CASE REPORT

Neuroendocrine tumour in pancreatic dorsal agenesis: a rare association

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Accepted 6 September 2017

SUMMARY

Pancreatic dorsal agenesis (PDA) is a rare congenital anomaly, usually asymptomatic, that can present with abdominal pain, pancreatitis, diabetes mellitus and jaundice. Pancreatic tumours in PDA background are extremely rare, and when they occur are mainly pancreatic ductal adenocarcinoma. We present a case of a 48-year-old female patient with incidental detection of a 26×20 mm nodular lesion of the cephalic pancreas on ultrasound. Surgery was performed and gross examination revealed PDA with a tumour developed around the Wirsung duct. Histology showed a neuroendocrine tumour G1 with neural and vascular invasion. Two and half years later, the patient is alive and without tumour relapse. Awareness of the association of PDA and pancreatic tumours is fundamental in order to develop personalised follow-up programmes.

BACKGROUND

Pancreatic dorsal agenesis (PDA) is a rare congenital anomaly. PDA is normally asymptomatic, but it can present with abdominal pain, pancreatitis, diabetes mellitus and jaundice. Pancreatic tumours in PDA background are extremely rare, with only 12 cases reported in the literature—five pancreatic ductal adenocarcinoma (PDAC), two solid pseudopapillary neoplasm, one intraductal papillary mucinous neoplasm with associated invasive mucinous adenocarcinoma, two ampullary and one periampullary carcinoma, and one neuroendocrine tumour (NET). As far as we know, this is the second case reported of a NET, developed in the context of PDA.

We report this case in order to increase awareness of the relation between PDA and pancreatic tumours.

CASE PRESENTATION

A 48-year-old obese female patient, with history of hepatic steatosis and gallbladder lithiasis, presented with incidental detection of a 26×20 mm nodular lesion on the pancreas head on routine ultrasound scan.

Pathological background included total thyroidectomy due to follicular adenoma 9 years before. Regular medication was limited to levothyroxine.

INVESTIGATIONS

Blood tests did not demonstrate relevant findings: haemoglobin and bilirubin, as well as neuron-specific enolase and chromogranin A, had normal serum levels.

Contrast-enhanced CT revealed a nodular and hypervascular lesion with 27 mm in size of the pancreas head (figure 1A), confirmed by MRI and positron emission tomography with somatostatin analogue 1-Nal3-octreotide (NOC) and gallium Ga 68-labeled 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) (DOTANOC) (figure 1B).

No surgical contraindications were present and a cephalic duodenopancreatectomy was performed.

Gross examination revealed a cephalic pancreatic lesion with a size of 30×28×20 mm on cut section composed of yellowish and firm tissue, developed around the Wirsung duct with a peripheral rim of pancreatic and adipose tissue (figure 2).

Histological examination was performed on H&E-stained slides observed in light microscope (Nikon Eclipse 50i), and images were obtained using a Nikon Digital Sight DS-Fi1 camera.

Microscopically the tumour was well-differentiated, composed of trabeculae and small nests, with polygonal and monotonous cells with well-defined boundaries, eosinophil cytoplasm, and nuclei with coarse and fine chromatin and visible nucleoli (figure 3A,B). No mitosis was registered. There was frequent neural invasion (figure 3C) and focal vascular invasion (figure 3D), with no lymph node metastasis on 16 lymph nodes.

Immunohistochemistry studies were performed on one representative block of the lesion, resorting to avidin-biotin-peroxidase complex detection system and performed on Ventana Marker

Figure 1 Nodular and hypervascular lesion with 27 mm in size of the pancreas head: contrast-enhanced CT (A) and hypermetabolic on positron emission tomography scan (B).

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To cite: Rodrigues P, Oliveira RC, Oliveira CM, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-221999

Figure 2 The tumour was composed of white and firm tissue, developed around the Wirsung.

Platform BenchMark ULTRA IHC/ISH, and showed diffuse positivity for synaptophysin (MRQ-40, Cell Marque, California, USA) and chromogranin A (LK2H10, Ventana, Tucson, Arizona, USA) (figure 4A). The Ki67 (30-9, Ventana) proliferative index, counted on a printed picture of 500 cells, was low at 1.4% (figure 4B), providing the final diagnosis of pancreatic NET G1.

The tumour was classified according to the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) (7th edition) and European Neuroendocrine Tumor Society (ENETS) classification as pTNM (tumor node metastasis) T2N0 and T3N0, respectively.

Figure 3 Microscopically the tumour was composed of trabeculae with polygonal cells with well-defined boundaries, with coarse and chromatin and visible nucleoli (A, H&E 100×; B, H&E 400×), neural invasion (C, H&E 200×) and vascular venous invasion (D, H&E 400×).

DIFFERENTIAL DIAGNOSIS

The diagnosis of NET was straightforward. Tumour morphology was typical and immunohistochemistry (IHC) confirmed the diagnosis.

TREATMENT

Surgical treatment was performed with no complications. Surgical exploration found a globus pancreas, only with cephalic portion, without body and tail, with its left limit at the right of the superior mesenteric vein. Reconstruction of the digestive tract was performed with a Roux-en-Y anastomosis.

Fluid therapy and analgesics were prescribed. During the post-operative period, the patient always had glycaemia values within the normal range. She was observed by an endocrinologist and discharged 5 days after surgery with indication for hypolipidaemic and hypoglycaemic diet, without the need for insulin. Pancreatin was added to her regular prescription.

OUTCOME AND FOLLOW-UP

Currently the patient is alive with no signs of disease after 3 years.

During follow-up a pituitary microadenoma was detected. The patient always maintained glycaemia values within the normal range without insulin administration.

Familiar history was investigated by the endocrinology department in order to rule out multiple neuroendocrine neoplasia type 1 (MEN1) syndrome, which was negative.

The patient also had history of liver abscess with 24 mm, due to infection by *Proteus mirabilis*, *Streptococcus viridans* and *Bacteroides fragilis*, successfully treated with antibiotics.

DISCUSSION

PDA is extremely rare, with literature reports accounting for less than 100 cases.¹ The pancreas is a retroperitoneal organ of the upper abdomen that weighs 70–150 g and measures 15–25 cm in length, with connection to the duodenum via the ampulla of Vater where the main pancreatic ducts coalesce with the common bile duct.² The pancreas develops by ventral and dorsal endodermal buds.^{1–3} The dorsal bud forms the upper part of the head, body and tail of the pancreas, which drains through the Santorini duct. The ventral bud gives rise to the major part of the head and uncinate process, which drains through the Wirsung duct.^{1,3} Agenesis of the ventral pancreas and complete agenesis of the pancreas are usually lethal conditions.³

PDA results of embryogenesis failure and most cases are asymptomatic, with diagnosis performed on autopsy, laparotomy exploration or radiology (ultrasound, CT and MRI) due to other causes.^{2,3} When symptomatic, the main symptoms are abdominal pain, pancreatitis, diabetes mellitus, weight loss and jaundice,² so pancreas divisum and autodigestion secondary to chronic pancreatitis must be considered in the clinical and radiological differential diagnosis.^{4,5}

Regarding classification, neuroendocrine tumors (NETs) are stratified according to WHO as NET G1, G2, G3, and as large-cell neuroendocrine carcinoma (NEC) and small-cell NEC, based on morphological and immunohistochemistry (IHC) characteristics; they may also be classified according to the hormone production status as gastrinoma, glucagonoma, insulinoma, somatostatinoma and VIPoma.^{6–9} Morphologically our case was a NET G1 and serological evaluation did not show any hormone production.

NET is a heterogeneous neoplasm with unknown clinical behaviour; however, some prognostic factors are well

Figure 4 Immunostaining for chromogranin A (A, 200×), synaptophysin (B, 200×) and Ki67 (C, 200×).

established, namely the ENETs classification, vascular invasion and hormone-producing status.⁹

PDA association with pancreatic tumours is extremely rare, the PDAC being the most frequent¹; NET developed in PDA is even rarer, with only two cases reported as far as the authors know, including the one described in this manuscript.¹⁰

Our patient was a 48-year-old woman with incidental discovery of pancreatic mass on routine follow-up. The other case described in the literature was also of a 48-year-old woman referred to surgical oncology clinic for evaluation of pancreatic mass; however, in this case there was a history of an endometrial stromal sarcoma.

In both cases surgery was the treatment of choice, without adjuvant radiotherapy or chemotherapy, without tumorous recurrence—in our case, with 3 years of follow-up. Further follow-up is mandatory due to the ability of NET to develop secondary disease.

Learning points

- ▶ PDA (pancreatic dorsal agenesis) is an uncommon congenital anomaly, rarely associated with pancreatic tumours.
- ▶ The most frequent tumour in association with PDDA is pancreatic ductal adenocarcinoma.
- ▶ This is the second case described of neuroendocrine tumour in a pancreatic dorsal agenesis background.
- ▶ Awareness of the association of PDDA and pancreatic tumours is fundamental in order to develop personalised follow-up programmes.

Contributors PR and RCO collected clinical data, analysed the histopathology and performed the draft of the manuscript. CMO performed radiology examination. MAC helped with the histopathological analysis and reviewed critically the article for important intellectual content. All authors read and approved the final version of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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