Revista Española de Enfermedades Digestivas
THE SPANISH JOURNAL OF GASTROENTEROLOGY

Title:
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DOI: 10.17235/reed.2017.5003/2017
Link: PubMed (Epub ahead of print)

Please cite this article as:
Costa Juliana M., Carvalho Sofia, Soares João B. . Synchronous intraductal papillary mucinous neoplasm and a pancreatic neuroendocrine tumor: more than a coincidence? . Rev Esp Enferm Dig 2017. doi: 10.17235/reed.2017.5003/2017.

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Synchronous intraductal papillary mucinous neoplasm and a pancreatic neuroendocrine tumor: more than a coincidence?

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Received: 29/04/2017

Accepted: 17/05/2017

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ABSTRACT

Although the association between intraductal papillary mucinous neoplasm of the pancreas (IPMN) and pancreatic neuroendocrine tumor (PNET) has been increasingly reported, whether this association is real or coincidence remains unclear. We report a case of synchronous IPMN and a PNET which were diagnosed preoperatively and discuss the tumorigenesis, clinicopathological features and management of these rare tumors based on the published literature.

A 56-year-old male was incidentally diagnosed with a 14 mm branch duct IPMN and a 3.6 mm non-functional PNET during an evaluation due to persistent upper abdominal pain via endoscopic ultrasound. Close follow-up of the patient was decided as the IPMN had no worrisome features.

A review of twenty-two previously reported cases of synchronous IPMN and PNET indicated that: a) only seven cases were diagnosed preoperatively; b) abdominal pain was the main presenting symptom; c) IPMN was the dominant tumor and presented with low grade dysplasia; d) the PNET was small and non-functional and had an indolent behavior; and e) only one case underwent radiologic follow-up.

IPMN are associated with other pancreatic and extrapancreatic malignancies. Thus, the entire pancreatic parenchyma should be examined closely during the evaluation of an

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IPMN in order to exclude other pancreatic lesions, for example, a PNET.

Key words: Endoscopic ultrasound. Intraductal papillary mucinous neoplasm. Pancreatic neuroendocrine tumor. Synchronous neoplasms.

INTRODUCTION

Intraductal papillary mucinous neoplasm of the pancreas (IPMN) is a relatively uncommon tumor which is associated with other pancreatic and extrapancreatic malignancies (1). Synchronous IPMN and a pancreatic neuroendocrine tumor (PNET) is extremely rare, and whether this is a real association or a coincidence remains unclear (1,2). We report a case of synchronous IPMN and PNET which were diagnosed preoperatively and discuss the tumorigenesis, clinicopathological features and management of these rare tumors based on a review of published literature.

CASE REPORT

A 56-year-old male with no significant past medical history was incidentally diagnosed with a 10 mm cystic lesion in the pancreatic body (Fig. 1) by abdominal computed tomography (CT) that was performed to evaluate persistent upper abdominal pain.

An endoscopic ultrasound (EUS) examination was performed and demonstrated two lesions in the pancreatic body. One was a 14 x 12 mm cystic lesion that communicated with the main pancreatic duct (no dilation) without mural nodules that was suspected to be a branch duct IPMN (BD-IPMN). In addition, a 3.6 mm solid hypoechoic lesion was observed (Fig. 2), and three additional cystic lesions of 2.8 to 4.4 mm were found in the pancreatic tail that were thought to be multifocal BD-IPMN. Fine-needle-aspiration (FNA) of the solid lesion revealed relatively uniform cells with oval nuclei, coarsely stippled chromatin and positive staining for chromogranin and synaptophysin. These features favored the diagnosis of a PNET (Fig. 3). No representative material for cytological analysis was obtained through EUS-FNA of the largest cystic lesion. However, the tumor markers carcinoembryonic antigen (CEA) and amylase were increased, with 8.3 ng/ml (reference: < 5 ng/ml) and 205 U/l (reference: 25-115 U/l), respectively. There were no symptoms suggestive of a clinical syndrome related to the

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PNET, thus it was considered as a non-functional tumor.

The IPMN had no high risk or worrisome features and the PNET was not advanced. Thus, after discussion in multidisciplinary meeting with the patient, close follow-up of the lesions was decided. After one year of follow-up the patient remains asymptomatic and EUS showed that both lesions were stable.

DISCUSSION

IPMN can be associated with other pancreatic and extrapancreatic malignancies (1). The diagnosis of PNET in a patient with IPMN is very rare, with a frequency of 2.8-4.6% (2,3). Although the association between IPMN and PNET has been increasingly reported in the literature, whether this association is real or fortuitous remains unclear (3,4). Several authors have attempted to explain the concomitant origin of the IPMN and PNET, however, the mechanism is not yet understood.

Marrache F et al. proposed that these tumors may have a common neoplastic progenitor or may be due to transdifferentiation of one cell type into another by the gastrin signaling pathway (4). However, Stukavec J et al. do not support this hypothesis, and suggest that the association is fortuitous and corresponds to a collision of two distinct tumors (5). Some studies corroborate this hypothesis and have shown that the incidence of small PNET is probably higher than previously thought due to the use of multiple imaging techniques such as EUS. The use of EUS may have contributed to the improvement in the preoperative diagnosis of very small PNET (6). Moreover, the genetic and histopathologic studies of IPMN and PNET suggest that there are obvious differences in terms of the genetic and histopathologic profile (7,8).

A review of the literature identified 22 case reports of synchronous IPMN and PNET to date. The review of these reports revealed the following aspects: a) the concomitant occurrence of these tumors was diagnosed preoperatively by cross sectional imaging in only seven cases; b) the male:female ratio was 10:12; c) the mean age at diagnosis was 65 years; d) symptoms include abdominal or epigastric pain in most cases (only six cases were asymptomatic at presentation; e) IPMN was the dominant tumor (mean size was 31 mm) and in most cases it had low grade dysplasia; f) the PNET was small (mean size 14 mm), non-functional and had indolent behavior in most cases

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(metastasis was observed in three cases); and g) almost all cases underwent a total or partial pancreatectomy (except one case) (1,2,5-7).

The optimal management of small and incidental non-functional PNET (NF-PNET) is currently a controversial topic. Recent studies have shown that small (< 20 mm) NF-PNET usually exhibit minimal or no growth over many years. Moreover, similar mortality rates were observed in non-operative and operative management cases. There is an advantage of non-operative management as surgical resection is associated with a higher morbidity rate (up to 40%, which includes pancreatic leakage and abscess formation) (9).

These studies suggest that small NF-PNETs have an indolent course, and therefore can be managed safely (without an increased risk of disease progression) with radiologic surveillance. Increasing size (which has not been specified in these studies) suggests that the neoplasm is a more aggressive type and should be considered for resection (9).

On the other hand, there are several guidelines for the management of BD-IPMN. Asymptomatic BD-IPMNs (without symptoms related to the pancreas such as jaundice, diabetes and acute pancreatitis), less than 40 mm in diameter and without worrisome features (mural nodules, dilation of the main pancreatic duct > 6 mm diameter) can be followed-up by imaging (10).

CONCLUSION

In most cases, synchronous IPMN and PNET were diagnosed incidentally after surgery. Only seven cases with a preoperative diagnosis of synchronous IPMN and PNET have been reported to date. This report emphasizes the importance of close observation of the entire pancreatic parenchyma during the evaluation of an IPMN. This neoplasm can be associated with other small pancreatic lesions that occasionally have a different origin to the main lesion (IPMN). Moreover, surveillance instead of surgical treatment can be offered in cases of concomitant small NF-PNET.

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Fig. 1. Abdominal computed tomography (CT) showing a cystic lesion in the body of the pancreas (white arrow).

Figure 3.

Fig. 2. Endoscopic ultrasound (EUS) examination. A. Synchronous 14 mm cystic lesion suggestive of an intraductal papillary mucinous neoplasm (IPMN). B. 3.6 mm solid lesion in the pancreatic body (white arrows).

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Figure captions:

Figure 1. Abdominal computed tomography (CT) showing a cystic lesion in the body of the pancreas (circled and white arrow).

Fig. 3. Cytological examination of a fine-needle-aspiration (FNA) of the solid lesion. A. Uniform cells with oval nuclei and coarsely stippled chromatin, with hematoxylin and eosin stain (magnification x400). B. Positive chromogranin staining (magnification x400). C. Synaptophysin staining (magnification x400) which favors a pancreatic neuroendocrine tumor (PNET).

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