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Case Study

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MALIGNANT TRANSFORMATION OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS: A NEW CASE REPORT

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ABSTRACT

Intraductal papillary mucinous neoplasms (IPMN) are a heterogeneous group of mucin producing cystic tumours that involve the main pancreatic duct and/or branch ducts and may be associated with invasive carcinoma. A 71 year-old male patient with a past medical history of hypertension and ischemic heart disease, presented with paroxysmal epigastralgia, weight loss, asthenia and steatorrhea. Abdominal computed CT scan showed a cystic lesion of the pancreas communicating with an accessory pancreatic duct associated with segmental dilation of the wirsung duct. The preoperative diagnosis was mixed type IPMN. The patient underwent pancreatoduodenectomy. Histopathological examination of the surgical specimen coupled with immunohistochemical study established the diagnosis of intestinal type IPMN associated with invasive ductal adenocarcinoma. Postoperative course was uneventful. At present, the patient is still being followed-up. Despite recent advanced technologies, diagnosis of IPMN is still challenging, especially in western countries due to its rarity. Early identification and resection of lesions, even in asymptomatic or minimally symptomatic patients, are however important prognostic factors.

KEYWORDS: Pancreas, pathology, intraductal papillary mucinous neoplasm, malignant transformation.

INTRODUCTION

Intraductal papillary mucinous neoplasm (IPMN) is the most frequent cystic tumour of the pancreas, accounting for approximately 8-20% of all resected pancreatectomy specimens.[1] Considered to be precursor of invasive carcinoma, these lesions can undergo malignant transformation.[2-3] To date, there remain conflicting results particularly concerning predictors of malignancy in IPMN. In this paper, the authors a new case of IPMN with an associated invasive carcinoma. The aim of the present study was to highlight the clinicopathological features and prognosis of this entity.

CASE REPORT

A 71 year-old male patient with a past medical history of hypertension and ischemic heart disease, presented with paroxysmal epigastralgia, weight loss, asthenia and steatorrhea.

Physical examination of the patient did not disclose any anomaly. Biological tests were within normal limits. Abdominal ultrasonography showed a dilated duct of wirsung associated with a suspected hypoechoic lesion of the pancreatic head measuring 36 mm (Fig 1a). Abdominal computed CT scan showed a cystic lesion of the pancreas communicating with an accessory pancreatic duct associated with segmental dilation of the wirsung duct (Fig.1b). Magnetic resonance imaging demonstrated a cystic lesion of the head of the pancreas measuring 5,5 x 2 cm, hyperintense on T2 and hypointense on T1 associated with multiple enhancing parietal nodules (Fig.1c). The main pancreatic duct was dilated measuring 9,8 mm in diameter and the adjacent pancreas was atrophic. The preoperative diagnosis was mixed type IPMN. The patient underwent pancreatoduodenectomy. Macroscopic examination of the surgical specimen showed that the wirsung duct was dilated filled with mucin (Fig.1d). The adjacent pancreatic tissue was fibrotic and firm in consistency with dialed accessory pancreatic ducts. Histological examination of the surgical specimen revealed that the dilated main pancreatic duct and connecting dilated branch ducts were filled with nodular growth of tumour cells consisting of intestinal-type adenoma with intestinal gland-like structures (Fig.2a & 2b). In the main pancreatic duct, a transition from intestinal-type adenoma to intestinal-type carcinoma was observed. In addition, in a dilated branch duct, some components of intestinal-type carcinoma with marked arborizing structures were observed. A minimally invasion was observed around branch ducts with several irregular tubular glands set in a fibrous stroma (Fig. 2c). Immunohistochemical study revealed positive immunostaining of the neoplastic epithelium for MUC2 (Fig. 2d), MUC5AC and CDX2. The final pathological diagnosis was mixed and intestinal-type IPMN of the pancreas with an associated invasive ductal carcinoma.

Postoperative course was uneventful. At present, the patient is still being followed-up.

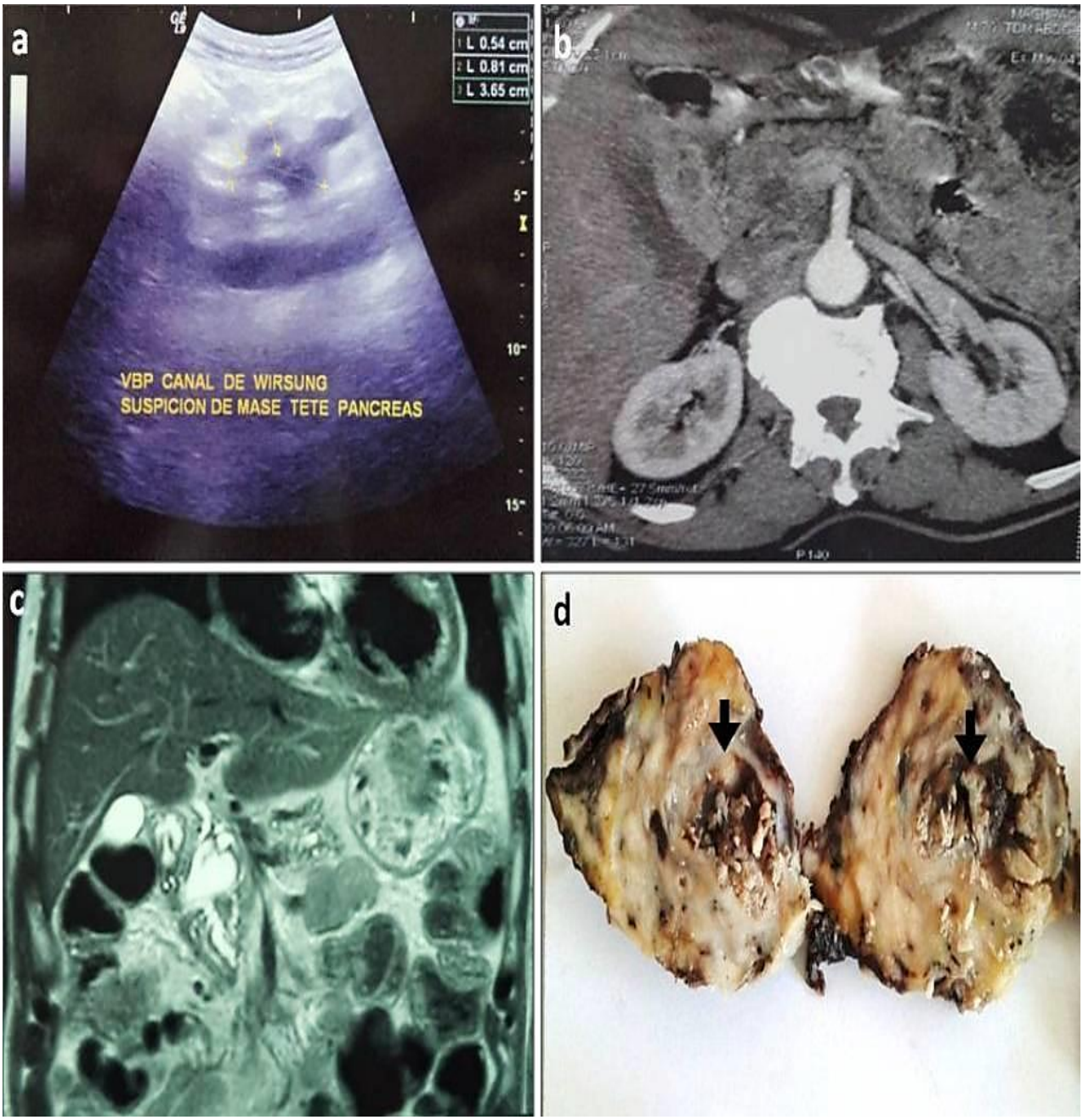

Figure 1a: Abdominal ultrasonography showed a dilated duct of wirsung measuring 6, 9 mm associated with a hypoechoic lesion of the pancreatic head.
Figure 1b: Abdominal computed CT scan revealed a cystic lesion of the pancreas communicating with an accessory pancreatic duct associated with segmental dilation of the wirsung duct.
Figure 1c: Magnetic resonance imaging demonstrated a cystic lesion of the pancreatic head measuring 5,5 x 2 cm, hyperintense on T2 and hypointense on T1 associated with multiple enhancing parietal nodules.
Figure 1d: Macroscopic findings of mixed type IPMN. The main pancreatic duct (arrows) was dilated filled with mucin. The accessory pancreatic ducts were also dilated.

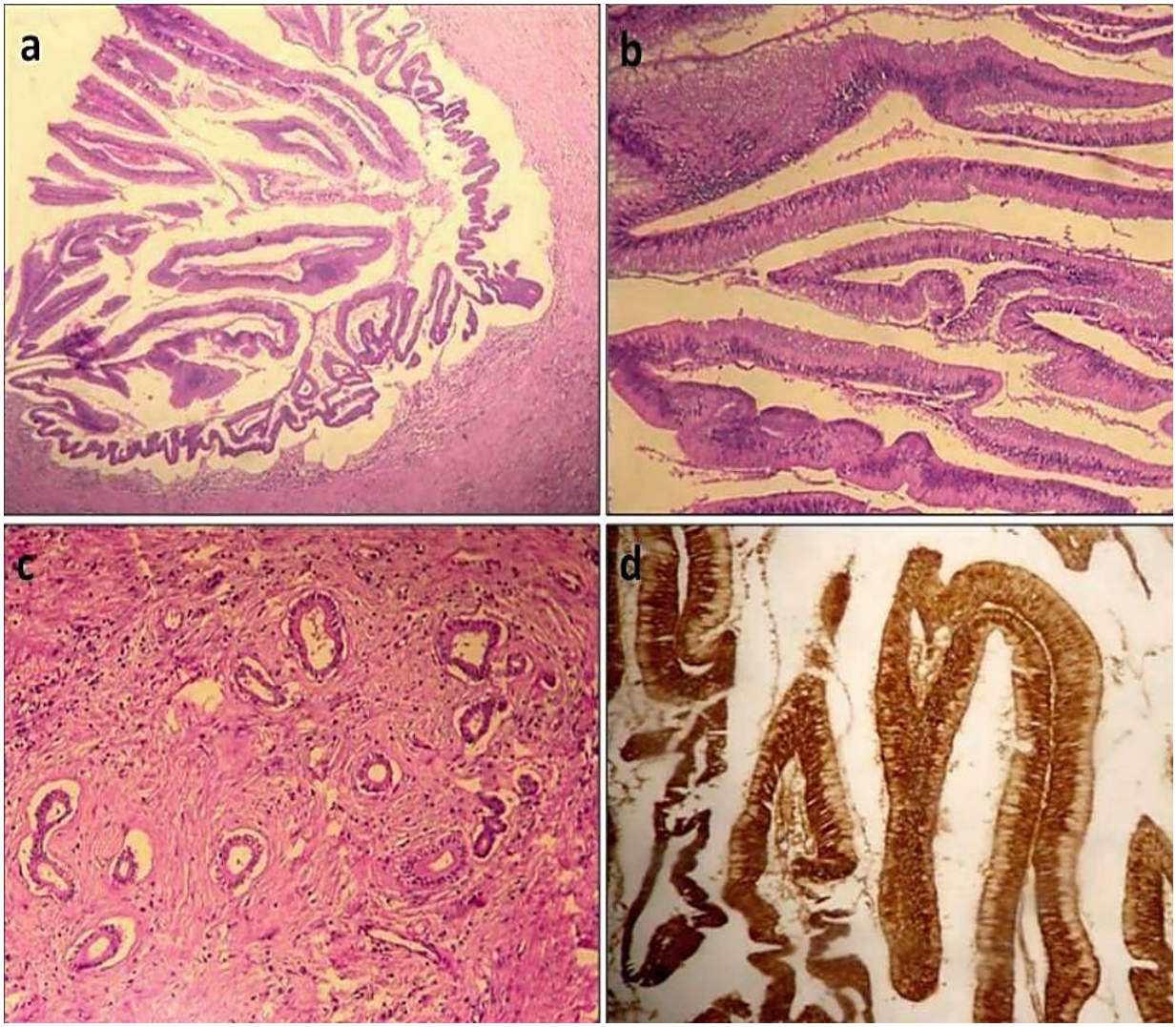

Figure 2a: Intraductal proliferation of columnar mucin producing cells with several finger-like projections lined by a pseudostratified epithelium, (Hematoxylin and eosin, magnification × 40).
Figure 2b: Pseudostratified tall columnar cells line the papillae with several goblet cells (Hematoxylin and eosin, magnification × 200).
Figure 2c: Invasive component: well differentiated ductal adenocarcioma, (Hematoxylin and eosin, magnification × 100).
Figure 2d: The neoplastic epithelium showed positive immunostaining for MUC2, (Immunohistochemistry, magnification × 200).

DISCUSSION

Intraductal papillary mucinous neoplasms are distinct cystic pancreatic neoplasms characterized by mucin production, cystic dilation of the pancreatic ductal system, and intrapapillary epithelial growth.[4] The true prevalence of IPMN is unknown. It is estimated that they represent about 20- 50% of all pancreatic cystic neoplasms.[1,3] Intraductal papillary mucinous neoplasms encompass a spectrum of cystic neoplasms with different malignant potential following a progressive pathway of low-grade dysplasia to high grade dysplasia to invasive pancreatic ductal adenocarcinoma.[5,6] Intraductal papillary mucinous neoplasms are equally distributed in gender. They usually occur between the sixth and seventh decade of life and are mostly located in the head of the pancreas.[7] Patients with malignant transformation of IPMN are generally 3 to 5 years older than those with noninvasive IPMNs, suggesting that it takes years for an IPMN to progress to invasive cancer.[4,7] Our patient was 71 years old. Intraductal papillary mucinous neoplasms may present with a broad spectrum of symptoms ranging from nonspecific abdominal pain to pancreas-related symptoms such as jaundice or acute pancreatitis.[8,9] Our patient presented with paroxysmal epigastralgia, weight loss, asthenia and steatorrhea. Preoperative imaging techniques such as MRI with magnetic resonance cholangiopancreatography, contrast-enhanced CT, endoscopic ultrasonography and endoscopic retrograde choledochopancreatography are usually sufficient to confirm the diagnosis and classify the IPMN type.[8] Anatomically, IPMN is classified into three types according to the involvements of pancreatic ducts: main

duct (MD) IPMN, branch duct (BD) IPMN and mixed type IPMN. Main duct IPMN and mixed IPMN carry a higher risk of malignant transformation (62% and 58% of surgically resected cases respectively), whereas BD-IPMN have a much more indolent behavior.[10] Fine needle aspiration with analysis of cyst fluid is often used for characterizing cystic lesions. Pancreatic cyst fluid contains glycoproteins including carcinoembryonic antigen (CEA) and cancer antigen (CA) 19-9. High CEA levels (>192ng/ml) are associated with mucinous cysts (including IPMN), with lower levels (<5 ng/ml) found in non-mucinous cysts (sensitivity 50%, specificity 95%).[11] CEA cannot differentiate IPMN from mucinous cystic neoplasm, or accurately identify malignancy.[12] Cyst fluid cytology has a limited role in the diagnosis of IPMN. It can differentiate between mucinous and non-mucinous cysts by identifying columnar epithelium or extracelluar mucin. Histologically, IPMN are characterized by the intraductal proliferation of columnar mucin-producing cells. The epithelium of IPMN can be flat or form papillae with fibrovascular cores.[4] Based on the predominant architectural and cell differentiation pattern, we classify IPMN into four subtypes: gastric (70%), intestinal (20%), pancreatobiliary (7%) and oncocytic (3%).[4] Noninvasive IPMN are classified as having low-grade, intermediate grade or high-grade dysplasia based on the highest degree of architectural and cytological atypia identified.[4] Most invasive carcinomas arise in association with main-duct type IPMN with high-grade dysplasia.[4] We distinguish two distinct types of invasive carcinoma. Invasive colloid carcinoma usually arises in association with intestinal-type IPMN and tubular (conventional ductal) adenocarcinoma which is morphologically similar to usual ductal adenocarcinoma. Sampling is extremely important for IPMNs with no obvious invasive carcinoma. If a resection specimen is not well sampled, there is a good chance of missing a small invasive carcinoma. Therefore, unless there is a grossly identifiable invasive carcinoma associated with an IPMN, some authors recommend that the entire lesion should be submitted for histological examination.[4] When issuing a diagnostic report, it is critical that the invasive and noninvasive components of an IPMN are clearly and separately documented. The size of invasive carcinoma should be measured separately from the noninvasive IPMN. Immunohistochemically, ductal markers including keratins 7 and 19, CA19-9, B72.3 and CEA are strongly expressed in most IPMN. The expression of mucin glycoproteins (MUC) is useful for distinguishing the morphological subtypes.[4] Intestinal type IPMN are positive for MUC2, MUC5AC and CDX2 but are negative for MUC1 and MUC6 as it was the case in our patient.[4] Activating point mutations in codon 12 of the KRAS oncogene have been reported in 30-80% of IPMN and the prevalence of these mutations increases with increasing degree of dysplasia.[4,13] PIK3CA gene mutations occur in about 10% of IPMN. Mutations in the BRAF gene are found in a small fraction of IPMN.[4,13] Allelic losses involving loci of tumour-suppressor genes, including CDKN2A, TP53 and SMAD4 are found in up to 40% of IPMN and these losses increase with increasing degree of dysplasia. TP53 gene mutations have been reported in IPMN with high-grade dysplasia.[4,13] The prognosis of IPMN with an associated invasive carcinoma is worse than for noninvasive IPMN. The 5-year survival rates for IPMN with an associated invasive carcinoma are reported to be between 27% and 60%, depending upon the extent and histological type of the invasive component.[7] Because of the well-documented frequency of malignancy in MD-IPMN, surgical resection is recommended in all fit patients. In patients with BD-IPMN, the indication for surgical resection is still the subject of controversy. Nevertheless, there is a consensus that all young and surgically fit elderly patients with BD-IPMNs should be resected if they present with an enhanced solid component, obstructive jaundice, a main pancreatic duct size of greater than 6 mm, or cytology that is suspicious or positive for malignancy.[14] The role of radiation and adjuvant chemotherapy in patients with invasive IPMNs has not been well defined.

In conclusion, the knowledge of molecular biology of IPMN has developed over the last few years, but more research is needed to use this information for clinical intent, to better define the natural history of these tumors. The presence of IPMN in the pancreas increases the risk for developing carcinoma, and surveillance of the entire pancreas or continued surveillance of the remnant pancreas is essential in order to detect an invasive carcinoma arising in a separate area of the pancreas.[14] A multidisciplinary approach involving gastroenterologists, radiologists, surgeons, and pathologists is essential to the optimal management of these patients.

REFERENCES

1. Farrell JJ, Brugge WR. Intraductal papillary mucinous tumor of the pancreas. Gastrointest Endosc, 2002; 55(6): 701-14.
2. Nara S, Shimada K, Kosuge T, Kanai Y, Hiraoka N. Minimally invasive intraductal papillary-mucinous carcinoma of the pancreas: clinicopathologic study of 104 intraductal papillary-mucinous neoplasms. Am J Surg Pathol, 2008; 32(2): 243-55.
3. Niedergethmann M, Grutzmann R, Hildenbrand R. Outcome of invasive and noninvasive intraductal papillary-mucinous neoplasms of the pancreas (IPMN): a 10-year experience. World J Surg, 2008; 32(10): 2253-60.
4. Adsay NV, Fukushima N, Furukawa T, Hruban RH, Klimstra DS, Kloppel G et al. intraductal neoplasm of the pancreas. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, editors. WHO classification of tumours of digestive system. Lyon: WHO Press, 2010; 304-313.
5. Hruban RH, Pitman MB, Klimstra DS. Tumors of the pancreas. In: Silverberg SG, editor. AFIP Atlas of tumor pathology series 4, vol.6. Washington: ARP Press, 2007; 75-110.

6. Sessa F, Solcia E, Capella C et al. Intraductal papillary mucinous tumours represent a distinct group of pancreatic neoplasms: an investigation of tumour cell differentiation and k-ras, p53 and c-erbB-2 abnormalities in 26 patients. Virchows Arch, 1994; 425: 357-367.
7. Chanjuan Shi, Ralph H. Hruban. Intraductal papillary mucinous neoplasm. Human Pathology, 2012; 43: 1-16.
8. Fernandez-del Castillo C, Adsay NV. Intraductal papillary mucinous neoplasms of the pancreas. Gastroenterology, 2010; 139: 708-713.
9. Farrell JJ, Fernandez-del Castillo C. Pancreatic cystic neoplasms: management and unanswered questions. Gastroenterology, 2013; 144: 1303-1315.
10. Velez M, Ganguly E. Intraductal papillary mucinous neoplasms of pancreas- A Review. Ann Clin Pathol, 2014; 2(2): 1021-28.
11. Van der Waaij LA, van Dullemen HM, Porte RJ. Cyst fluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. See comment in PubMed Commons below Gastrointest Endosc., 2005; 62: 383-9.
12. Ngamruengphong S, Bartel MJ, Raimondo M. Cyst carcinoembryonic antigen in differentiating pancreatic cysts: a meta-analysis. See comment in PubMed Commons below Dig Liver Dis, 2013; 45: 920- 26.
13. Paini M, Crippa S, Partelli S, Scopelliti F, Tamburrino D, Baldoni A, Falconi M. Molecular pathology of intraductal papillary mucinous neoplasms of the pancreas. World J Gastroenterol, 2014; 20(29): 10008-10023.
14. Adsay V, Mino-Kenudson M, Furukawa T. Pathologic evaluation and reporting of intraductal papillary mucinous neoplasms of the pancreas and other tumoral intraepithelial neoplasms of pancreatobiliary tract. Recommendations of Verona consensus meeting. Ann Surg., 2016; 263: 162-77.