ducts fail to merge together. In this case the ventral pancreatic duct appears small and most of the pancreatic juice is drained through the minor papilla into the duodenum. Intraductal papillary mucinous neoplasia (IPMN) represents a heterogeneous group of pancreatic neoplasms. This kind of tumor may have its development in PD. Recently, owing to the progress in imaging and endoscopic ultrasound (EUS) techniques about the evaluation of the pancreas; the IPMN has been more and more identified and referred by the literature.

Keywords: Endoscopic Ultra Sound (EUS); Intraductal Papillary Mucinous Neoplasia (IPMN); Pancreas Divisum (PD); Pancreatic Cancer

Intraductal papillary mucinous neoplasia (IPMN) was firstly described by Ohashi et al. in 1982 [1]. These kind of tumors of the exocrine pancreas represent a group of ductal lesions, that only in 1996 were incorporated into the WHO classification [2]. The lesions may arise from the dysplasia and the invasive carcinoma as well and are characterized by intraductal papillary growth, mucin production and cystic dilatation of the pancreatic ducts. IPMNs are cystic tumors involving the main pancreatic duct and/or the branch ducts. There are three wide kinds of IPMNs, according to the extent of duct involvement: principal duct, secondary branches or mixed presentations [2].

Pancreas divisum (PD) has been recognized to be the most common congenital variant of the pancreas, consisting of a defect of fusion between the ventral and the dorsal ducts. As a result, the major drainage of the pancreas comes from the dorsal duct, which flows into the minor papilla, while the ventral duct drains the less part of it and flows into the major papilla. An incomplete PD may arise in some cases. In this condition, only a narrow connection joins the ventral and the dorsal ducts, but most of the pancreatic drainage takes place through the minor papilla [3].

According to autopsy series, PD can be approximately found in 8% to 12.6% of the Western population [4]. The referred prevalence of PD in patients who undergo ERCP is about 4-8% in the Western population and less than 2% in the Asian one [5-7].

In recent years, very little has been published on the relationship between IPMN and PD.

Data come from a personal overview of articles selected among the main literature Medline works (1966-2013).

Totally 13 articles have been analysed. Results concerning IPMN associated to PD are summarized in the Table 1. Thirteen cases have been identified (8 female and 5 male).

The reported average was 61.7 years (range: 33-79).

It is well known that IPMN is thought to be a rare neoplasia of the exocrine pancreas, with a reported incidence of 1 in 281.000 patients per year [21]. IPMN is more common in men between 60 and 70 years of age [16].

Also in cases of IPMN associated with PD, it seems that the age of diagnosis and the sex prevalence are the same of those patients without congenital anomalies of the pancreas.

In these kinds of patients, recurrent episodes of acute pancreatitis are the typical clinical expression of the disease, with abdominal pain, due to chronic, intermittent obstruction of the pancreatic duct both by mucus secretion and intraductal tumor growth [22]. Other symptoms may include weight loss, anorexia, abdominal pain, steatorrhea, jaundice, and vomiting [16].

The relationship between pancreas divisum and pancreatic cancer is still unknown, but some Authors support the hypothesis that pancreatic duct obstruction would cause stasis, also allowing a prolonged exposure to oncogenic agents, while some others believe that the obstruction may simply be the consequence of the tumor [23]. Nishino et al. [24] demonstrated that there was a significantly higher prevalence of pancreatic cancer in pancreas divisum (p=0.008), but the meaning of this association is still unclear. In fact, the Authors concluded that patients with PD should receive a careful follow-up on the risk of developing cancer.

Kamisawa et al. [12] in a retrospective study found 4 cases of pancreas divisum associated with pancreatic tumors. Among them, 3 were associated with pancreatic carcinoma and 1 with intraductal papillary mucinous tumor. All tumors developed from the dorsal pancreas of pancreas divisum. Periductal and interlobular fibrosis detected in the margin of the distal pancreatectomy of a non-carcinomatous pancreas implied that chronic dorsal pancreatitis, associated with pancreas divisum, preceded carcinoma. The Authors argued that in pancreas divisum, longstanding pancreatic duct obstruction caused by relative stenosis of the minor duodenal papilla, might be an ontogenetic factor.

In fact, it is well known that patients with chronic pancreatitis are reported to have a higher prevalence of pancreatic cancer than the general population [25].

Taking into account that the sensitivity of pancreatic imaging has improved with high-resolution magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS), early detection of small curable pancreatic cancers (IPMN) now seems to be possible [26]. Actually,

***Corresponding author:** Maddalena Zippi, Unit of Gastroenterology and Digestive Endoscopy, Sandro Pertini Hospital Via dei Monti Tiburtini 385, 00157 Rome, Italy, Tel: +39-06-41733310; Fax: +39-06-41733847; E-mail: maddyzip@yahoo.it

Received January 23, 2014; **Accepted** January 21, 2014; **Published** March 05, 2014

Citation: Zippi M, Quarto AD (2014) Intraductal Papillary Mucinous Neoplasm Associated to Pancreas Divisum. J Gastroint Dig Syst 4: 171. doi:10.4172/2161-069X.1000171

Author	Year	Number of pts (age)	Sex	Type of PD	Location IPMN	Surgery
Thayer et al. [8]	2002	1 (71 yrs)	female	complete	DPD	dorsal. pancreatectomy
Yarzeet al. [9]	2003	1 (33 yrs)	female	complete	DPD	pylorus-preserving pancreatoduodenectomy
Sakateet al. [10]	2004	1 (34 yrs)	male	complete	VPD	pylorus-preserving pancreatoduodenectomy
Sakurai et al. [11]	2004	1 (74 yrs)	male	complete	DPD	pylorus-preserving pancreaticoduodenectomy
Kamisawaet al. [12]	2005	1 (63 yrs)	female	complete	DPD	distal. pancreatectomy
Akizukiet al. [13]	2005	1 (75 yrs)	female	complete	DPD	distal. pancreatectomy
Tal.boltet al. [14]	2005	1 (51 yrs)	female	complete	DPD	dorsal. pancreatectomy
Scattonet al. [15]	2006	1 (45 yrs)	male	complete	DPD	dorsal. pancreatectomy
Sterling et al. [16]	2007	1 (70 yrs)	female	incomplete	DPD	unresectable (during surgery)
Kim et al. [17]	2009	1 (79 yrs)	male	complete	DPD	not performed for poor general. condition
Santi et al. [18]	2010	1 (74 yrs)	female	complete	DPD and VPD	not performed
Ringold et al. [19]	2010	1 (65 yrs)	male	complete	DPD	not perfomed
Nakagawa et al. [20]	2013	1 (70yrs)	female	complete	DPD	not specificated

Table 1: Results regardless IPMN associated to PD: Number of patients (with age at diagnosis) affected by IPMN; Type of PD (complete/incomplete); Location of IPMN (Dorsal. Pancreatic Duct –DPD-/Ventral. Pancreatic duct –VPD-); Type of surgical. approach.

there is no evidence that diagnosing these lesions will improve survival, but data suggesting that resection of very early disease is associated with a better prognosis are now available [27].

When imaging exams are used to study IPMN lesions, it is necessary to check mural nodules and to determine whether the tumor communicates with the main pancreatic duct or above all with the dorsal duct in case of PD. EUS shows better spatial resolution than computer tomography (CT) and furthermore can more clearly visualize the internal structure of cystic tumors of the pancreas [28]. For this reason, EUS is often used for the follow-up of IPMNs, in order to assess any changes in cystic lesions. In a recent article, Kamata et al. [29] have studied 167 patients with IPMNs using four techniques (EUS, ultrasonography, CT, MRI) to diagnose concomitant adenocarcinoma and IPMN-derived adenocarcinoma during the first examination and throughout 5 years of follow-up. EUS was shown to be superior to other imaging procedures both at the first examination than during the exam itself. The sensitivity and the specificity of these methods are as follows: at the first examination, for concomitant adenocarcinoma, EUS (61%, 100%), ultrasonography (39%, 99%), CT (39%, 100%) MRI (33%, 100%); for IPMN-derived adenocarcinoma, EUS (100%, 85%), ultrasonography (47%, 99%), CT (53%, 97%), MRI (53%, 92%) and throughout the exam EUS (100%, 100%), ultrasonography (39%, 99%), CT (56%, 100) and MRI (50%, 100%) [29].

In conclusion, the connection between pancreas divisum and IPMN is currently unknown. In pancreas divisum longstanding pancreatic duct obstruction caused by a relative stenosis of the minor papilla might be an oncogenetic factor. Thanks to the progress in radiologic diagnosis (especially EUS) and the increase of cases, the study of the pathogenesis of IPMN associated to PD will go on.

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Citation: Zippi M, Quarto AD (2014) Intraductal Papillary Mucinous Neoplasm Associated to Pancreas Divisum. J Gastroint Dig Syst 4: 171. doi:10.4172/2161-069X.1000171