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Intraductal papillary mucinous neoplasms of the pancreas with concurrent pancreatic and periampullary neoplasms

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Abstract

Background: Intraductal papillary mucinous neoplasms (IPMN) have been reported to be associated with concurrent, distinct pancreatic ductal adenocarcinoma (con-PDAC) in about 8% (range, 4–10%) of resected branch duct (BD) lesions. In addition, other pancreatic and ampullary tumors are occasionally diagnosed with IPMN in patients undergoing pancreatic surgery. The objective of this study is to describe the prevalence, clinicopathologic characteristics and prognosis of IPMN with concurrent pancreatic and ampullary neoplasms, especially con-PDAC.

Methods: The combined databases of pancreatic resections from the Massachusetts General Hospital and the Negrar Hospital, Italy, were analyzed for patients who had been diagnosed with IPMN and concurrent pancreatic or ampullary neoplasms.

Results: 2762 patients underwent pancreatic surgery from January 2000 to December 2012. Sixteen percent (n = 441) had pathologically confirmed IPMN and 11% of these (n = 50) had a different distinct synchronous pancreatic neoplasm. The majority of these, 62%, were con-PDAC, followed by neuroendocrine neoplasms (10%) and ampullary carcinoma (10%). Less frequently, mucinous (6%) as well as serous cystic neoplasms (6%), adenosquamous carcinoma (4%) and distal bile duct cancer (2%) were diagnosed. Among all patients with synchronous neoplasms, 66% harbored BD-IPMN, 28% combined IPMN and 6% main duct IPMN. Abdominal pain and/or jaundice were the leading symptoms in half of patients.

Conclusion: IPMN, mainly BD-IPMN, are associated with con-PDAC in about 7% of patients and account for 62% of all concurrent pancreatic/ampullary neoplasms. Other synchronous neoplasms may be found sporadically with IPMN without a suspected association.

Keywords: Pancreas; Intraductal papillary mucinous noeplasm; Concurrent neoplasm; Pancreatic cancer

Introduction

Much knowledge about the unique biological characteristics of intraductal papillary mucinous neoplasms (IPMN) of the pancreas has been gained since its initial characterization by the WHO more than 2 decades ago.[1] IPMN originate from the pancreatic ductal epithelium and represent a majority of mucin producing cystic tumor of the pancreas. Following an adenoma carcinoma sequence, all IPMN harbor potential risk of progression into invasive cancer

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originating from the IPMN (IPMN-Ca).[2,3] The individual risk of cancer derived from IPMN, is directly related to the ductal involvement.[4–6] In main-duct (MD) IPMN the reported prevalence of high-grade dysplasia and invasive cancer is about 62% (range 36–100%), while branch-duct (BD) IPMN have a more indolent biology (mean prevalence in resected lesions is 25%, range 6–46%).[7–13] Consequently, pancreatic resection is recommended by the 2012 International Association of Pancreatology (IAP) guidelines for all IPMN involving the main pancreatic duct, while BD-IPMN without worrisome features can be followed by observation.

In addition to the risk of malignant transformation within IPMN (IPMN-Ca), an association with concurrent, distinct pancreatic ductal adenocarcinoma (con-PDAC) has been found in 2–10% of resected IPMN. Con-PDAC is defined as a distinct invasive ductal carcinoma that develops away from the corresponding IPMN with an uninvolved, segment of the pancreatic duct present in-between. An increased risk of con-PDAC has also been described for low-risk branch-duct IPMNs undergoing surveillance[14–21] and of metachronous con-PDAC developing in the pancreatic remnant after resection of IPMN.[17,22–24] As a consequence, close lifelong surveillance has been recommended by these authors for all patients under observation and for those who have had a resection for IPMN. In addition to con-PDAC, other pancreatic and ampullary tumors have occasionally been diagnosed with IPMN.[25–29] Those described have been mostly neuroendocrine neoplasms, and there are only a few case reports of other synchronous tumors like serous cystadenoma[28] and solid pseudopapillary neoplasms.[29]

The objective of this study is two-fold. First, to describe the prevalence and clinicopathologic characteristics of all concurrent, distinct pancreatic and ampullary neoplasms in a large cohort from two high-volume centers and second, to examine the characteristics of the IPMNs that presented with a synchronous pancreatic and ampullary neoplasm.

Patients and methods

With the approval of the institutional review board (IRB), the combined databases of pancreatic resections from the Massachusetts General Hospital, USA, (IRB-protocol # 2012P000620) and the Negrar Hospital (no local IRB approval required), Italy, were analyzed to identify patients who underwent pancreatic surgery and had pathologically proven IPMN and concurrent pancreatic or ampullary neoplasms between 2000 and 2012. Patient's demographics and clinicopathologic characteristics were extracted. Factors analyzed included gender, age at the time of surgery, personal medical history, details on diagnosis, surgical procedure, postoperative course, final pathologic findings and follow-up information.

Patients were regularly followed after resection by imaging studies such as computerized tomography, magnetic resonance imaging or endoscopic ultrasound. In addition, patients were further contacted by a study nurse if no more clinical follow up was done within the Institution. Follow-up time was calculated from the date of surgery until the last date of contact or the day of death.

Histopathologic evaluation

Histologic assessment was performed according to the WHO criteria for IPMN by senior staff pathologists specialized in pancreatic disease (GZ and MMK) and each case of IPMN was graded as low-, intermediate-, or high-grade dysplasia, or invasive carcinoma.[30] The intraductal components were classified into four distinct epithelial subtypes—gastric, intestinal, pancreatobiliary and oncocytic—on the basis of their epithelial morphology on routine hematoxylin and eosin staining. If necessary immunohistochemistry against mucin glycoproteins was performed according to previously described criteria.[31,32] The term malignancy was only used for invasive carcinoma according the 2012 IAP Fukuoka guidelines.[33] Con-PDAC was defined as an invasive ductal carcinoma that developed away from the corresponding IPMN with an uninvolved, segment of the pancreatic duct present in-between. Other synchronous pancreatic and ampullary neoplasms were identified by standardized histopathological work-up. TNM staging was performed according to the 2010 classification of the American Joint Committee on Cancer.[34]

Statistical analysis

Categorical variables were compared using a x2 test. Continuous variables are expressed by median and range, and compared by the Mann–Whitney U test, or, if they had a normal distribution, using a 2-sample Student t test. For survival analysis, Kaplan–Meier method was used to assess survival time distribution, and log-rank test was applied. P values of less than .05 were considered statistically significant. The SPSS 18 software for Mac OsX (SPSS Inc., Chicago, IL) was used for all analyses.

Results

From January 2000 to December 2012, a total of 2762 patients underwent pancreatic surgery at the Massachusetts General Hospital (n = 2232), Boston, USA and the Negrar Hospital (n = 530), Italy. Among these patients, 16% (n = 441) had pathologically confirmed IPMN and 11% of these (n = 50) had a different synchronous pancreatic neoplasm. The majority of these patients (68%) underwent surgery after 2005. Patient characteristics are shown in Table 1.

Most synchronous neoplasms found with IPMN were con-PDAC (62%), followed by neuroendocrine neoplasms (10%) and ampullary carcinoma (10%). Less frequent were mucinous (6%) as well as serous cystic neoplasms