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CASE REPORT

Acinar cell carcinoma of the pancreas in childhood

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Abstract A 12-year-old Japanese girl with pancreatic acinar cell carcinoma is presented. She was referred to our hospital with upper abdominal pain on exercise. Computed tomography scan showed a 17 × 17 × 12 cm heterogeneous mass in the right abdominal cavity centering around the pancreatic head to the anterior pararenal space. We performed pylorus-preserving pancreatoduodenectomy, because the tumor invaded the pancreatic head. Macroscopically, the tumor was a 19 × 18 cm, encapsulated mass derived from the pancreatic head without invasion to the surrounding organs, and consisted of solid and cystic portions. Histological examination showed tumor cells proliferating in an acinar pattern and invading the duodenal muscle layer. Immunohistochemically, tumor cells were positive for α1 trypsin and α1 chymotrypsin. From these histological findings, we diagnosed the lesion as an acinar cell carcinoma of the pancreas. We report this case of childhood acinar cell carcinoma, which is extremely rare, with a review of the literature.

Keywords Acinal cell carcinoma · Pancreas · Childhood · α-Fetoprotein

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Abbreviations

ACC	Acinar cell carcinoma
AFP	α-Fetoprotein

Introduction

Acinar cell carcinoma (ACC) of the pancreas is a rare cancer that originates from acinar cells in the pancreatic parenchyma and accounts for approximately 1 % of pancreatic exocrine malignancies [1, 2]. Reports of ACC in children are very rare, with only 25 cases in the literature. Since adult ACC is also rare, the prognosis has been unclear due to lack of data. Large-scale studies have been published recently, and the results have suggested that ACC has a better prognosis than pancreatic ductal carcinoma. However, the prognosis of pediatric ACC remains unclear due to the scarcity of reports. Here, we report a 12-year-old Japanese girl who underwent radical resection of pancreatic ACC, and we also review the relevant literature.

Case report

A 12-year-old girl developed upper abdominal pain on exercise that was improved by rest. However, mild upper abdominal pain persisted and the patient consulted a local physician after 3 days. Imaging studies revealed a very large mass in the abdomen, and the patient was referred to our department. There was no relevant past history or family history. On examination, a poorly mobile periumbilical mass was palpated and abdominal tenderness was noted. Blood chemistry tests did not show any abnormalities. Regarding tumor markers, AFP was increased to

173.1 ng/ml and elastase 1 was elevated to 36,440 ng/dl, but CEA, CA19-9, and DUPAN-2 were normal at 0.8 ng/l, <0.2 and <25 U/ml, respectively (Table 1). CT scans showed a 17 × 17 × 12 cm mass lesion with a clear and regular margin that occupied the right abdominal cavity, being centered around the right anterior pararenal space posterior to the head of the pancreas and below the liver. The mass was heterogeneous, containing cystic areas and solid areas with uneven contrast enhancement. No dilation of the bile ducts or pancreatic duct was noted. The duodenum was displaced laterally, but there was no evidence of ileus. The large and small intestines were markedly displaced to the left by the mass, but the right ureter was not dilated. The border between the mass and the liver parenchyma was clear. No metastasis to other organs was identified (Fig. 1a–d). MRI revealed that mass contained a small amount of fat. On T2-weighted images, the solid areas showed a high signal intensity, as well as slow and uneven contrast enhancement (Fig. 1e). On PET scanning, the solid areas of the mass were seen as hot spots (SUV-max = 2.7), but there were no hot spots suggestive of metastasis. From these findings, a retroperitoneal tumor (e.g., immature teratoma) or a pancreatic tumor (e.g., solid pseudopapillary tumor) was suspected, and surgery was performed. At operation, the tumor was continuous with the head of the pancreas, but there was no invasion of other organs. Accordingly, we performed pylorus-preserving pancreatoduodenectomy with D1 (+12, 8a) lymphadenectomy and reconstruction by the modified Child procedure, and pancreatojejunostomy with complete drainage (Fig. 2a). The resected specimen contained a tumor measuring 19 × 18 cm that arose from the head of the pancreas, and the cut surface showed both yellowish-white solid areas and cystic areas (Fig. 2b–d). The cysts were filled with brown liquid that was considered to represent old blood. Histopathological examination demonstrated tumor cells with an acinar pattern of proliferation that had small round nuclei, mild atypia, and eosinophilic cytoplasm (Fig. 3a, b). The tumor had a fibrotic capsule and featured internal hemorrhage and necrosis. It invaded the adjacent pancreatic tissue and duodenal muscle layer through the capsule, but no vascular invasion was noted. All of the resection margins were negative. The results of immunostaining were as follows: α1 trypsin (+) (Fig. 3c), α1 chymotrypsin (+) (Fig. 3d), S-100 (−), NSE (−), chromogranin A (−), synaptiphysin (−), amylase (−), vimentin (−), β-catenin (cell membrane (+), nucleus (−)), CD10 (+), CD56 (−), ER (−), and PgR (−). In addition, AFP was slightly positive in some areas (Fig. 3e). These findings were consistent with a diagnosis of ACC of the pancreas (T3N0M0, stage IIA). No complications occurred after surgery, and the patient was discharged on the 32nd postoperative day. Since the tumor was of low malignancy and radical surgery was performed, postoperative adjuvant chemotherapy was not given. AFP and elastase-1 levels were elevated preoperatively, but were normalized after surgery and did not increase again during the follow-up period. At present (52 months after surgery), the patient is alive without recurrence. She has no postoperative growth disorder, and no symptoms such as abdominal pain or diarrhea. Her height and body weight were low before surgery, being 132.5 cm (−2.2 SD) and 29.4 kg (−1.3 SD), respectively, but showed improvement to 154.7 cm (−0.6 SD) and 53.9 kg (−0.1 SD) at the latest review.

Discussion

Because ACC is rare, only a few patients have been reported from each institution and there is no consensus concerning the treatment or prognosis. The first large-scale study was published in 2007, which was a report by Kitagami et al. on 115 patients with pancreatic ACC in the Cancer Registry of the Japan Pancreas Society [3]. Resection was performed in 76.5 % of these patients, and their 5-year survival rate was 43.9 % (median survival

Table 1 Laboratory data for the patient (normal range)

WBC	5600/μℓ		(3400–9600)	Amy	100	IU/ℓ	(40–126)
Hb	12.9	g/dℓ	(10.9–15.1)	Cr	0.49	mg/dℓ	(0.5–1.0)
Plt	30.7 × 104	/μℓ	(12.9–41.0 × 104)	BUN	9	mg/dℓ	(8–20)
TP	7.9	g/dℓ	(6.5–8.3)	Tumor markers			
Alb	4.5	g/dℓ	(3.8–5.2)	AFP	173.1	ng/mℓ	(−13.4)
T-Bil	7.9	mg/dℓ	(0.2–1.2)	Elastase-1	36,440	ng/dℓ	(−300)
AST	26	IU/ℓ	(13–34)	CEA	0.8	ng/mℓ	(−5.0)
ALT	11	IU/ℓ	(8–37)	CA19-9	<0.2	U/mℓ	(−37.0)
LDH	233	IU/ℓ	(119–214)	DUPAN-2	<25	U/mℓ	(−150)
ALP	480	IU/ℓ	(107–340)	NSE	10.5	ng/mℓ	(−12.0)
γ-GTP	5	IU/ℓ	(9–44)	HCG-β	≤0.1	ng/mℓ	(−0.10)
ChE	272	IU/ℓ	(217–491)	CA125	29.2	U/mℓ	(−35.0)

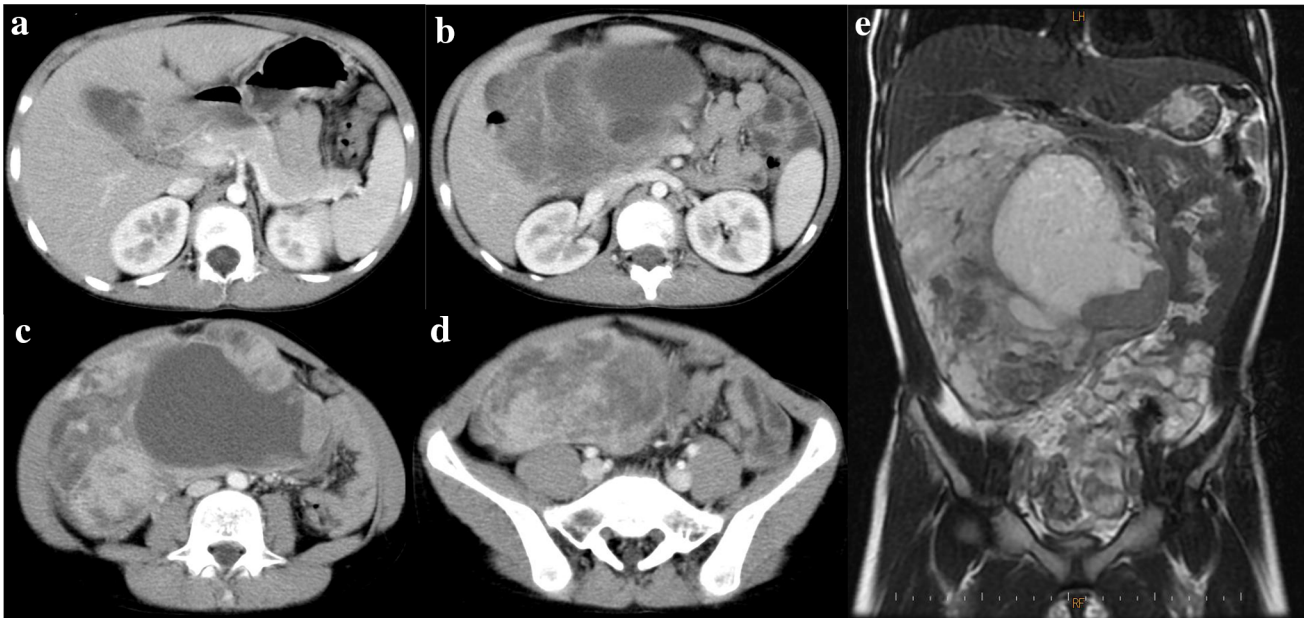

Fig. 1 Enhanced CT (**a**–**d**) and MR (**e**) images of the pancreatic acinar cell carcinoma. A 17 × 17 × 12-cm, heterogeneous mass occupied the right abdominal cavity. The tumor had solid and cystic lesions, and the solid lesion showed enhanced heterogeneity

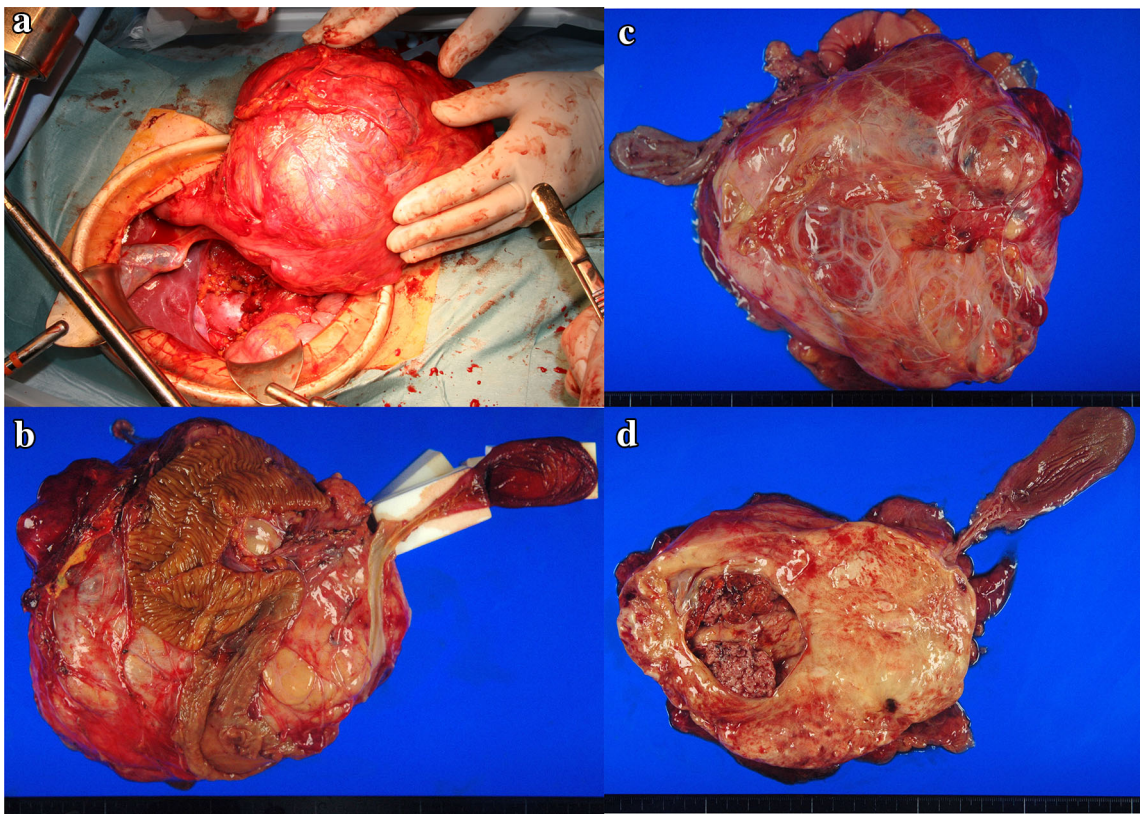

Fig. 2 Scene of the operation (**a**). A pylorus-preserving pancreatoduodenectomy was performed, because the tumor invaded the pancreatic head. Macroscopic findings (**b**–**d**). The tumor was an encapsulated 19 × 18-cm mass derived from the pancreatic head, and the cut surface (**d**) had yellowish white solid parts and cystic parts

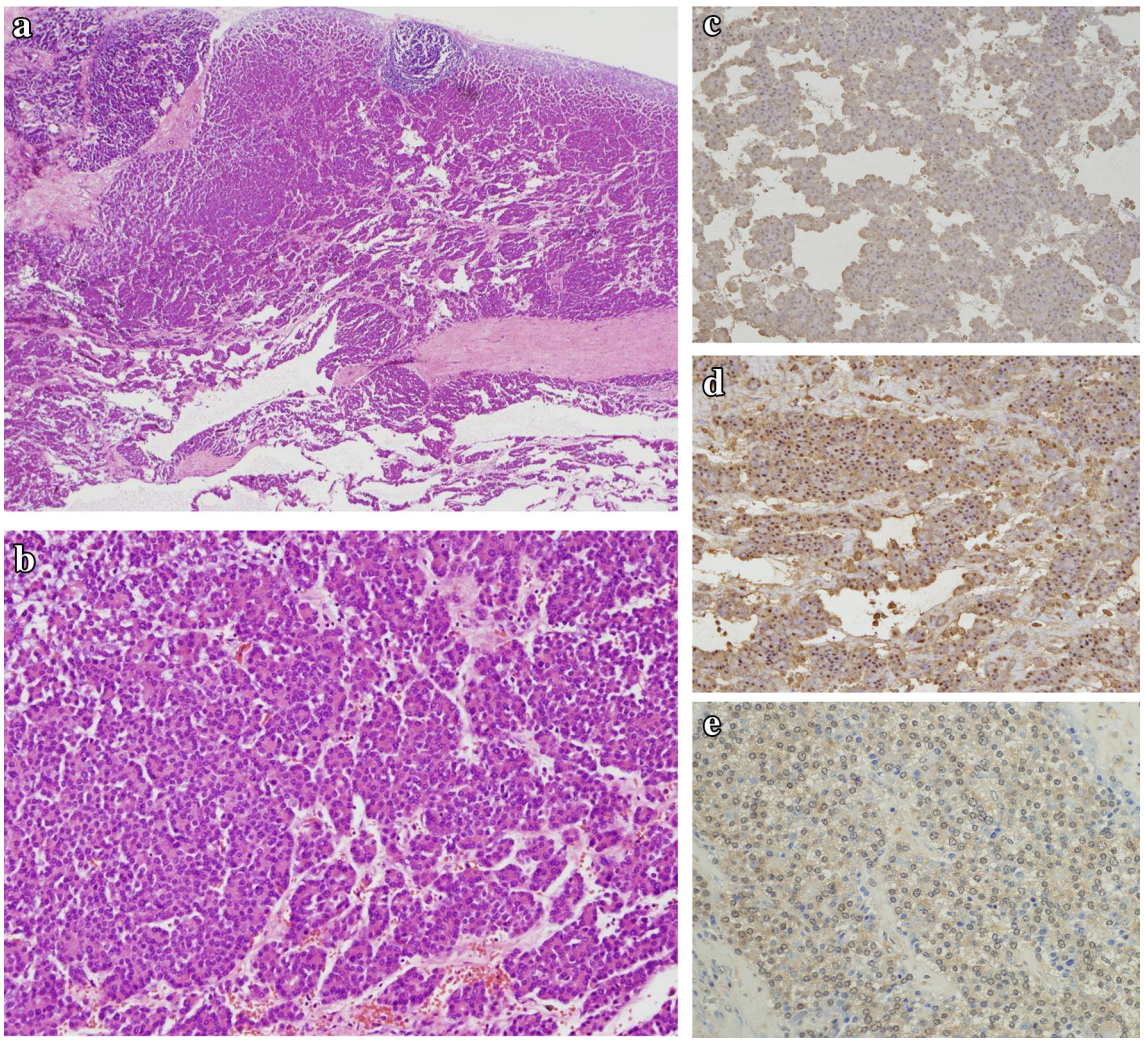

Fig. 3 Histological examination. The tumor cells had small, round nuclei with mild atypia, and showed an acinar arrangement. **a** hematoxylin and eosin (H&E) stain, ×. **b** H&E stain, ×. Immunohistochemically, tumor cells showed positive staining for α1 trypsin, α1 chymotrypsin, and AFP. **c** Immunohistochemical staining of α1 trypsin (×). **d** Immunohistochemical staining of α1 chymotrypsin (×). **e** Immunohistochemical staining of AFP (×)

time: 41 months). In 2008, Nicolas et al. published an analysis of 672 patients with pancreatic ACC registered in the Surveillance, Epidemiology, and End Results (SEER) database, reporting a resection rate of 38.7 % and a 5-year survival rate after resection of 71.6 % (median 123 months) [4]. However, the 5-year survival rate of unresectable patients was 0 % according to Kitagami et al. and 22 % according to Nicolas et al., indicating that unresectable ACC has a very poor prognosis. Despite differences between the two reports, which are considered to be due to differences of the surgical indications, the data at least suggest that the prognosis of resectable ACC is more favorable than that of pancreatic ductal carcinoma and that resectable tumors should be treated surgically. Chemotherapy and radiotherapy could also be considered, but there are insufficient data on the efficacy of these modalities for ACC and large-scale studies are needed.

There have been fewer reports of pancreatic ACC in children, and no large-scale analyses. Among 55 cases of pancreatic exocrine tumors in patients aged 16 years or younger accumulated in Germany by Ellerkamp et al. [5] between 1980 and 2007, 5 patients had ACC and this is the largest series. In addition, Dall'igna et al. [6] reviewed 21 patients aged 18 years or younger with pancreatic tumors reported in Italy between 2000 and 2009, including 2 cases of ACC. Table 2 summarizes the 26 reported pediatric cases, including the patients from the above reports and our case [5–21]. Although the details are often unclear, the following characteristics of pediatric ACC can be suggested: (1) the tumors tend to be very large at diagnosis, (2) distant metastasis is rare and in most cases lesions are

Table 2 Case of acinar cell carcinoma in childhood in the literature

Case	Age/sex	Size	Stage	Treatment	Follow-up	AFP	References
1	13/F	ND	N0M0	DP	14 M, dead	7582 μg/L↑	Ellerkamp V [5]
2	7/F	ND	N0M0	DP	72 M, D-free	32,000 μg/L↑	Ellerkamp V [5]
3	16/M	ND	N1M1	PD	36 M, dead	19,856 μg/L↑	Ellerkamp V [5]
4	15/M	ND	N × M1	Biopsy	ND	5387 μg/L↑	Ellerkamp V [5]
5	11/M	ND	N × M1	Biopsy	28 M, dead	1546 μg/L↑	Ellerkamp V [5]
6	3/F	15 cm (head)	N × M0	TP	15 M, D-free	1520 kIU/L↑	Matarazzo P [8]
7	7/M	16 cm (body)	N0M0	Resection	24 M, alive	Normal	Dall'Igna P [6]
8	6/F	9 cm (head)	N0M0	Resection	3 M, alive	Positive↑	Dall'Igna P [6]
9	10/M	13 cm (tail)	N × M0	DP	24 M, D-free	ND	Tapia B [9]
10	10/M	10 cm (body)	ND	Biopsy	2Y, died	7664 IU/ml↑	Illees G [10]
11	4/M	18 cm (head)	N0M0	PD	12 M, D-free	ND	Huang Y [11]
12	14/M	11 cm (head)	ND	PD	ND	43 μg/ml↑	Rouleau C [12]
13	16/F	ND (tail)	N0M0	DP	3Y, D-free	ND	Shorter NA [13]
14	10/M	ND	N × M0	Resection	8Y, D-free	ND	Kimstra DS [14]
15	10/M	8 cm	ND	Resection	10 M, dead	ND	Kimstra DS [14]
16	6/F	8 cm	N × M0	Resection	13Y, D-free	ND	Ichijima K [7]
17	3/F	8 cm (head)	ND	PD	20 M, dead	ND	Lack EE [15]
18	1/M	8 cm (head)	ND	PD	35 M, dead	ND	Lack EE [15]
19	9/M	20 cm (head)	N × M1	Biopsy	28 M, dead	ND	Osborne BM [16]
20	10/F	6 cm	N × M0	Resection	15 M, D-free	ND	Taxy JB [17]
21	6/M	12 cm (body)	N0M0	DP	1Y, D-free	ND	Wilander E [18]
22	9/M	8 cm	ND	PD	10 M, dead	Normal	Mah PT [19]
23	7/M	ND	ND	PD	26 M, alive	ND	d'Ambrosio G [20]
24	6/F	ND	ND	PD	41 M,alive	ND	d'Ambrosio G [20]
25	6/M	12 cm (ectopic)	N0M0	Resection	5 M, D-free	1393 ng/ml↑	Sharma S [21]
26	12/F	19 cm (head)	N0M0	PD	52 M, D-free	173 ng/ml↑	Our case

M male, *F* female, *ND* no data, *DP* distal pancreatectomy, *PD* pancreaticoduodenectomy, *TP* total pancreatectomy, *D-free* disease-free alive, *M* months, *Y* years

resectable, (3) patients who undergo resection show long survival and a high long-term survival rate, and (4) many patients have a high AFP level. Similarly to adult ACC, long-term survival can be expected after radical surgical resection.

One characteristic of ACC in children is that all of the tumors were very large masses ranging from 6 to 20 cm in diameter, probably because asymptomatic children are rarely examined for tumors. Despite the large size of their tumors, few of the patients had distant metastasis. There was no mention of lymph node metastasis in the other reports. Since the tumors were very large and preoperative diagnosis was difficult, it is likely that few patients underwent lymphadenectomy. With respect to adult patients, Kitagami et al. [3] reported that the disease was N0 in 57.6 % of 115 patients with ACC, suggesting that lymph node metastasis is less frequent than in pancreatic ductal carcinoma. In our patient, the tumor was also very large (19 cm in diameter), but there was no distant metastasis or lymph node involvement. On the basis of these results, surgery should be the first option even in children and even if the tumor is very large. However, considering the possibility of long-term survival and subsequent growth of juvenile patients, it is important to avoid lymphadenectomy around the pancreatic head plexus. The AFP level was high in most patients in whom it was measured, although AFP was not mentioned in many reports. In adult patients, Shimizu et al. [22] reported that ACC accounted for 27 % of AFP-producing pancreatic tumors and that AFP is frequently elevated in patients with this disease. AFP was also elevated in our patient. Therefore, an increase of AFP may be frequent in ACC patients and it seems to be a useful tumor marker, particularly in children.

In conclusion, we encountered a 12-year-old girl with pancreatic ACC who underwent surgical resection. At

present, she is alive without recurrence at 52 months after surgery, and we hope for long-term survival, as reported in many cases. Many points about ACC remain unclear because of the small number of cases, including the usefulness of postoperative adjuvant chemotherapy, but information regarding effective treatment is expected to increase with accumulation of further reports.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Chen J, Baithun SI (1985) Morphological study of 391 cases of exocrine pancreatic tumors with special reference to the classification of exocrine pancreatic carcinoma. J Pathol 146:17–29
2. Cubilla AL, Fitzgerrald PJ (1984) Tumors of the exocrine pancreas. In: Hartmann WH, Sobine LH (eds) Atlas of tumor pathology, 2nd ser, fasc 19. Armed Forces Institute of Pathology, Washington DC, pp 208–212
3. Kitagami H, Kondo S, Hirano S et al (2007) Acinar cell carcinoma of the pancreas: clinical analysis of 115 patients from Pancreatic Cancer Registry of Japan Pancreas Society. Pancreas 35:42–46
4. Wisnoski NC, Townsend CM, Nealon WH et al (2008) 672 Patients with acinar cell carcinoma of the pancreas: a population-based comparison to pancreatic adenocarcinoma. Surgery 144:141–148
5. Ellerkamp V, Warmann SW, Vorwerk P et al (2012) Exocrine pancreatic tumors in childhood in Germany. Pediatr Blood Cancer 58:366–371
6. Dall'Igna P, Cecchetto G, Bisogno G et al (2010) Pancreatic tumors in children and adolescents: the Italian TREP project experience. Pediatr Blood Cancer 54:675–680
7. Ichijima K, Akaishi K, Toyoda N et al (1985) Carcinoma of the pancreas with endocrine component in childhood. Am J Clin Pathol 83:95–100
8. Matarazzo P, Tuli G, Tessaris D et al (2011) Cushing syndrome due to ectopic adrenocorticotropic hormone secretion in a 3-year-old child. J Pediatr Endocrinol Metab 24:219–222
9. Tapia B, Ahrens W, Kenney B et al (2008) Acinar cell carcinoma versus solid pseudopapillary tumor of the pancreas in children: a comparison of two rare and overlapping entitles with review of the literature. Pediatr Dev Pathol 11:384–390
10. Illés G, Luczay A, Benyó G et al (2007) Cushing's syndrome in a child with pancreatic acinar cell carcinoma. Endocr Pathol 18:95–102
11. Huang Y, Cao YF, Lin JL et al (2006) Acinar cell cystadenocarcinoma of the pancreas in a 4-year-old child. Pancreas 33:311–312
12. Rouleau C, Serre I, Roger P et al (2005) Acinar cell carcinoma of the pancreas in a young patient with cells immunoreactive for somatostatin. Histopathology 48:306–309
13. Shorter NA, Glick RD, Klimstra DS et al (1967) Malignant pancreatic tumors in childhood and adolescence: the Memorial Sloan-Kettering experience, 1967 to present. J Pediatr Surg 37:887–892
14. Kimstra DS, Heffess CS, Oertel JE et al (1992) Acinar cell carcinoma of the pancreas. A clinicopathologic study of 28 cases. Am J Surg Pathol 16:815–837
15. Lack EE, Cassady JR, Levey R et al (1983) Tumors of the exocrine pancreas in children and adolescents. A clinical and pathologic study of eight cases. Am J Surg Pathol 7:319–327
16. Osborne BM, Culbert SJ, Cangir A et al (1977) Acinar cell carcinoma of the pancreas in a 9-year-old child: case report with electron microscopic observations. South Med J 70:370–372
17. Taxy JB (1976) Adenocarcinoma of the pancreas in childhood. Report of a case and a review of the English language literature. Cancer 37:1508–1518
18. Wilander E, Sundström C, Meurling S et al (1976) A highly differentiated exocrine pancreatic tumour in a young boy. Acta Paediatr Scand 65:769–772
19. Mah PT, Loo DC, Tock EP (1974) Pancreatic acinar cell carcinoma in childhood. Am J Dis Child 128:101–104
20. d'Ambros G, del Prete L, Grimaldi C et al (2014) Pancreaticoduodenectomy for malignancies in children. J Pediatr Surg 49:534–538
21. Sharma S, Agarwal S, Nagendla MK et al (2015) Omental acinar cell carcinoma of pancreatic origin in a child: a clinicopathological rarity. Pediatr Surg Int 32:307–311
22. Shimizu E, Kikuyama M, Hashimoto M et al (1996) A case of alpha-fetoprotein-producing pancreatic carcinoma: review of 41 cases reported in Japan (in Japanese). Nihon Shokakibyo Gakkai Zasshi 93:921–926