Pancreatic hamartoma: A rare and benign cause of pancreatic incidentaloma☆

Hamartoma pancreático: una causa benigna y poco frecuente de incidentaloma pancreático

Pancreatic hamartomas (PH) represent less than 1% of all hamartomas. They are composed of disorganized acinar, islet, and ductal cells[1,2]. Given their low incidence, it is difficult to differentiate them from other low-grade benign or malignant tumors, requiring pathological and immunohistochemical studies of the surgical specimen for definitive diagnosis[2]. We present the first case of PH described in Spain.

A 41-year-old male patient was evaluated at our hospital for an incidental finding of abdominal magnetic resonance imaging (MRI) of a 17 × 12 × 15 mm pancreatic mass. Blood levels of amylase, bilirubin, carcinoembryonic antigen, Ca 19-9, gastrin, and neuron-specific enolase were normal, as were 5-hydroxyindoleacetic acid levels.

After 10 months of follow-up, the abdominal MRI revealed a lesion in the pancreatic body measuring 20 × 18 × 17 mm that was hyperintense on T2, suggestive of a cystic component vs central necrosis, and slightly hypointense in the periphery with progressive enhancement in the portal and late phase (Fig. 1). Given the presence of a solid component, malignancy could not be ruled out. We suspected a neuroendocrine tumor and requested an octreotide scan, which was normal.

Endoscopic ultrasound revealed a 19 mm lesion in the body of the pancreas that was hypoechogenic, well defined and solid with a central cystic area. Fine-needle aspiration biopsy showed a columnar epithelium with mucinous cells and no atypia. The patient was initially diagnosed with a mucinous tumor (not intraductal mucinous papillary tumor), ruling out solid pseudopapillary tumor (SPT) or a neuroendocrine tumor.

Given the patient's age, the limited growth of the lesion and the inability to clarify its nature, we performed open spleen-preserving distal pancreatectomy (DP). Macroscopically, the mass was firm and whitish, measuring 1.8 × 1.8 cm. Microscopically, it consisted of randomly distributed ductal, acinar, and neuroendocrine structures embedded in a fibrocellular stroma, with no significant inflammatory infiltrates. Immunohistochemically, the stroma was positive for ß-catenin; negative for IgG, IgG4, synaptophysin, chromogranin, actin, CD34, S100, and Bcl2. In the end, the patient was diagnosed with PH.

The patient developed a type A pancreatic fistula, which was treated conservatively, and he was discharged on the 7th postoperative day with a pancreatic drainage tube, which was removed on the 10th postoperative day. After 5 months of follow-up, he has not presented recurrence of the disease.

PH are extremely rare. Described for the first time in 1977 by Anthony et al.[3], 43 cases have been published since, including the present one (Table 1). They can appear at any age, although the average age is 40–60 years. There is no tendency for PH to affect either sex. Most are either diagnosed incidentally or present with nonspecific signs and symptoms, such as abdominal pain or weight loss. Only one case has been reported that began with obstructive jaundice[4]. PH can appear anywhere in the pancreas, although most frequently in the head, with a size of 1.0–14.0 cm[5].

Two types of PH are distinguished according to the macroscopic findings: solid type and solid-cystic type[6]. On

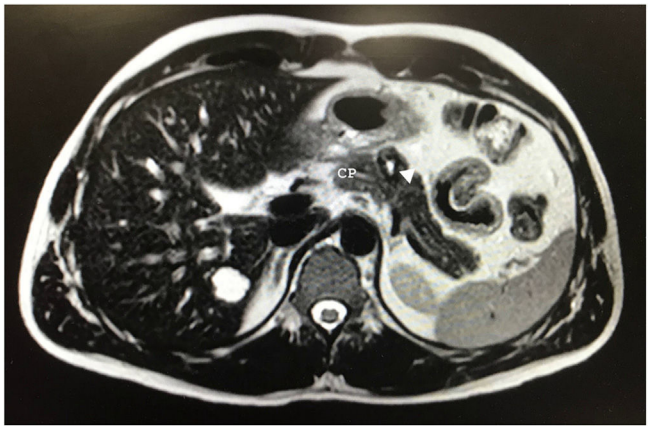

Fig. 1Magnetic resonance showing a 20-mm lesion, well defined and hyperintense in T2, in the body of the pancreas (white arrow) and its relationship with the pancreatic duct.

☆ Please cite this article as: Santana Valenciano Á, Molina Villar JM, Barranquero AG, Sanjuanbenito Dehesa A, Fernández Cebrián JM. Hamartoma pancreático: una causa benigna y poco frecuente de incidentaloma pancreático. Cir Esp. 2022;100:251–255.

Table 1 – Clinical-pathological characteristics of pancreatic hamartomas described in the literature (n = 43).

Author	Age	Sex	Symptoms	Location	Size (cm)	Dilatation of the pancreatic duct	Preoperative diagnosis	Image	Surgery	Pathological type	Follow-up (months/results
Anthony et al.[3] (1977)	46	M	Asymptomatic	Head	1.6	NR	NR	NR	PD	S/C	NR/NR
Anthony et al.[3] (1977)	35	M	Epigastric pain	Tail	Multiple	–	NR	NR	LR	NR	NR/NR
Anthony et al.[3] (1977)	58	M	Asymptomatic	Head	1	NR	NR	NR	Autopsy	NR	NR/Exitus
Burt et al.[11] (1983)	0	F	Hypoglycemia and hypercalcemia	Diffuse	11.5	–	NR	S	Total pancreatectomy	S	3/Exitus
Flaherty and Benjamin[12] (1992)	20 meses	F	Abdominal distension	Head	9	NR	NR	S/C	LR	S/C	9/alive
Izbicki et al.[13] (1994)	25	M	Epigastric pain	Head	10.6	NR	NR	S/C	PD	S/C	48/alive
Wu et al[14] (1998)	39	M	Abdominal pain and weight loss	Head	8	NR	NR	NR	PD	NR	9/alive
McFaul et al.[15] (2004)	29	M	Abdominal pain and weight loss	Head	1	–	NET	NR	PD-PP	NR	24/alive
McFaul et al.[15] (2004)	62	M	Abdominal pain and weight loss	Head	3.5	–	NR	NR	PD	NR	3/alive
Pauser et al.[16] (2005)	36	F	Epigastric pain	Head	7	–	NR	S/C	PD	S/C	15/NR
Pauser et al.[16] (2005)	55	F	Abdominal pain	Neck	3	–	NR	S/C			DP + splenectomy
S/C	23/ alive										
Pauser et al.[17] (2005)	51	M	Asymptomatic	Tail	3	–	Tumor of unknown origin	NR	LR	S	24/alive
Pauser et al.[17] (2005)	54	F	Abdominal pain	Body	2	–	NR	NR	DP	S	48/alive
Nagata et al.[1] (2007)	58	F	Asymptomatic	Body	2	–	NET	NR	DP	S	6/alive
Thrall et al.[18] (2008)	3	M	Abdominal pain	Head	3	NR	NR	S/C	PD	S/C	NR/NR
Sampelean et al.[19] (2009)	46	M	Abdominal mass	Head	8	NR	NR	NR	PD	S	NR/NR
Durczynski et al.[8] (2010)	69	M	Asymptomatic	Body	3	–	NR	NR	CP	S	55/alive
Kim et al.[2] (2012)	52	F	Abdominal pain	Head	2.2	–	SPT or cystic serous neoplasm	S/C	PD-PP	S/C	10/alive
Kawakami et al.[20] (2012)	78	F	Asymptomatic	Head	Multiple	–	Pancreatic carcinoma	S	DP	S	30/alive
Sueyoshi et al.[21] (2013)	14 meses	M	Abdominal distension	Tail	14	–	Pseudo-cystic blastoma	S/C	LR	S/C	26/alive
Yamaguchi et al.[6] (2013)	78	F	Asymptomatic	Head	1.7	NR	Pancreatic carcinoma	NR	NR	S	32/alive
Yamaguchi et al.[6] (2013)	61	F	Abdominal pain	Head	4	NR	SPT	NR	NR	S	7/alive
Yamaguchi et al.[6] (2013)	71	F	Asymptomatic	Body	5	NR	Cystic tumor	NR	NR	S/C	68/alive
Yamaguchi et al.[6] (2013)	59	F	Abdominal pain	Tail	1	NR	NET	NR	NR	S	10/alive
Yamaguchi et al.[6] (2013)	53	M	Abdominal pain	Head	8	NR	SPT	NR	NR	S/C	9/alive
Yamaguchi et al.[6] (2013)	53	M	Asymptomatic	Head	2.5	NR	Mass-forming pancreatitis	NR	NR	S/C	12/alive
Inoue et al.[4] (2014)	65	M	Obstructive jaundice	Head	4	+	NR	S	PD	S	36/alive
Addeo et al.[22] (2014)	61	F	Asymptomatic	Body	2.6	+	NR	S	Robotic		DP + splenectomy
S	NR/NR										
Shahbaz et al.[23] (2015)	62	F	Epigastric pain	Head	1.4	–	Pancreatic carcinoma	NR	PD	NR	NR/NR

Table 1 (*Continued*)

Author	Age	Sex	Symptoms	Location	Size (cm)	Dilatation of the pancreatic duct	Preoperative diagnosis	Image	Surgery	Pathological type	Follow-up (months/results
Zhang et al. (2016)[7]	53	F	Abdominal pain and weight loss	Head	2.3	–	Tumor of unknown origin	NR	PD	S	55/alive
Nagano et al.[24] (2017)	72	F	Asymptomatic	Head	2	+	NR	NR	PD-PP subtotal	S	36/alive
Delgado et al.[25] (2017)	0	F	Asymptomatic	NR	1.2	–		NR	Autopsy	S/C	NR/Exitus
Han et al[9] (2018)	35	F	Hypoglycemia	Tail	1	–	NET	S	DP	S/C	NR/NR
Tanaka et al.[26] (2018)	54	M	Asymptomatic	Body	3.6	NR	IPMN, malignant lipomatous tumor	S	DP	S lipomatous	NR/NR
Tanaka et al.[26] (2018)	74	M	Asymptomatic	Head	5	NR	Lipoma	S	PD	S lipomatous	NR/NR
Tanaka et al.[26] (2018)	67	M	Asymptomatic	Tail	6.5	NR	Liposarcoma	NR	DP	S/C lipomatous	NR/NR
Shin et al.[27] (2019)	54	F	Asymptomatic	Head	2.2	–	SPT or NET	NR	Robotic PD-PP	S	6/alive
Nahm et al.[28] (2019)	42	F	Abdominal pain	Neck	2.8	–	SPT	S/C	CP	S/C	8/alive
Hosfield et al.[29] (2019)	4	M	Abdominal pain, steatorrhea	Head	9.5	NR	SPT,				
pancreatoblastoma, IPMN	S/C	PD	S/C	1/alive							
Cui et al.[5] (2020) ()	57	F	Asymptomatic	Head	3	–	NET	S/C	PD	S/C	34/alive
Cui et al.[5] (2020)	69	M	Asymptomatic	Head	1.5	–	Tumor of unknown origin	S	PD	S	44/alive
Toyama et al.[10] (2020)	53	M	Asymptomatic	Head	3.7	–	NET, IPMN, SPT hemangioma	S/C	PD	S/C	NR/NR
Caso actual (2020)	41	M	Asymptomatic	Body	1.8	–	Mucinous tumor	S/C	DP	S/C	5/alive

PD: pancreaticoduodenectomy; PD-PP: PD with preservation of the pylorus; F: female; M: male; NR: no reported; CP: central pancreatectomy; DP: distal pancreatectomy; LR: local resection; S: solid; S/C: solid and cystic; NET: neuroendocrine tumor; IPMN: intraductal papillary mucinous neoplasms; SPT: solid pseudopapillary tumour.

[11]Pediatr Radiol. 1983;13:287-9.
[12]Hum Pathol. 1992;23:1309-12.
[13]Am J Gastroenterol. 1994;89:1261-2.
[14]Histopathology. 1998;33:485-7.
[15]Pancreatology. 2004;4:533-8.
[16]Am J Surg Pathol. 2005;29:797-800.
[17]Mod Pathol. 2005;18:1211-6.
[18]Pediatr Dev Pathol. 2008;11:314-20.
[19]J Gastrointest Liver Dis. 2009;18:483-486.
[20]World J Gastrointest Oncol. 2012;4:202.
[21]Int J Surg Case Rep. 2013;4:98-100.
[22]Surg (United States). 2014;156:1284-5.
[23]Am J Gastroenterol. 2015;110:S109.
[24]BMC Gastroenterol. 2017;17(1):146.
[25]Autops Case Reports. 2017;7(4):26-29.
[26]Am J Surg Pathol. 2018;42(7):891-7.
[27]Ann Hepato-Biliary-Pancreatic Surg. 2019;23:286.
[28]ANZ J Surg. 2019;89:E265-E267.
[29]J Pediatr Surg Case Reports. 2019;48:101258.

ultrasound, they appear to be hypoechoic masses with well-defined margins[4,5,7,8].

On computed tomography scans, PH are usually well defined, with a slightly unequal density in solid lesions, hypo- or isodense, with progressive heterogeneous enhancement in late phases. The margins are typically well defined after contrast enhancement[1,2,5,9]. Contrarily, pancreatic adenocarcinomas are characterized by low enhancement and the invasion of adjacent structures, while NET show clear enhancement in the initial phases after contrast[5,9]. SPT are similar but usually present encapsulation and peripheral calcifications[10]. Therefore, PH should be included in the differential diagnosis of pancreatic incidentalomas.

On MRI, the contour is regular, with well-defined edges in T2. The intensity of the interior of the lesion is slightly heterogeneous, hypointense on T1 and iso- or hyperintense on T2[5,7,9].

Microscopically, PH are composed of a variable proportion of acinar, ductal, and endocrine cells arranged in a disorganized manner, so fine-needle aspiration is not effective. The solid component consists of fibroadipose tissue, while the cystic component is made up of dilated pancreatic ducts. They present differentiated acinar cells, without forming well-organized lobules[1,6,7], and characteristically lack 3 structures: concentric elastic fibers around the pancreatic ducts, peripheral nerves, and well-formed Langerhans islets. This distinguishes PH from chronic pancreatitis and hamartoma of the pancreatic duct, where these 3 structures are well preserved[6].

Although PH is a benign disease, most patients undergo surgical resection because it is impossible to rule out malignant disease. Given the higher frequency of malignancy or premalignancy in pancreatic incidentalomas, surgery is the indicated treatment, be it pancreaticoduodenectomy, DP, or conservative surgery (central pancreatectomy or enucleation), even though this may be too aggressive in the case of benign tumors[8].

Some authors suggest that conservative surgery should be performed to preserve the integrity of the gastrointestinal tract and the endocrine and exocrine function of the pancreas and spleen due to the indolent nature of this tumor[7]. We opted for spleen-preserving DP due to the initial suspicion, and we decided against performing parenchyma-sparing surgery due to the risk of fistula, given the proximity of the tumor to the main pancreatic duct (Fig. 1).

REFERENCES

1. Nagata S, Yamaguchi K, Inoue T, Yamaguchi H, Ito T, Gibo J, et al. Solid pancreatic hamartoma. Pathol Int. 2007;57:276–80.
2. Kim HH, Cho CK, Hur YH, Koh YS, Kim JC, Kim HJ, et al. Pancreatic hamartoma diagnosed after surgical resection. J Korean Surg Soc. 2012;83:330–4.
3. Anthony PP, Faber RG, Russell RCG. Pseudotumours of the pancreas. Br Med J. 1977;1:814.
4. Inoue H, Tameda M, Yamada R, Tano S, Kasturahara M, Hamada Y, et al. Pancreatic hamartoma: a rare cause of obstructive jaundice. Endoscopy. 2014;46:157–8.
5. Cui H, Lian Y, Chen F. Imaging findings for pancreatic hamartoma: two case reports and a review of the literature. BMC Gastroenterol. 2020;20:1–5.
6. Yamaguchi H, Aishima S, Oda Y, Mizukami H, Tajiri T, Yamada S, et al. Distinctive histopathologic findings of pancreatic hamartomas suggesting their ''hamartomatous'' nature: a study of 9 cases. Am J Surg Pathol. 2013;37:1006–13.
7. Zhang J, Wang H, Tang X, Jiang Q, Wang C. Pancreatic hamartoma, a rare benign disease of the pancreas: a case report. Oncol Lett. 2016;11:3925–8.
8. Durczynski A, Wiszniewski M, Olejniczak W, Polkowski M, Sporny S, Strzelczyk J. Asymptomatic solid pancreatic hamartoma. Arch Med Sci. 2011;7:1082–4.
9. Han YE, Park BJ, Sung DJ, Kim MJ, Han NY, Sim KC, et al. Computed tomography and magnetic resonance imaging findings of pancreatic hamartoma: a case report and literature review. Clin Imaging. 2018;52:32–5.
10. Toyama K, Matsusaka Y, Okuda S, Miura E, Kubota N, Masugi Y, et al. A case of pancreatic hamartoma with characteristic radiological findings: radiological-pathological correlation. Abdom Radiol. 2020. http://dx.doi.org/10.1007/s00261-020-02425-6.
11. Burt TB, Condon VR, Matlak ME. Fetal pancreatic hamartoma. Pediatr Radiol. 1983;13:287–9.
12. Flaherty MJ, Benjamin DR. Multicystic pancreatic hamartoma: a distinctive lesion with immunohistochemical and ultrastructural study. Hum Pathol. 1992;23:1309–12.
13. Izbicki JR, Knoefel WT, Miiller-Höcker J, Mandelkow UK. Pancreatic hamartoma: a benign tumor of the pancreas. Am J Gastroenterol. 1994;89:1261–2.
14. Wu SS, Vargas HI, French SW. Pancreatic hamartoma with Langerhans cell histiocytosis in a draining lymph node. Histopathology. 1998;33:485–7.
15. McFaul CD, Vitone LJ, Campbell F, Azadeh B, Hughes ML, Garvey CJ, et al. Pancreatic hamartoma. Pancreatology. 2004;4:533–8.
16. Pauser U, Kosmahl M, Kruslin B, Klimstra DS, Klöppel G. Pancreatic solid and cystic hamartoma in adults. Am J Surg Pathol. 2005;29:797–800.
17. Pauser U, Da Silva MTS, Placke J, Klimstra DS, Klöppel G. Cellular hamartoma resembling gastrointestinal stromal tumor: a solid tumor of the pancreas expressing c-kit (CD117). Mod Pathol. 2005;18:1211–6.
18. Thrall M, Jessurun J, Stelow EB, Adsay NV, Vickers SM, Whitson AK, et al. Multicystic adenomatoid hamartoma of the pancreas: a hitherto undescribed pancreatic tumor occurring in a 3-year-old boy. Pediatr Dev Pathol. 2008;11:314–20.
19. Sampelean D, Adam M, Muntean V, Hanescu B, Domsa I. Pancreatic hamartoma and SAPHO syndrome: a case report. J Gastrointest Liver Dis. 2009;18:483–6.
20. Kawakami F, Shimizu M, Yamaguchi H, Hara S, Matsumoto I, Ku I, Itoh T. Multiple solid pancreatic hamartomas: a case report and review of the literature. World J Gastrointest Oncol. 2012;4:202.
21. Sueyoshi R, Okazaki T, Lane GJ, Arakawa A, Yao T, Yamataka A. Multicystic adenomatoid pancreatic hamartoma in a child: case report and literature review. Int J Surg Case Rep. 2013;4:98–100.
22. Addeo P, Tudor G, Oussoultzoglou E, Averous G, Bachellier P. Pancreatic Hamartoma Surg (United States). 2014;156:1284–5.
23. Shahbaz O, Patel M. Pancreatic hamartoma: a mimicker of pancreatic adenocarcinoma. Am J Gastroenterol. 2015;110:S109.
24. Nagano H, Nakajo M, Fukukura Y, Kajiya K, Tani A, Tanaka S, et al. A small pancreatic hamartoma with an obstruction of the main pancreatic duct and avid FDG uptake mimicking

a malignant pancreatic tumor: a systematic case review. BMC Gastroenterol. 2017;17:146.
25. Delgado PI, Correa-Medina M, Rojas CP. Pancreatic hamartoma in a premature Trisomy 18 female. Autops Case Rep. 2017;7:26–9.
26. Tanaka M, Ushiku T, Ikemura M, Takazawa Y, Igari T, Shimizu M, et al. Pancreatic lipomatous hamartoma. A hitherto unrecognized variant. Am J Surg Pathol. 2018;42:891–7.
27. Shin DH, Rho SY, Hwang HK, Lee WJ, Kang CM. A case of pancreatic hamartoma pathologically confirmed after robot-assisted pancreaticoduodenectomy. Ann Hepato-Biliary-Pancreatic Surg. 2019;23:286.
28. Nahm CB, Najdawi F, Reagh J, Kaufman A, Mittal A, Grill AJ, et al. Pancreatic hamartoma: a sheep in wolf's clothing. ANZ J Surg. 2019;89:E265–7.
29. Hosfield BD, Grayson BL, Nakeeb A, Albright EA, Markel TA. Multicystic adenomatoid hamartoma of the pancreas. J Pediatr Surg Case Rep. 2019;48101258.

Ángela Santana Valenciano*, José Manuel Molina Villar, Alberto G. Barranquero, Alfonso Sanjuanbenito Dehesa, José María Fernández Cebrián

Servicio de Cirugía General y del Aparato Digestivo, Hospital Universitario Ramón y Cajal, Madrid, Spain

*Corresponding author.
E-mail address: santanavalenciano.a@gmail.com
(Á. Santana Valenciano).

http://dx.doi.org/10.1016/j.cireng.2022.03.010
2173-5077/