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Original Article

Solid pseudopapillary neoplasm of the pancreas in children: a clinical and pathological study of 16 cases

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Abstract: Introduction: Solid pseudopapillary neoplasm of the pancreas is an uncommon pancreatic neoplasm with malignant potential. There are many unique differences between children and adults in solid pseudopapillary neoplasm of the pancreas. Our study aimed to illustrate the clinical and pathological features of solid pseudopapillary neoplasm of the pancreas in children. Method: The clinical and pathological data of 16 pediatric cases of solid pseudopapillary neoplasm of the pancreas were retrieved and reviewed from the medical records in the Kunming Children's Hospital. Results: There were 11 girls and 5 boys, the sex ratio was 2.2:1 (female-to-male); the median age was 9.5 years, and the average age was 9.56±3.65 years (ranging from 3 to 15 years). The chief complaint was abdominal pain (8/16) and a mass in the abdomen (3/16). The median size of the tumors was 7.9 cm in maximum diameter (ranging from 2.8 to 16.4 cm). The lesions were located at the head (7 cases, 43.75%), the body (4 cases, 25%), the tail (1 case, 6.25%), both the head and the body (1 cases, 6.25%), and both the body and the tail (3 cases, 18.75%). 9 cases (including 4 boys) of solid pseudopapillary neoplasm of the pancreas were cystic and solid (56.25%), 6 cases were purely solid (37.5%), and only 1 case was purely cystic (6.25%). Distal pancreatectomy was the choice for the body/tail tumors (50%), pancreaticoduodenectomy and total mass excision for the head tumors (43.75%), and total pancreatectomy for the head and body tumors (6.25%). Histologically, pseudopapillaes, solid cell sheets surrounded by fibrovascular stroma, nuclear grooves, areas of myxoid change and haemorrhage were the rudimentary histological patterns of solid pseudopapillary neoplasm of the pancreas. On immunohistochemistry the tumors variably expressed vimentin, neuron-specific enolase, alpha-1-antitrypsin, progesterone receptor, β-catenin, CD99 (dot-like intracytoplasmatic), cytokeratin, synaptophysin, Ki-67 (2-4%), and were negative to chromogranin A. The prognosis was satisfying. The average follow-up was 22.88±16.69 months (ranging from 3 to 61 months) and all the patients were event-free after operation. Conclusion: Solid pseudopapillary neoplasm of the pancreas was a borderline tumor with malignant potential and was uncommon in children. Compared with the adults, the pediatric patients showed many different characteristics: gender disparity, main clinical manifestations, the tumor location distribution, the size and configuration, and degenerative changes. Immunohistochemical markers such as β-catenin and CD99 were useful for the diagnosis. Although with malignant potential, metastases and recurrence were rarely observed in children.

Keywords: Solid pseudopapillary neoplasm of the pancreas, children, pathology, immunohistochemistry

Introduction

Solid pseudopapillary neoplasm of the pancreas (SPNP) is an uncommon pancreatic neoplasm with malignant potential and accounts for 0.13-2.7% of all exocrine pancreatic tumors and about 9-15% of cystic pancreatic tumors [1]. It was first described by Lichtenstein in 1934 [2]. The first case as a mucinous cystic neoplasm of the pancreas was reported by Frantz in 1959 [3, 4]. In 1970 Hamoudi et al. described the ultrastructural features of the tumor which led to its acceptance as a separate clinicopathological entity [5]. Later the World Health Organization designated these tumors as solid pseudopapillary tumors in 1996 [6] and reclassified them as solid pseudopapillary neoplasms in 2010 [7].

SPNP predominantly affected women 40% of which were during the second decade of life, and only approximately 6-8% of SPNP occurred in children [8]. A Korean review showed that there were only 11 pediatric cases in the total

Table 1. Primary antibodies used in the immunohistochemical study

Antigens	Clone	Host species	Working dilution	Source
Vimentin	IR630	Mouse	1:50	Dako, America
Neuron-specific enolase	IR612	Mouse	1:400	Dako, America
Chromogranin A	IR502	Mouse	1:400	Dako, America
Synaptophysin	IR776	Mouse	1:50	Dako, America
Cytokeratin	IR053	Mouse	1:200	Dako, America
Ki-67	IR626	Mouse	1:50	Dako, America
CD99	IR057	Mouse	1:200	Dako, America
β-catenin	IR702	Mouse	1:100	Dako, America
Alpha-1-antitrypsin	IR505	Mouse	1:200	Dako, America
Progesterone receptor	IR068	Mouse	1:50	Dako, America

116 SPNP cases and they had obviously different clinical features compared with adults [9]. Herein, we report a series of 16 cases of SPNP and make a study of their clinical and pathological features with a literature review.

Clinical presentations of SPNP include abdominal pain, palpable abdominal mass, nausea/vomiting, weight loss, jaundice, fever, constipation, diarrhea or fatigue [10]. Most of symptoms are nonspecific [11] and insufficient for diagnosis.

Computed tomography can detect a huge well-encapsulated mass with heterogeneous densities or intensities reflecting degeneration or haemorrhage within classic SPNP [12].

Pathological features are the mainstay for the diagnosis of SPNP. The classic features of SPNP include an evident fibrous capsule and typical pseudopapillary structures. In addition, solid cell sheets surrounded by fibrovascular stroma, nuclear grooves, degeneration and haemorrhage were the auxiliary histological patterns of SPNP [13].

Recently, some of the latest researches suggestted that the pediatric patients of SPNP showed different clinical and pathological features compared with adults [14]. Owing to the paucity of SPNP in children, this case series study was conducted to elucidate the clinical and pathological features of SPNP in children.

Materials and methods

Medical records

16 cases of SPNP were retrieved from the medical records in Kunming Children's Hospital between 1996 and 2015 with the permission of the ethics committee. The data we collected included the sex, age, complaints, lesion size, site, histopathological information, treatment, and follow-up.

Histopathological studies

With pathologic examination, all of the resected pancreatic specimens were fixed in 10% buffered formalin and embedded in paraffin. Block step sections (5 μm) were cut and stained conventionally with hematoxylin and eosin.

Immunohistochemistry

Immunohistochemical staining was performed using the EnVision method. The antibodies were listed in **Table 1**. Vimentin, Cytokeratin (CK), Synaptophysin (Syn), Chromogranin A (CgA), NSE (Neuron-specific enolase) and α1-AT (Alpha-1-antitrypsin) were expressed in membrane and Ki-67 and progesterone receptor (PR) were positive in nucleus. Particularly, β-catenin was positive in nucleus and cytoplasm, and CD99 showed dot-like intracytoplasmatic positivity.

Results

The clinicopathological data of 16 cases were collected and summarized in **Table 2**. There were 11 girls and 5 boys, the sex ratio was 2.2:1 (female-to-male); the median age was 9.5 years (ranging from 3 to 15 years), and the average age was 9.56±3.65 years (boys and girls was 8.8±3.7 years and 9.91±3.75 years, respectively). Abdominal pain (8 cases, 50%) and abdominal mass (3 cases, 18.75%) was the chief complaint, and the left (5 cases, 31.25%) were asymptomatic. The median size of tumors was 7.9 cm in maximum diameter (ranging from 2.8 to 16.4 cm). The median size of boys and girls in maximum diameter was 4.8 cm (ranging from 4.0 to 9.6 cm) and 8.0 cm (ranging from 2.8 to 16.4 cm), respectively.

Computed tomograpy showed that all tumors had clear circumscription and originated from the pancreas (**Figure 1**). The lesions were located at the head (7 cases, 43.75%), the body (4 cases, 25%), the tail (1 case, 6.25%), both the head and the body (1 cases, 6.25%), and both the body and the tail (3 cases, 18.75%). 9 cases (including 4 boys) of SPNP were cystic

Table 2. Clinical and pathological features of SPNP in children

NO	Sex	Age (year)	Complaints	Size in maximum diameter (cm)	Site	Cut section	Circumscription	Pseudo-papillae	Degeneration	Treatment	Follow-up (months)	Metastasis and Recurrence
1	F	3	Asymptomatic	2.8	Head	Solid	Clear	Exist	Hemorrhage, myxoid	TME	54	No
2	M	3	Abdominal mass	4.0	Head	Solid And Cystic	Clear	Exist	Hemorrhage myxoid necrosis	PDD	15	No
3	F	6	Abdominal pain	8.0	Body and tail	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid, necrosis	DP	28	No
4	F	7	Asymptomatic	10.2	Head	Solid	Clear	Exist	Hemorrhage, myxoid	PDD	10	No
5	M	8	Abdominal pain	9.6	Body	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid	DP	12	No
6	F	8	Asymptomatic	9.5	Head	Solid	Well demarcated	Exist	Hemorrhage, myxoid, necrosis	PDD	10	No
7	F	9	Asymptomatic	8.9	Body	Solid	Clear	Exist	Hemorrhage, myxoid	DP	36	No
8	M	9	Abdominal pain	4.8	Body	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid	DP	32	No
9	F	10	Abdominal mass	6.0	taill	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid, necrosis	DP	7	No
10	F	11	Abdominal pain	7.8	Head	Solid And Cystic	Well demarcated	Exist	Hemorrhage, myxoid, necrosis	PDD	61	No
11	M	12	Abdominal mass	8.2	Head	Solid	Clear	Exist	Hemorrhage, myxoid	PDD	25	No
12	F	12	Abdominal pain	5.5	Head	Cystic	Clear	Exist	Hemorrhage, myxoid, necrosis	PDD	8	No
13	M	12	Abdominal pain	5.0	Body and tail	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid, necrosis	DP	3	No
14	F	14	Asymptomatic	6.8	Body	Solid	Well demarcated	Exist	Hemorrhage, myxoid	DP	15	No
15	F	14	Abdominal pain	8.5	Body and tail	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid	DP	22	No
16	F	15	Abdominal pain	16.4	Head and body	Solid And Cystic	Clear	Exist	Hemorrhage, myxoid, hyaloid	TP	28	No

Abbreviations: F, female; M, male; DP, distal pancreatectomy; PDD, pancreaticoduodenectomy; TME, total mass excision; TP, total pancreatectomy.

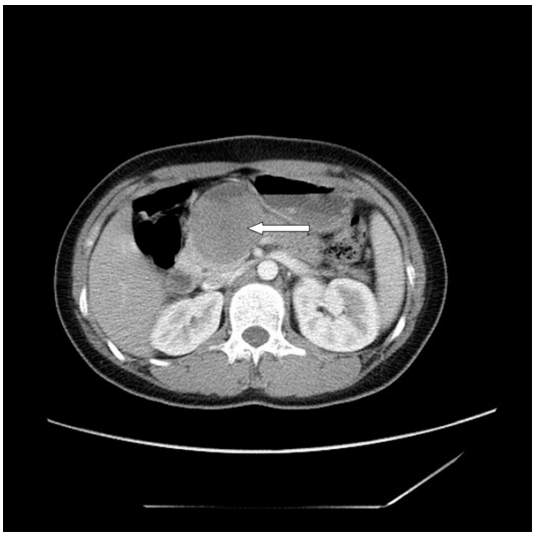

Figure 1. CT scan showed an equal-density cystic and solid mass of the pancreas in case 2 (Arrow).

and solid (56.25%), 6 cases were purely solid (37.5%), and only 1 case was purely cystic (6.25%).

Distal pancreatectomy was the choice for the body/tail tumors (50%), pancreaticoduodenectomy and total mass exicision for the head tumors (43.75%), and total pancreatectomy for the head and body tumors (6.25%).

Histologically, all the tumors were well-circumscribed with a fibrotic pseudocapsule. Monomorphic tumor cells were polygonal or oval with prominent pink or hyaline cytoplasm (**Figure 2A**) and some eosinophilic globules could be detected in or outside the cytoplasm (**Figure 2B**). Most tumor cells arranged around the blood vessels in a pseudopapillary pattern (**Figure 2C**) or in sheets with thin fibrovascular septa (**Figure 2D**). Some tumor cells displayed just like the pseudorosettes (**Figure 2E**). Large areas of cellular cystic degeneration (**Figure 2F**), hemorrhage (**Figure 2G**), and necrosis (**Figure 2G**) were highlighted. Pseudoglandular pattern with hyalinized collagenous stroma was observed partially (**Figure 2H**). Cellular mitosis was not observed.

On immunohistochemistry the tumor cells variably expressed vimentin, NSE, α1-AT, PR, CK and Syn, and did not express CgA. The characteristic markers of SPNP were CD99 and β-catenin. β-catenin was positive in nucleus and cytoplasm, and CD99 was dot-like intracytoplasmatic. Ki-67 index was 2-4% (**Figure 3**).

The prognosis of our patients was satisfying. The average follow-up was 22.88±16.69 months (ranging from 3 to 61 months), and all the patients were event-free after operation.

Discussion

To date, about 1000 cases of SPNP have been reported, and more than two-thirds of them appeared in the last 10 years [15, 16]. This probably reflected the increasing awareness of the clinicopathologic and radiographic features of SPNP and the uniformity of the nomenclature used for SPNP. However, the etiology and the differentiation status of SPNP remained challenging and still enigmatic [17].

Although the age of patients ranged widely from 2 to 85 years, SPNP mainly affected women during the second decade of life [18]. The largest reported pediatric case series showed the median age was 11.2 years [19], and our patient's median age of 9.5 years was lower than it. The sex ratio (female-to-male) was 9.78:1 in adults [20], and 3:1 [21] or 4.5:1 [22] in children. Our sex ratio of 2.2:1 (female-to-male) was lower than the previously reported in children, which suggested a lower female preponderance of SPNP in children in accord with Jung's report [23].

The common clinical manifestation of SPNP was abdominal pain and mass. Allison L. Speer reported most of 11 pediatric cases presented with abdominal pain (73%) [24]. Some literatures [25] demonstrated a significant difference in symptoms between adults and children in their comparative study. Although in adults it most commonly manifested as an incidental finding (38.3%) followed by abdominal pain (34%), SPNP in children most frequently presented with abdominal pain and a palpable mass [26]. The abdominal pain (50%) and abdominal mass (18.75%) was the chief complaint in our study which was also confirmed by other studies.

There were 8 cases at head (50%) which was similar to the literature in children (66.7% head) [27], but different from adults (80.9% body or tail) [28]. The median size of our tumors was 7.9 cm (ranging from 2.8 to 16.4 cm) in maximum diameter, and the size of girls was larger than that of boys (8.0 cm vs. 4.8 cm) similar to the previous study [29]. Lee et al. [30] demonstrated that the size in children was significant-

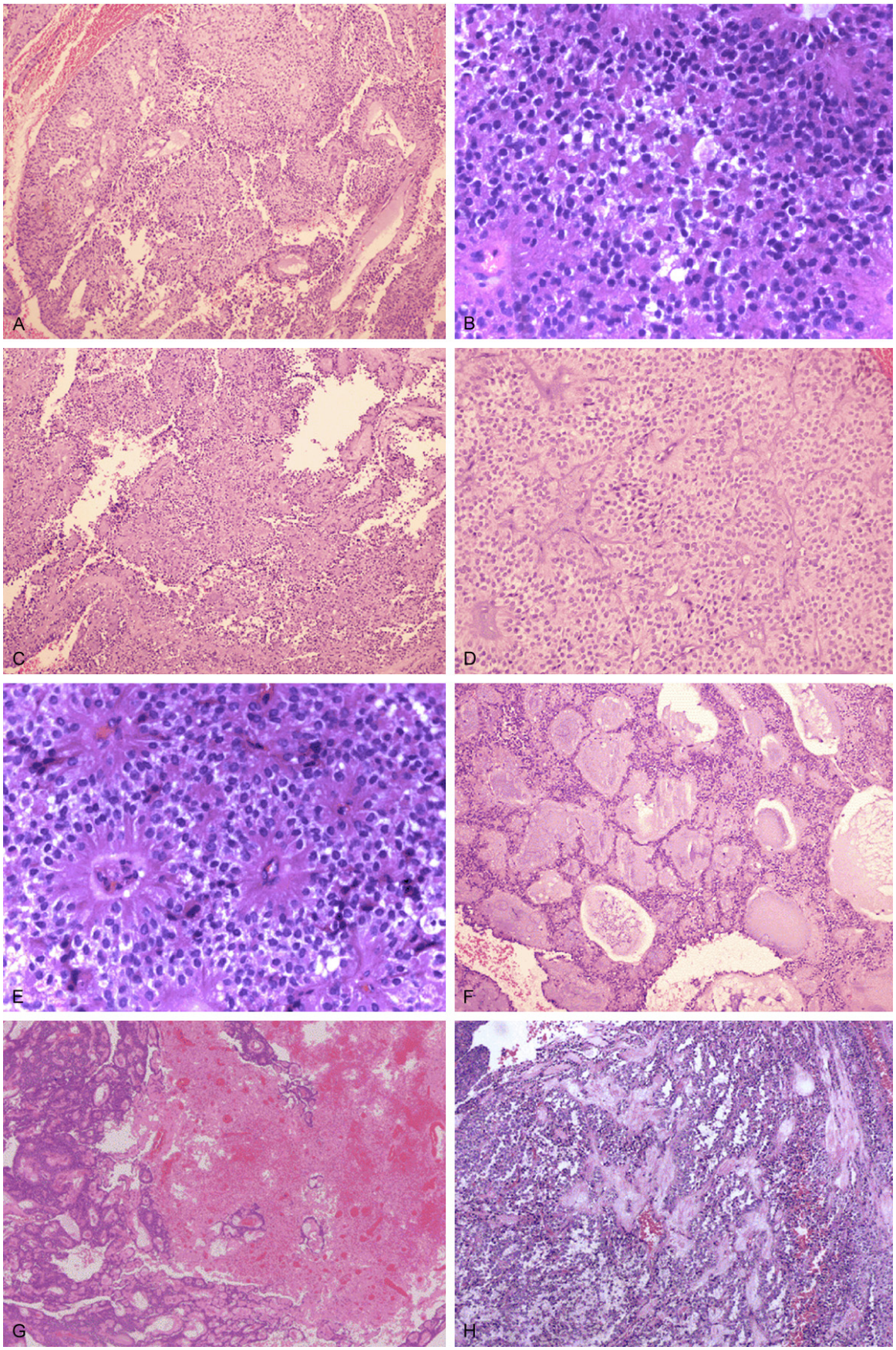
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Figure 2. (A) The tumor cells were uniform with plenty of cytoplasm (×100). (B-D) Eosinophilic globules (B, ×400), pseudopapillary pattern (C, ×100) and thin fibrovascular septa (D, ×200) was highlighted. (E) Elongated tumour cells radiated around blood vessels and were similar to pseudorosettes in ependymoma (×400). (F, G) Cystic degeneration (F, ×100), hemorrhage (G, ×50), and necrosis (G, ×50) was shown. (H) There was obvious pseudoglandular structure and hyalinized collagenous stroma (×100).

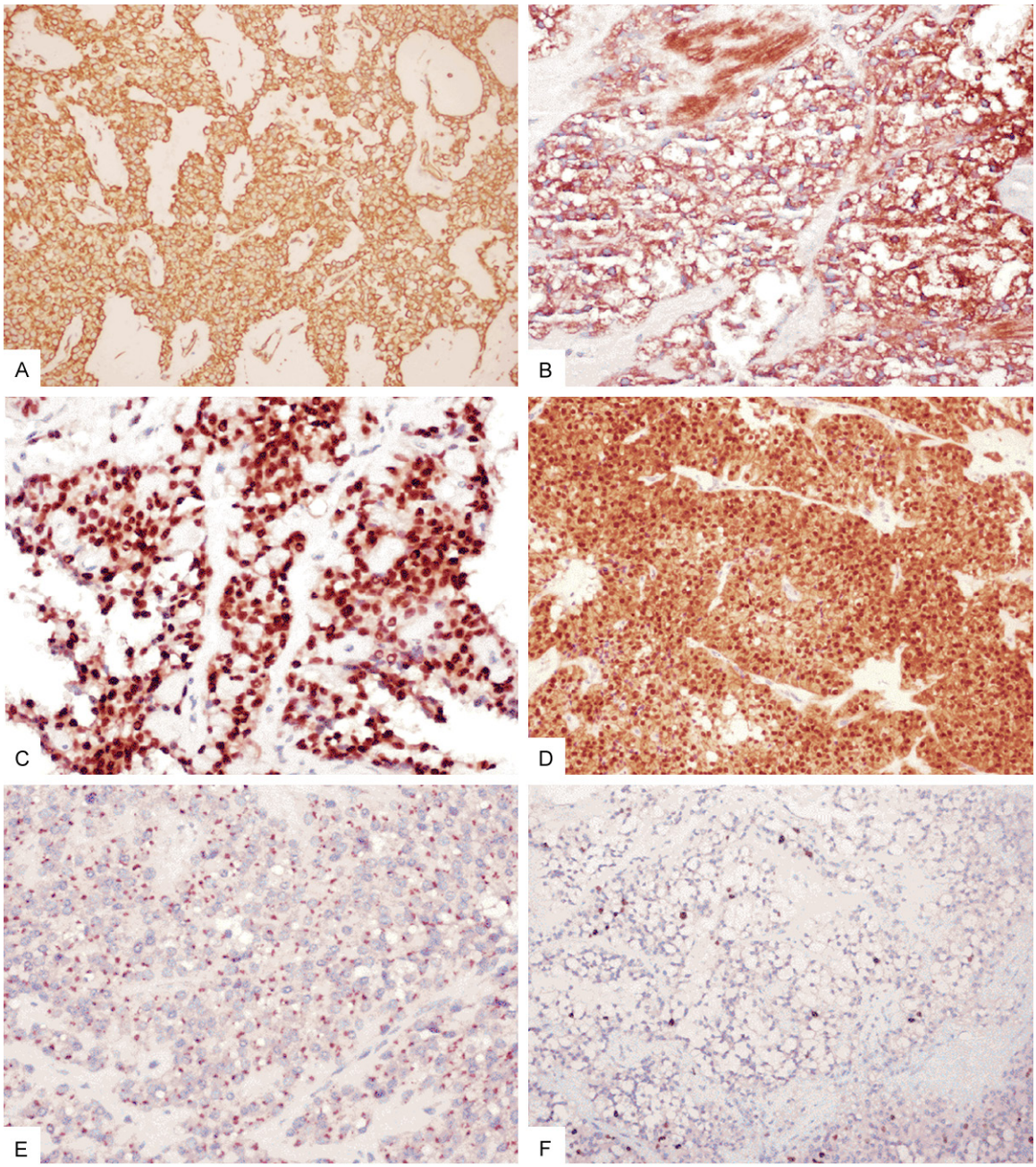

Figure 3. (A-C) Vimentin (A, ×200), α1-AT (B, ×400) and PR (C, ×400) was diffusely positive in tumor cells. (D) β-catenin showed unique positivity in nucleus and cytoplasm (×200). (E) CD99 was dot-like intracytoplasmatic (×400). (F) The Ki-67 index was about 2-4% (×400).

ly larger than that in adults (7.1 cm vs. 4.9 cm), and the bigger tumors easily occurred haemorrhage and/or myxoid, which gave rise to cystic spaces, ischemia and degenerations.

Histologically, all of our cases were macroscopically large and well encapsulated by a fibrous capsule. The tumor cells appeared pseudopapillaes, solid sheets surrounded by fibrovascular stroma, nuclear grooves, and areas of degeneration change, which were in accord with the rudimentary histological patterns of SPNP [31, 32]. Degenerative cysts, haemorrhage, necrosis and myxoid areas were common [33, 34]. According to the previous literatures, many studies found that SPNP in women showed cystic or degenerative changes and grew rapidly in early stage. Compared to women, SPNP in men were more likely to occur as a solid mass and to degenerate less frequently and more slowly during their growth [35-37]. Nishihara et al. reached almost the same conclusion and found that the mean age of men with degeneration in SPNP was higher than that of women (31.4 vs. 25.5 years) [38]. However, some researchers reported that the degenerative changes have no obvious gender discrepancy in pediatric SPNP [39]. Most of our cases were cystic and solid (56.25%) including 4 boys (80% of male) and 5 girls (45.45% of female). Small case number in our study might be the explanation for the high degeneration rate in boys.

Non-specific immunohistochemical markers were discovered in SPNP. The tumor cells variably expressed Vimentin, NSE, α1-AT, PR, CK and Syn but did not express CgA [40]. β-catenin and CD99 may be helpful in the diagnosis of SPNP for their unique pattern. β-catenin was positive in nucleus and cytoplasma, and CD99 showed dot-like intracytoplasmatic expression. According to the recent studies, almost SPNP had active mutations of the β-catenin (CTNNB1) gene, and expressed β-catenin in a diffuse cytoplasmic and aberrant nuclear pattern, which was accompanied by a lack of membranous E-cadherin [41, 42]. Except for some acinar cell carcinoma of the pancreas and pancreatoblastoma, pancreatic neuroendocrine tumor (PET) consistently lacks the nuclear expression of β-catenin. Thus, β-catenin was specific for SPNP [43]. Our patients' immunoprofiles were consistent with previous studies. Recently published data showed that a particular dot-like intracytoplasmatic expression of CD99 appeared to be highly unique for SPNP [44]. CD99 was a glycoprotein encoded by the pseudoautosomal gene MIC2, and was expressed in the cellular membrane of Ewing sarcoma (ES), primitive neuroectodermal tumor (PNET), lymphoblastic lymphoma, synovial sarcoma and other solid tumors [45]. The characteristic cytoplasmatic paranuclear "dot-like" pattern described in SPNP had also been found in colonic adenomas/adenocarcinomas, pituicytomas and endometrial serous carcinomas with ES differentiation, but to date it was rarely described in other types of endocrine or exocrine pancreatic tumors included in the differential diagnosis of SPNP [46]. The pseudopapillary regions of all our samples displayed the distinctive CD99 staining pattern which was consistent with previous reports. Some studies suggested that sex hormones might be involved in the origin of the tumor [47]. Many researchers found that the tumor cells in SPNP always expressed PR, but did not express estrogen receptor and/or androgen receptor [40]. Hence, some scholars proposed that no differences in immunohistochemical stains for sex hormone receptors in clinicopathological characteristics had been found attributable to gender alone [39]. Ki-67 index was about 2-4% in our studies suggesting the proliferative activity of the tumor cells was low.

Pancreatoblastoma, PET, acinar cell carcinoma of the pancreas, and ductal adenocarcinoma of pancreas should come to the differential diagnosis of SPNP. Pancreatoblastoma usually affects children younger than 10 years and has no female predilection. It is more aggressive than SPNP, and usually has liver metastasis [48]. Histologically, it shows clusters of primitive polygonal cells with hypercellular stroma and the characteristic squamoid corpuscles. PET has characteristic morphological features, such as solid monomorphous growth pattern and rosette-like structures. In addition, it also expresses neuroendocrine markers, such as Syn, NSE, and CD56 [49]. Acinar cell carcinoma of the pancreas is manignant and usually occurs in adults.It has uniform tumor cells arranged in solid and acinar pattern.The expression of pancreatic enzymes such as trypsin,chymotrypsin, and lipase may be useful. Ductal adenocarcinoma of pancreas is a malignant epithelial carcinoma exclusively seen in adults.It has an unique expression of a cytokeratin antibody panel.

Complete surgical resection is very effective for SPNP. Distal pancreatectomy, pancreaticoduodenectomy, total mass exicision and pancreatectomy was the treatment for the tumors in the different sites respectively [50-52]. Our patients also received the different surgical

procedure according to the different location. Routine lymphadenectomy was not recommended due to the rare incidence of metastasis [53, 54].

The overall 5-year survival rate of SPNP was about 95% [55]. Approximately 10-15% of SPNP patients developed metastasis and most often involved the liver or peritoneum lymph node [56]. Predicting aggressive behavior was still challenging because there were no reliable prognostic factors [57]. Our follow-up was satisfying and all the patients were alive without events. Metastases and recurrence were not observed in our study.

Conclusion

SPNP is an uncommon pancreatic neoplasm in children. The presentations of SPNP in children are different from those of adults. They have many unique features: the patients lack relatively obvious gender ratio; abdominal pain and abdominal symptoms are main clinical manifestations; the tumors frequently locate at the head and body; the size and configuration of tumors lack obvious gender difference; most tumors are composed of cystic and solid configurations, and degenerative changes occur earlier in tumor growth.

In summary, we report 16 pediatric SPNP and make a preliminary clinicopathological study. More data are needed to promote the progressive realization and diagnosis of SPNP in children.

Disclosure of conflict of interest

None.

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References

[1] Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. J Am Coll Surg 2005; 200: 965-972.

[2] Lichtenstein L. Papillary cystadenocarcinoma of the pancreas. Am J Cancer 1934; 21: 542-553.

[3] Frantz VK. Tumors of the pancreas (atlas of tumor pathology). Washington, DC: US Armed Forces Institute of Pathology; 1959. pp. 79-141.

[4] Frantz VK. Tumors of the pancreas. In: Bumberg CW, editor. Atlas of tumor pathology, VII. fascicles 27 and 28. Washington, DC: Armed Forced Institute of Pathology; 1959. pp. 32-33.

[5] Hamoudi AB, Misugi K, Grosfeld JL, Reiner CB. Papillary epithelial neoplasm of pancreas in a child. Report of a case with electron microscopy. Cancer 1970; 26: 1126-1130.

[6] Klo¨ppel G, Luttges J, Klimstra D, Hruban R, Kern S, Adler G. World Health Organization Classification of Tumours: pathology and genetics of tumours of the digestive system. Lyon: IARC Press; 2000. pp. 246-248.

[7] Salvia R, Bassi C, Festa L, Falconi M, Crippa S, Butturini G, Brighenti A, Capelli P, Pederzoli P. Clinical and biological behavior of pancreatic solid pseudopapillary tumors: report on 31 consecutive patients. J Surg Oncol 2007; 95: 304-310.

[8] Adamthwaite JA, Verbeke CS, Stringer MD, Guillou PJ, Menon KV. Solid pseudopapillary tumour of the pancreas: diverse presentation, outcome and histology. JOP 2006; 7: 635-642.

[9] Lee WJ, Park YT, Choi JS, Chi HS, Kim BR. Solid and papillary neoplasms of the pancreas. Yonsei Med J 1996; 37: 131-141.

[10] Martin RC, Klimstra DS, Brennan MF, Conlon KC. Solid-pseudopapillary tumor of pancreas: a surgical enigma? Ann Surg Oncol 2002; 9: 35-40.

[11] Buetow PC, Buck JL, Pantongrag-Brown L, Beck KG, Ros PR, Adair CF. Solid and papillary epithelial neoplasm of the pancreas: imaging-pathologic correlation in 56 cases. Radiology 1996; 199: 707-711.

[12] Cantisani V, Mortele KJ, Levy A, Glickman, JN, Ricci P, Passariello R, Ros PR, Silverman SG. Silverman. MR imaging features of solid pseudopapillary tumor of the pancreas in adult and pediatric patients. AJR Am J Roentgenol 2003; 181: 395-401.

[13] Pelosi G, Iannucci A, Zamboni G, Bresaola E, Iacono C, Serio G. Solid and cystic papillary neoplasm of the pancreas: a clinicocytopathologic and immunocytochemical study of five new cases diagnosed by fine-needle aspiration cytology and a review of the literature. Diagn Cytopathol 1995; 13: 233-246.

[14] Albores-Saavedra J, Simpson KW, Bilello SJ. The clear cell variant of solid pseudopapillary tumor of the pancreas: a previously unrecognized pancreatic neoplasm. Am J Surg Pathol 2006; 30: 1237-1242.

[15] Cai H, Zhou M, Hu Y, He H, Chen J, Tian W, Deng Y. Solid-pseudopapillary neoplasms of the pancreas: clinical and pathological features of 33 cases. Surg Today 2013; 43: 148-154.

[16] Yang F, Jin C, Long J, Yu XJ, Xu J, Di Y, Li J, Fu de L, Ni QX. Solid pseudopapillary tumor of the pancreas: a case series of 26 consecutive patients. Am J Surg 2009; 198: 210-215.
[17] Kloppel G, Kosmahl M. Cystic lesions and neoplasms of the pancreas. The features are becoming clearer. Pancreatology 2001; 1: 648-655.
[18] Todani T, Shimada K, Watanabe Y, Toki A, Fujii T, Urushihara N. Franz's tumor: a papillary and cystic tumor of the pancreas in girls. J Pediatr Surg 1988; 23: 116-121.
[19] Choi SH, Kim SM, Oh JT, Park JY, Seo JM, Lee SK. Solid pseudopapillary tumor of the pancreas: a multicenter study of 23 pediatric cases. J Pediatr Surg 2006; 41: 1992-1995.
[20] Zampieri N, Schiavo N, Capelli P, Scarpa A, Bassi C, Camoglio FS. Pseudopapillary tumor in pediatric age: clinical and surgical management. Pediatr Surg Int 2011; 27: 1271-1275.
[21] Lee SE, Jang JY, Hwang DW, Park KW, Kim SW. Clinical features and outcome of solid pseudopapillary neoplasm: differences between adults and children. Arch Surg 2008; 143: 1218-1221.
[22] Butte JM, Brennan MF, Gonen M, Tang LH, D'Angelica MI, Fong Y. Solid pseudopapillary tumors of the pancreas. Clinical features, surgical outcomes, and long-termsurvival in 45 consecutive patients from a single center. J Gastrointest Surg 2011; 15: 350-357.
[23] Jung SE, Kim DY, Park KW, Lee SC, Jang JJ, Kim WK. Solid and papillary epithelial neoplasm of the pancreas in children. World J Surg 1999; 23: 233-236.
[24] Madiba TE, Ramdial PK, Pirie F. Solid and cystic papillary epithelial neoplasm of the pancreas. A report of 3 cases. S Afr J Surg 2000; 38: 58-60.
[25] Laje P, Bhatti TR, Adzick NS. Solid pseudopapillary neoplasm of the pancreas in children: a 15-year experience and the identification of a unique immunohistochemical marker. J Pediatr Surg 2013; 48: 2054-2060.
[26] Low G, Panu A, Millo N, Leen E. Multimodality imaging of neoplastic and nonneoplastic solid lesions of the pancreas. Radiographics 2011; 31: 993-1015.
[27] Shorter NA, Glick RD, Klimstra DS, Brennan MF, LaQuaglia MP. Malignant pancreatic tumors in childhood and adolescence: the Memorial Sloan-Kettering experience, 1967 to present. J Pediatr Surg 2002; 37: 887-892.
[28] Yu DC, Kozakewich HP, Perez-Atayde AR, Shamberger RC, Weldon CB. Childhood pancreatic tumors: a single institution experience. J Pediatr Surg 2009; 44: 2267-2272.
[29] Cavallini A, Butturini G, Daskalaki D, Salvia R, Melotti G, Piccoli M, Bassi C, Pederzoli P. Laparoscopic pancreatectomy for solid pseudopapillary tumors of the pancreas is a suitable technique; our experience with long-term follow-up and review of the literature. Ann Surg Oncol 2011; 18: 352-357.
[30] Klöppel G, Maurer R, Hofmann E, Luthold K, Oscarson J, Forsby N, Ihse I, Ljungberg O, Heitz PU. Solid-cystic (papillary-cystic) tumours within and outside the pancreas in men: report of two patients. Virchows Arch A 1991; 418: 179-183.
[31] Chen C, Jing W, Gulati P, Vargas H, French SW. Melanocytic differentiation in a solid pseudopapillary tumor of the pancreas. J Gastroenterol 2004; 39: 579-583.
[32] Daum O, Sima R, Mukensnabl P, Vanecek T, Brouckova M, Benes Z, Michal M. Pigmented solid-pseudopapillary neoplasm of the pancreas. Pathol Int 2005; 55: 280-284.
[33] Lam KY, Lo CY, Fan ST. Pancreatic solid-cystic-papillary tumor: clinicopathologic findings in eight patients from Hong Kong and review of the literature. World J Surg 1999; 23: 1045-1050.
[34] Abraham SC, Klimstra DS, Wilentz RE, Yeo CJ, Conlon K, Brennan M, Cameron JL, Wu TT, Hruban RH. Solid-pseudopapillary tumors of the pancreas are genetically distinct from pancreatic ductal adenocarcinomas and almost always harbor beta-catenin mutations. Am J Pathol 2002; 160: 1361-1369.
[35] Mancini GJ, Dudrick PS, Grindstaff AD, Bell JL. Solid-pseudopapillary tumor of the pancreas: two cases in male patients. Am Surg 2004; 70: 29-31.
[36] Ohashi K, Nakajima Y, Hisanaga M, Nakano H, Tsutsumi M, Kondoh S, Konishi Y. A solid and papillary (solid-cystic) tumor of the pancreas occurring in a 36-year-old man: report of a case. Surg Today 1993; 23: 551-555.
[37] Nishihara K, Tsuneyoshi M, Ohshima A, Yamaguchi K. Papillary cystic tumor of the pancreas: is it a hormone-dependent neoplasm? Pathol Res Pract 1993; 189: 521-526.
[38] Geers C, Moulin P, Gigot JF, Weynand B, Deprez P, Rahier J, Sempoux C. Solid and pseudopapillary tumor of the pancreas review and new insights into pathogenesis. Am J Surg Pathol 2006; 30: 1243-1249.
[39] Kim MJ, Choi DW, Choi SH, Heo JS, Sung JY. Surgical treatment of solid pseudopapillary neoplasms of the pancreas and risk factors for malignancy. Br J Surg 2014; 101: 1266-1271.
[40] Kim HH, Yun SK, Kim JC, Park EK, Seoung JS, Hur YH, Koh YS, Cho CK, Shin SS, Kweon SS, Kim HS, Kim HJ. Clinical features and surgical outcome of solid pseudopapillary tumor of the pancreas: 30 consecutive clinical cases. Hepatogastroenterology 2011; 58: 1002-1008.
[41] Tanaka Y, Notohara K, Kato K, Ijiri R, Nishimata S, Miyake T, Fukunaga M, Horisawa M, Naka-

tani Y. Usefulness of beta-catenin immunostaining for the differential diagnosis of solid-pseudopapillary neoplasm of the pancreas. Am J Surg Pathol 2002; 26: 818-820.
[42] Guo Y, Yuan F, Deng H, Wang HF, Jin XL, Xiao JC. Paranuclear dot-like immunostaining for CD99: a unique staining pattern for diagnosing solid-pseudopapillary neoplasm of the pancreas. Am J Surg Pathol 2011; 35: 799-806.
[43] Li L, Li J, Hao C, Zhang C, Mu K, Wang Y, Zhang T. Immunohistochemical evaluation of solid pseudopapillary tumors of the pancreas: the expression pattern of CD99 is highly unique. Cancer Lett 2011; 310: 9-14.
[44] Makhoul R, Schwartz AM, Williams R, Lee NH. Paranuclear dot-like immunostaining for CD99: presence in colonic adenomas and adenocarcinomas. Am J Surg Pathol 2011; 35: 1749-1750.
[45] Kwon MJ, Suh YL. Pituicytoma with unusual histological features. Pathol Int 2011; 61: 598-602.
[46] Quddus MR, Rashid L, Sung CJ, Steinhoff MM, Zhang C, Lawrence WD. Ewing's sarcoma/peripheral primitive neuroectodermal tumor (ES/PNET) differentiation in endometrial serous carcinomas. Reprod Sci 2009; 16: 591-595.
[47] Hu S, Huang W, Lin X, Wang Y, Chen KM, Chai W. Solid pseudopapillary tumour of the pancreas: distinct patterns of computed tomography manifestation for male versus female patients. Radiol Med 2014; 119: 83-89.
[48] Klimstra DS, Wenig BM, Adair CF, Heffess CS. Pancreatoblastoma: a clinicopathologic study and review of the literature. Am J Surg Pathol 1995; 19: 1371-1389.
[49] Kosmahl M, Seada LS, Jänig U, Harms D, Klöppel G. Solid-pseudopapillary tumor of the pancreas: its origin revisited. Virchows Arch 2000; 436: 473-480.
[50] Campanile M, Nicolas A, LeBel S, Delarue A, Guys JM, De Lagausie P. Frantz's tumor: is mutilating surgery always justified in young patients? Surg Oncol 2011; 20: 121-125.
[51] Tipton SG, Smyrk TC, Sarr MG, Thompson GB. Malignant potential of solid pseudopapillary neoplasm of the pancreas. Br J Surg 2006; 93: 733-737.
[52] Kang CM, Kim KS, Choi JS, Kim H, Lee WJ, Kim BR. Solid pseudopapillary tumor of the pancreas suggesting malignant potential. Pancreas 2006; 32: 276-280.
[53] Miyazaki Y, Miyajima A, Maeda T, Yuge K, Hasegawa M, Kosaka T, Kikuchi E, Kameyama K, Jinzaki M, Nakagawa K, Oya M. Extrapancreatic solid pseudopapillary tumor: case report and review of the literature. Int J Clin Oncol 2012; 17: 165-168.
[54] Deshpande V, Oliva E, Young RH. Solid pseudopapillary neoplasm of the ovary: a report of 3 primary ovarian tumors resembling those of the pancreas. Am J Surg Pathol 2010; 34: 1514-1520.
[55] Campbell F, Azadeh B. Cystic neoplasms of the exocrine pancreas. Histopathology 2008; 52: 539-551.
[56] Matos JM, Grützmann R, Agaram NP, Saeger HD, Kumar HR, Lillemoe KD, Schmidt CM. Solid pseudopapillary neoplasms of the pancreas: a multiinstitutional study of 21 patients. J Surg Res 2009; 157: e137-e142.
[57] Peng CH, Chen DF, Zhou GW, Yang WP, Tao ZY, Lei RQ, Zhange SD, Li HW. The solid-pseudopapillary tumor of pancreas: the clinical characteristics and surgical treatment. J Surg Res 2006; 131: 276-282.