CASE REPORT

Intraductal papillary mucinous neoplasm presenting with recurrent pancreatitis: a report of a painful 3-decade-long history

Samuel Raimundo Fernandes, Luís Araújo Correia, Teresa Antunes, Helena Cortez-Pinto

Serviço de Gastrenterologia e Hepatologia, Hospital de Santa Maria, Lisbon, Portugal

Correspondence to

Dr Samuel Raimundo Fernandes,
Samuelrfernandes@gmail.com

Accepted 4 March 2016

SUMMARY

Intraductal papillary mucinous neoplasm represents the most common pancreatic cystic neoplasm and harbours significant malignant potential. Duct obliteration can lead to recurrent episodes of pancreatic inflammation mimicking acute and chronic pancreatitis. We report a case of a patient with multiple episodes of idiopathic pancreatitis occurring over a period of three decades. Following admission with severe upper gastrointestinal bleeding, the patient was diagnosed as having invasive pancreatic adenocarcinoma. Examination of the surgical specimen confirmed an intraductal papillary mucinous neoplasm with multiple foci of invasive adenocarcinoma. This case is of significant interest, highlighting the long delay until diagnosis seen in this situation. Intraductal papillary mucinous neoplasm should be considered in the presence of recurrent acute or chronic pancreatitis of unknown aetiology.

BACKGROUND

Previously thought to be rare, intraductal papillary mucinous neoplasms (IPMNs) are increasingly being recognised as the most common pancreatic cystic neoplasms, accounting for up to 50% of all pancreatic cystic lesions.^{1 2} The neoplasm is characterised by intraductal proliferation of papillary mucin-secreting cells, multiple cysts and variable degrees of cellular atypia.³ Hypersecretion of mucin eventually leads to duct dilation and obstruction. Clinical presentation includes recurrent episodes of abdominal pain mimicking acute pancreatitis or overt signs of chronic pancreatitis due to duct destruction. Although IPMNs are usually benign and slow-growing, up to one-third may eventually become invasive and metastasise.⁴

We report a case of a patient with recurrent episodes of pancreatitis over a period of 30 years. The patient eventually developed signs of overt exocrine and endocrine pancreatic insufficiency. The diagnosis of IPMN with adenocarcinoma transformation was finally made after admission with gastrointestinal bleeding due to duodenal invasion by the neoplasm. This represents the longest undiagnosed case of IPMN to date. We present this case, highlighting the clinical and pathophysiological findings and review the available literature.

CASE PRESENTATION

A 67-year-old man was admitted to our gastroenterology clinic, with abdominal pain, melena and

asthenia. His medical history was relevant for multiple admissions due to recurrent pancreatitis starting at the age of 37 years. Even though the patient referred only mild alcohol consumption, this was consistently considered the cause for his recurrent pancreatitis. By 38 years of age, he had undergone a cholecystectomy and endoscopic retrograde cholangiopancreatography. Neither gallstones nor biliary duct abnormalities were noted on examination, although a reference to an abnormally enlarged papilla with mucoid secretion was noted at the time. At 40 years of age, the patient underwent pancreatic-jejunal drainage for relief of chronic pain. Even though he experienced considerable relief of symptoms, by 48 years of age, his abdominal CT showed evidence of severe pancreatic atrophy with pancreatic duct dilation and multiple parenchymal calcifications. By the age of 61 years, the patient was diagnosed with insulin-dependent diabetes mellitus. He was a moderate smoker and frequently took painkiller medication. There was no family history of pancreatitis. At admission, his physical examination was relevant for skin pallor and moderate epigastric pain on palpation.

Figure 1 Upper gastrointestinal endoscopy showing a postpapillary ulcerated lesion protruding into the duodenal lumen.

CrossMark

To cite: Fernandes SR, Correia LA, Antunes T, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-214640

Figure 2 Contrast-enhanced CT showing a heterogeneous and enlarged pancreas head with a small calcification (arrow).

INVESTIGATIONS

Laboratory tests showed severe anaemia (8.6 g/dL) with normal leucocytes and C reactive protein. Upper gastrointestinal endoscopy revealed a proliferating lesion below the second duodenal loop, roughly occupying half the circumference and a third of the lumen (figure 1). The pathological examination was compatible with a high-grade epithelial papillary neoplasm. Abdominal CT revealed an enlargement and heterogeneity of the head of the pancreas. The gland showed severe atrophy and multiple parenchymal calcifications (figure 2).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis should include periampullary neoplasms (ampulloma, cholangiocarcinoma or duodenal cancer) or

a pancreatic neoplasm arising in the background of chronic pancreatitis.

TREATMENT

Faced with these results, we made the diagnosis of pancreatic head carcinoma and the patient was referred for surgical resection (Whipple's operation). Macroscopically, the tumour was a vegetative, ulcerated lesion measuring approximately 4.2×4.4 cm, in contiguity with a pancreatic tumour measuring 5.5×6.9 cm (figure 3A). The architectural surface of the pancreas was severely disturbed showing multiple small parenchyma cysts measuring 1–2 mm in size. Histological examination was suggestive of an IPMN of the pancreatobiliary subtype with high-grade dysplasia and foci of well-differentiated adenocarcinoma invading the duodenum (figure 3B–D).

OUTCOME AND FOLLOW-UP

The postoperative period was uneventful and the patient was proposed for chemotherapy with gemcitabine. One year later, the patient has been diagnosed with disease recurrence and is receiving palliative care.

DISCUSSION

In recent years, owing to the development of more accurate imaging techniques, there has been a substantial rise in the diagnosis of IPMN.⁵ The natural history of IPMN is thought to be a consequence of duct obstruction and dilation from mucin accumulation, leading to the classic formation of multiple pancreatic cysts. Although previously thought to be benign, up to a quarter of patients with IPMN will develop chronic abdominal pain resembling acute pancreatitis, and half will eventually develop signs of pancreatic insufficiency similar to chronic pancreatitis.⁵ There has also been an increasing recognition that IPMN can progress to adenocarcinoma.³ Four subtypes of IPMN are currently recognised: gastric, intestinal, oncocytic and

Figure 3 (A) Macroscopic and microscopic pathological findings. (B) The mucinous epithelium showing multiple papillary projections; (C) the tumour consists of mucin-containing cuboidal cells with features of high-grade cellular atypia and (D) foci of well-differentiated adenocarcinoma can be seen invading the duodenal mucosa.

pancreatobiliary. The pancreatobiliary histological subtype is estimated to progress to tubular adenocarcinoma in over 50% of patients. This carcinoma resembles conventional ductal adenocarcinoma in both morphology, diagnosis and prognosis.⁶ Some authors have suggested that progression from adenoma to carcinoma can occur within 5–6 years.⁷ Nevertheless, several reports in the literature describe patients lacking a diagnosis for over two decades.^{8–9} Despite a highly symptomatic disease, our patient remained undiagnosed for over three decades, eventually developing pancreatic carcinoma. This makes our patient's the longest running case reported to date. Unfamiliarity with the diagnosis and the morphological changes induced by surgery may have contributed to the long delay between symptoms and diagnosis. Although not performed in our case, a biopsy at the time of surgery might have allowed for an earlier diagnosis. This is similar to the case reported by Abu-Hilal, where a palliative bypass controlled the patient's symptoms for over 20 years.⁸ Although unrecognised at the time of cholangiopancreatography, the finding of a 'bulging papilla with mucoid secretion' is nowadays referred to as the 'fish-eye sign', which, although observed in only about 25% of cases, is considered by some authors to be pathognomonic for IPMN.¹⁰ IPMNs appear to have distinct epidemiology and risk factors. Unlike typical chronic pancreatitis, patients are usually older women, smoke fewer cigarettes and consume less alcohol.¹¹ The development of insulin-dependent diabetes mellitus may be a clue to the development of malignant transformation similarly to ductal adenocarcinoma.¹² The diagnosis of IPMN typically includes cross-sectional imaging (MR with cholangiopancreatography or CT) or endoscopic ultrasound. All these methods are capable of identifying features associated with increased risk of malignancy

including mural nodules, thickened or enhancing cyst walls and pancreatic duct dilation. Endoscopic ultrasound with fine-needle aspiration can further improve diagnostic yield by providing tissue for analysis. Surgery remains the treatment of choice with excellent survival at 5 years in localised disease (70–100%). Survival in patients with advanced disease is more modest and roughly estimated at 40% in IPMN with an invasive component.^{13–14}

Acknowledgements The authors acknowledge Dr Cristina Ferreira for providing the anatomopathological examination and Professor José Velosa for reviewing the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Kosmahl M, Pauser U, Peters K, *et al.* Cystic neoplasms of the pancreas and tumor-like lesions with cystic features: a review of 418 cases and a classification proposal. *Virchows Arch* 2004;445:168–78.
- Allen PJ, D'Angelica M, Gonen M, *et al.* A Selective Approach to the Resection of Cystic Lesions of the Pancreas: Results From 539 Consecutive Patients. *Annals of Surgery* 2006;244:572–82.
- Longnecker D, Adsay N, Castillo C, *et al.* Histopathological diagnosis of pancreatic intraepithelial neoplasia and intraductal papillary-mucinous neoplasms: interobserver agreement. *Pancreas* 2005;31:344–9.
- Adsay N, Longnecker D, Klimstra D. Pancreatic tumors with cystic dilatation of the ducts: intraductal papillary mucinous neoplasms and intraductal oncocytic papillary neoplasms. *Semin Diagn Pathol* 2000;17:16–30.
- Balzano G, Zerbi A, Di Carlo V. Intraductal papillary mucinous tumors of the pancreas: incidence, clinical findings and natural history. *JOP* 2005;6(1 Suppl):108–11.
- Adsay N, Merati K, Basturk O, *et al.* Pathologically and biologically distinct types of epithelium in intraductal papillary mucinous neoplasms. *Am J Surg Pathol* 2004;28:839–48.
- Grützmann R, Niedergethmann M, Pilarsky C, *et al.* Intraductal papillary mucinous tumors of the pancreas: biology, diagnosis, and treatment. *Oncologist* 2010;15:1294–309.
- Abu-Hilal M, Salvia R, Casaril A, *et al.* Obstructive chronic pancreatitis and/or intraductal papillary mucinous neoplasms (IPMNs): a 21-year long case report. *JOP* 2006;7:218–21.
- Petrou A, Papalambros A, Brennan N, *et al.* Intraductal papillary mucinous neoplasm (IPMN) and chronic pancreatitis: overlapping pathological entities? Two case reports. *JOP* 2011;12:50–4.
- Maguchi H, Tanno S, Mizuno N, *et al.* Natural history of branch duct intraductal papillary mucinous neoplasms of the pancreas: a multicenter study in Japan. *Pancreas* 2011;40:364–70.
- Talamini G, Zamboni G, Salvia R, *et al.* Intraductal papillary mucinous neoplasms and chronic pancreatitis. *Pancreatol* 2006;6:626–34.
- Salvia R, Castillo C, Bassi C, *et al.* Main-duct intraductal papillary mucinous neoplasms of the pancreas. *Ann Surg* 2004;239:678–87.
- Sohn T, Yeo C, Cameron J, *et al.* Intraductal papillary mucinous neoplasms of the pancreas. *Ann Surg* 2004;239:788–99.
- Chari S, Yadav D, Smyrk T, *et al.* Study of recurrence after surgical resection of intraductal papillary mucinous neoplasm of the pancreas. *Gastroenterology* 2002;123:1500–7.

Learning points

- ▶ Intraductal papillary mucinous neoplasms (IPMNs) are the most common pancreatic cystic neoplasms and have malignant potential.
- ▶ Mucin production can lead to duct obstruction and dilation simulating acute and chronic pancreatitis.
- ▶ These lesions should be included in the differential diagnosis of idiopathic pancreatitis.
- ▶ Early resection of the main duct of IPMNs should be considered before malignant transformation, while side branch IPMN should be monitored and resection considered when it reaches 3 cm or presents worrisome signs (main duct dilation, mural nodules, significant symptoms or positive cytology).

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow