UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département de radiologie médicale
Service de radiodiagnostic et radiologie interventionnelle

Solid pseudopapillary tumor of the pancreas in children: typical radiological findings and pathological correlation

THESE

préparée sous la direction du Professeur associé François Gudinchet

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Saad ALQAHTANI

Médecin diplômé d'Arabie Saoudite
Originaire d'Arabie Saoudite

Lausanne

2010

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse	*Monsieur le Professeur associé* **François Gudinchet**
Co-Directeur de thèse	
Expert	
Directrice de l'Ecole doctorale	*Madame le Professeur* **Stephanie Clarke**

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Saad Alqahtani

intitulée

Solid pseudopapillary tumor of the pancreas in children: typical radiological findings and pathological correlation

Lausanne, le 20 avril 2010

pour Le Doyen
de la Faculté de Biologie et de Médecine

Madame le Professeur Stephanie Clarke
Directrice de l'Ecole doctorale

Tumeurs solides pseudopapillaires du pancréas chez l'enfant : signes radiologiques typiques et corrélation anatomopathologique

Introduction : Les tumeurs solides pseudo-papillaires du pancréas (SPT) sont des tumeurs rares, d'étiopathogénie encore incertaine.

Le but de notre travail était de décrire les caractéristiques radiologiques des SPT dans le groupe d'âge pédiatrique et d'étudier leur corrélation avec les études anatomopathologiques en vue d'établir un diagnostic.

Patients et Méthodes : Nous avons étudié rétrospectivement trois malades pédiatriques pour lesquelles le diagnostic de tumeur solide pseudo-papillaire du pancréas a été porté à l'examen d'une pièce opératoire. Ce groupe comprenait 3 jeunes filles et femmes (âge médian: 13 ans).

Résultats : La tumeur a été découverte pendant le bilan de symptômes digestifs non spécifiques. Les examens biologiques n'étaient pas informatifs. Des investigations radiologiques complètes ont été réalisées y compris les ultrasons (US), la tomodensitométrie (CT) et l'imagerie par résonance magnétique (IRM).Celles-ci ont montré de volumineuses lésions nodulaires, peu vascularisées, de compositions habituellement hétérogènes, avec des composantes kystiques et hémorragiques identifiées dans les 3 cas. Un traitement chirurgical a été pratiqué chez toute les patientes. L'étude de la pièce opératoire a montré une tumeur encapsulée dans les 3 cas. Aucune métastase n'a été mise en évidence.

Conclusion : Les SPT doivent être considérées dans le diagnostic différentiel des masses pancréatiques pédiatriques, en particulier chez les adolescentes. Certaines caractéristiques radiologiques comme des masses volumineuses bien circonscrites, des lésions hétérogènes avec des zones kystiques et hémorragiques, de plus entourées d'une pseudocapsule fibreuse réactive, suggèrent fortement le diagnostic de SPT. Celui-ci devrait ensuite être confirmé par une biopsie avant que la résection chirurgicale soit effectuée. Chez les enfants, l'échographie abdominale reste la méthode de première intention, suivie par l'IRM comme technique d'imagerie de choix pour évaluer les caractéristiques et l'extension de la lésion, tout en évitant l'exposition des patients aux rayonnements ionisants.

ELSEVIER

Clinical Imaging 34 (2010) 152–156

CLINICAL IMAGING

Solid pseudopapillary tumor of the pancreas in children: typical radiological findings and pathological correlation

Saad Al-Qahtani[a], Francois Gudinchet[a], Tarek Laswed[a], Pierre Schnyder[a], Sabine Schmidt[a], Maria-Chiara Osterheld[b], Leonor Alamo[a,*]

[a]*Department of Diagnostic Radiology, Unit of Pediatric Radiology, Centre Hospitalier Universitaire Vaudois, Rue du Bugnon, 46, 1011 Lausanne, Switzerland*
[b]*Department of Pathology, Centre Hospitalier Universitaire Vaudois, Rue du Bugnon, 46, 1011 Lausanne, Switzerland*

Received 26 March 2009; accepted 15 May 2009

Abstract

We report a case series of three children with solid pseudopapillary tumor of the pancreas (SPT) in which a complete radiological work-up, including ultrasound, computed tomography scans, and MRI, has been carried out. The aim of this article is to highlight the characteristic imaging findings of SPT in the pediatric age group and to establish a correlation with typical histopathological findings of the lesion.

Keywords: Gastrointestinal radiology; Pancreatic tumor; Abdominal CT; Abdominal MRI

1. Introduction

Solid pseudopapillary tumor of the pancreas (SPT) is a very rare pancreatic tumor with a low potential for malignancy [1,2], occurring mainly in adolescent females [3,4]. Patients with SPT usually present with nonspecific clinical symptoms and without abnormalities in clinical laboratory tests [5,6]. However, SPT has some highly characteristic radiological features that support its diagnosis, including a large size at the time of presentation, a well-demarcated pseudocapsule, and central areas of necrosis and hemorrhage. Knowledge of this unusual tumor and its radiological findings may facilitate an accurate diagnosis and therefore enable appropriate treatment. We report a case series of three children with histologically proven SPT and describe the characteristic radiological findings of the tumor in correlation with its main pathological findings.

* Corresponding author. Department of Diagnostic and Interventional Radiology, Centre Hospitalier Universitaire Vaudois, Rue du Bugnon, 46, 1011 Lausanne, Switzerland. Tel.: +41 21 314 3054; fax: +41 21 314 4645.
E-mail address: leonor.alamo@chuv.ch (L. Alamo).

0899-7071/09/$ – see front matter
doi:10.1016/j.clinimag.2009.06.024

2. Description of cases

2.1. Case 1

A 14-year-old girl presented with a 5-month history of right upper abdominal swelling that was not associated with clinical symptoms (Fig. 1). Examination showed a firm, well-palpable, and painless mass in the right upper quadrant of the abdomen. Blood laboratory tests yielded normal results.

An abdominal ultrasound (US) showed a retroperitoneal mass in the right hypochondrium. The mass was well-delimitated and heterogeneous, with solid and cystic components. No signs of invasion of adjacent organs were seen. Doppler US revealed reduced tumor vascularity.

Contrast-enhanced computed tomography (CECT) demonstrated a well-defined and encapsulated retroperitoneal mass (7 cm in diameter) with solid and cystic components, as well as hemorrhagic areas. The mass displaced posterolaterally the processus uncinatus of the pancreas and the second part of the duodenum, and was associated with a discrete dilatation of the pancreatic duct. No dilatation of the bile ducts, focal hepatic lesions, or abdominal lymphadenopathies were found. The initial suggested diagnosis was a complicated duplication cyst.

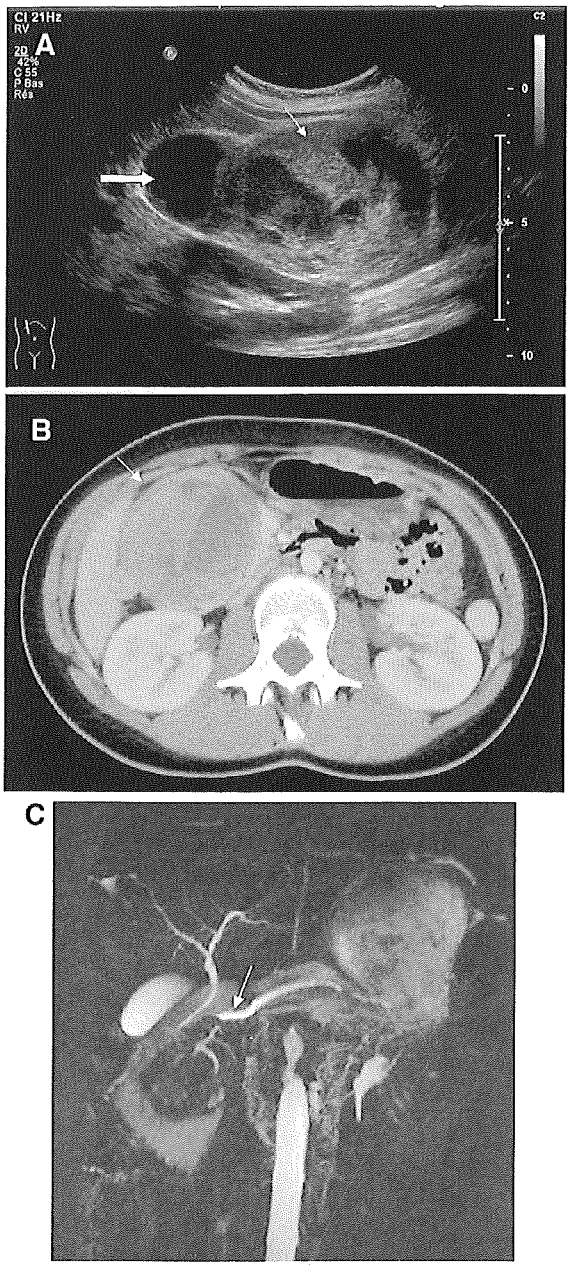

Fig. 1. Case 1: a 14-year-old girl. (A) Abdominal US shows a well-defined heterogeneous mass with both solid (arrow) and cystic (solid arrow) components. (B) CECT evidences the well-circumscribed mass with moderate enhancement of solid tumor components and the peripheral rim (white arrow). (C) Postoperative coronal MR cholangiography shows slight dilatation of the pancreatic duct (arrow) with no dilatation of the biliary tree.

Abdominal laparotomy failed to completely resect the mass because the thick pseudocapsule was strongly adhered to the second portion of the duodenum. On histology, the tumor revealed a proliferation of small neoplastic cells with a papillary pattern. Intratumoral areas of hemorrhage and necrosis were observed. The proposed diagnosis was SPT.

Postsurgical MRI confirmed the mass at the head of the pancreas and the presence of a thick fibrotic pseudocapsule adhering to the duodenal wall. Magnetic resonance cholangiography evidenced partial stenosis of the pancreatic duct as a result of the compression.

A Whipple operation with partial pancreatic and duodenal resection was then performed, and the tumor was completely resected. Microscopic examination revealed tumor cell proliferation surrounded by dense fibrous tissues. Surgical margins showed no tumor cell invasion. Local excised lymph nodes revealed no infiltration.

2.2. Case 2

A 13.5-year-old African girl presented with a well-palpable left upper abdominal mass (Fig. 2). She had been complaining of abdominal discomfort in the previous 3 months, with increasing postprandial abdominal pain for a week associated with light pruritus. Clinical examination revealed a firm, painful abdominal mass at the left hypochondrium. Blood laboratory tests yielded normal results.

Abdominal CECT was performed. The images revealed a well-defined, encapsulated, and solid mass (almost 10 cm in diameter) at the pancreatic head. On native CT, the tumor showed a central hyperdense area corresponding with spontaneous hemorrhage. No signs of infiltration of adjacent structures were observed; however, because of tumor compression, the right renal vein and the inferior vena cava were laminated, and the superior mesenteric vein was occluded. Evident signs of portal hypertension with collateral circulation were seen. No dilatation of the pancreatic or biliary ducts was detected.

On MRI, the lesion was solid and heterogeneous, with intratumoral hemorrhagic areas. The tumor showed moderate enhancement after an intravenous administration of gadolinium. A slight dilatation of the intrahepatic and extrahepatic biliary ducts was observed. A US-guided biopsy evidenced a thick, dense fibrous tissue adjacent to tumoral proliferation and associated with areas of hemorrhage and hemosiderin-containing macrophages.

Partial duodenopancreatectomy and partial gastrectomy were then performed. An iatrogenic operative damage of the portal vein required implantation of a vascular prosthesis. No complications were seen after the operation.

2.3. Case 3

An 11-year-old girl presented with nausea, vomiting, and acute periumbilical pain. She reported a chronic history of diffuse abdominal discomfort in the previous 6 years. On clinical examination, diffuse abdominal pain was noted. No palpable mass was detected. Blood analyses yielded normal results.

Abdominal US showed a well-defined and hyperechogenic mass (6 cm in diameter) with probable origin at the

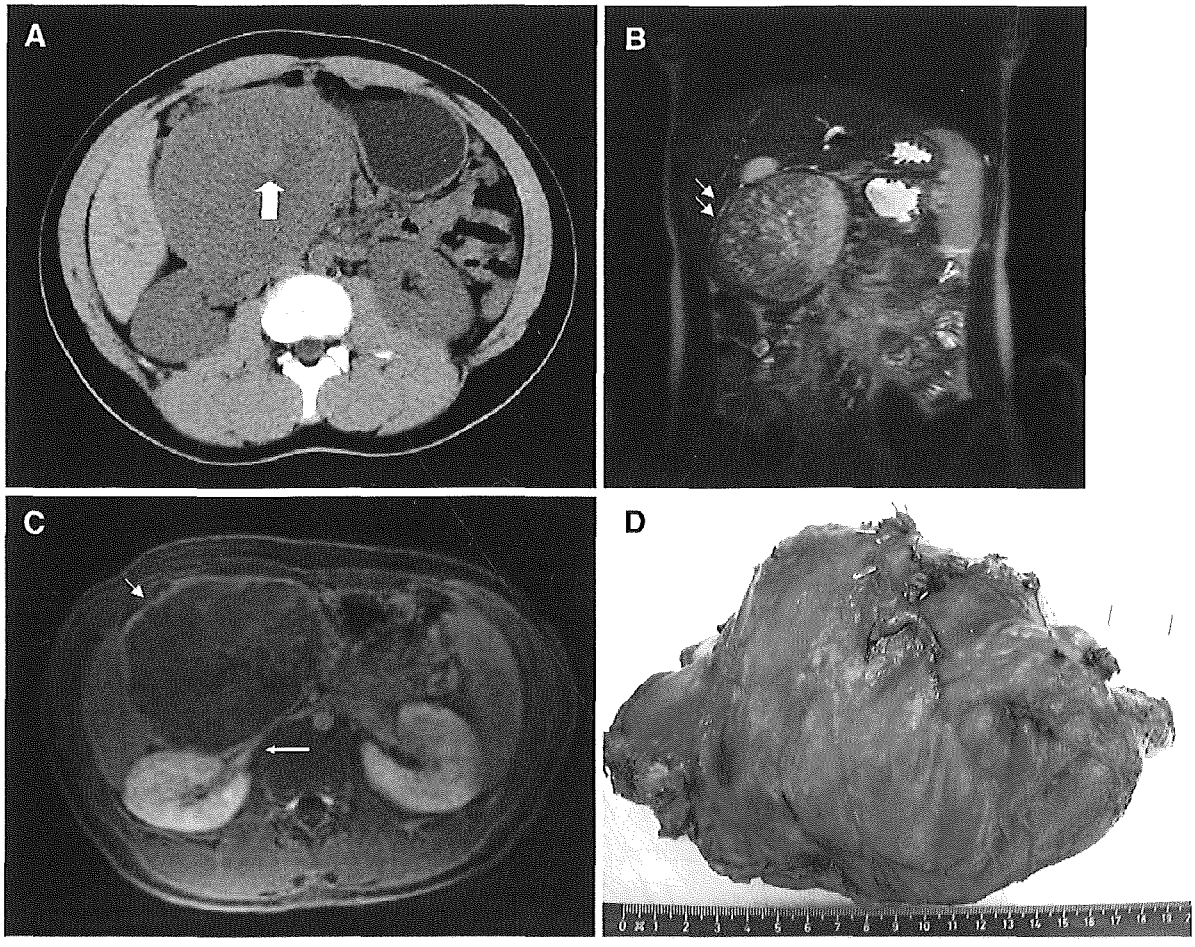

Fig. 2. Case 2. (A) Native CT scan reveals a well-defined encapsulated mass with hyperdense central hemorrhage (solid arrow). (B) Coronal T2-WI MRI reveals the heterogeneous character of the tumor of the well-delimitated mass. Observe the high degree of compression of the gastric outlet and the duodenum (double arrow). (C) Axial T1-WI MR after intravenous injection of contrast agent shows enhancement of the tumor's pseudocapsule (arrow) in an otherwise hypovascular tumor. Observe the compression of the right renal vessels. (D) Macroscopic view of duodenopancreatectomy, including the voluminous mass at the head of the pancreas.

head of the pancreas. No dilatation of the pancreatic or biliary duct was observed.

Abdominal CECT scan confirmed the pancreatic origin of the mass. The lesion was encapsulated and contained fine calcifications and cystic components. Small quantities of peritoneal fluid, as well as peritumoral infiltration of mesenteric fats, were seen.

MRI showed the pancreatic head mass, which was of high signal intensity in relation to the rest of the pancreas on T_2-weighted imaging (T2-WI). No dilatation of the pancreatic or bile duct was observed. No signs of infiltration of adjacent organs were seen, but the mass compressed and displaced the mesenteric vessels, which remained permeable.

A US-guided biopsy revealed foci of tumoral necrosis and areas of tumoral cells that were strongly positive for progesterone receptors but negative for estrogen receptors.

A Whipple operation with partial resection of the pancreatic head and duodenum was performed. The specimen revealed a voluminous, well-circumscribed, partially necrotic, and partially hemorrhagic mass delimited by a thick inflammatory wall, which was partially invaded by neoplastic trabecules.

3. Discussion

The term SPT was adopted by the World Health Organization Tumor Classification in 2000. Before that, different names such as papillary solid neoplasm, solid and papillary epithelial neoplasm, papillary cystic epithelial neoplasm, and Frantz tumor were used [3]. SPT is a rare low-grade malignant tumor, with an incidence of about 2–3% among primary pancreatic tumors. The tumor may present at all ages [5] and represents about 8–16.6% of pancreatic tumors in children [7]. It is most often located at the head of the organ [3], as was the case in our three cases.

SPT seems to occur more often in Asian and African-American adolescent females, suggesting a relationship between hormonal changes and tumor development. Indeed, our three cases were found in adolescent females, one of them of African origin.

Usually, an SPT displays a nonspecific clinical presentation. The most common symptom is light chronic abdominal pain, followed by a painless, slowly enlarging abdominal mass [3,5,6]. Not uncommonly, diagnosis is made in an incidental way when abdominal US is performed for other reasons. Occasionally, bowel obstruction or icterus secondary to obstruction of the biliary ducts is observed; however, in most cases, clinical laboratory tests results, including pancreatic endocrine or exocrine function, are preserved [8,9]. None of our cases had alterations in clinical laboratory tests.

On histology, SPT appears as an encapsulated tumor composed of a mixture of cystic, solid, and hemorrhagic components. Degenerative changes lead to extensive fibrosis, hemorrhage, focal calcification, and occasional ossification. A particular immunohistochemical aspect of this type of tumor is its positivity for progesterone receptor markers and its negativity for estrogen receptor markers [10], supporting hormonal influences on tumor development.

Because of the paucity of clinical symptoms, in most cases, the tumor is voluminous at the time of diagnosis and, therefore, easy to detect by imaging methods. Indeed, the contrast between the size of the lesion and the reduced symptomatology is one of the main characteristics of the lesion and may help to differentiate SPT from other pancreatic cystic neoplasms, including serous cystadenoma, mucin-producing tumors, islet cell tumor, or pancreatoblastoma [6].

US is the screening imaging method that is usually performed on children because of its wide accessibility and absence of radiation. On US, SPT is a well-circumscribed mass surrounded by a pseudocapsule of compressed pancreatic tissues and reactive fibroses [11–14]. Central cystic areas of necrosis are often visualized [3]. In our patients, US showed a well-defined heterogeneous mass with centrally located cystic and solid components.

Abdominal CT scan or MRI is then usually required for locoregional and distant staging. Native CT may identify hemorrhage and calcifications. Calcification is detected in almost 30% of published cases of adult patients, but only tiny calcifications have been reported in children, as was the case in one of our patients [11]. CECT reveals an enhancement of both tumor pseudocapsule and solid tumor components.

MRI should be considered the best imaging technique for children due to the absence of radiation and its improved capacity for visualizing tumor components, especially intratumoral areas of hemorrhage, with high signal intensity on T_1-weighted imaging (T1-WI) and heterogeneous signal intensity on T2-WI. The peripheral fibrous pseudocapsule is usually seen as a rim of heterogeneous signal intensity in T2-WI and of low signal intensity in T1-WI, which often enhances after gadolinium application. Both the fibrous capsule and the intramural hemorrhage are important clues for the final diagnosis because they are rarely found in other pancreatic neoplasms.

Because of its rarity, the tumor is often not included in the differential diagnosis of pancreatic masses, implying an inaccurate preoperative diagnosis [15]. Therefore, preoperative fine-needle aspiration or excisional biopsy should be performed.

Although the tumor shows low-grade malignancy, there may be local invasion of adjacent organs or local major blood vessels. This fact complicated surgical extirpation in one of our cases, where extensive venous thromboses with signs of portal hypertension were observed. Metastases are uncommon, occurring only in 7–9% of adult patients in large reviews, and are located mostly in the liver, omentum, and peritoneum [8,12,13].

The treatment of choice for SPT is complete surgical excision, preserving as much pancreatic tissues as possible. This treatment is curative in more than 95% of patients with SPT limited to the pancreas [9,13]. Radiotherapy has been suggested in cases of incomplete or impossible surgical resection [15].

In conclusion, SPT should be considered in the differential diagnosis of pediatric pancreatic masses, especially in adolescent females. Certain characteristic radiological findings such as a voluminous, well-circumscribed, and heterogeneous lesion with central cystic and hemorrhagic zones and surrounded by a fibrous reactive pseudocapsule strongly suggest the diagnosis of SPT, which should then be confirmed by biopsy before surgical resection is performed. In children, abdominal US remains as the initial screening method, followed by MRI as the imaging technique of choice to evaluate the characteristics and extension of the lesion, avoiding patient exposure to CT scan radiation.

References

[1] Rebhandl W, Felberbauer FX, Puig S, Paya K, Hochschoner S, Barlan M, Horcher E. Solid-pseudopapillary tumor of the pancreas (Frantz tumor) in children: report of four cases and review of the literature. J Surg Oncol 2001;76:289–96.

[2] Lam KY, Lo CY, Fan ST, Chan GC, Khong PL, Tam PK. Pancreatic solid–cystic–papillary tumor: clinicopathologic features in eight patients from Hong Kong and review of the literature. World J Surg 1999;23:1045–50.

[3] Coleman KM, Doherty MC, Bigler SA. Solid-pseudopapillary tumor of the pancreas. Radiographics 2003;23:1644–8.

[4] 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;23:233–6.

[5] 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;41:1992–5.

[6] Chung EM, Travis MD, Conran RM. Pancreatic tumors in children: radiologic–pathologic correlation. Radiographics 2006;26:1211–38.

[7] Jaksic T, Yaman M, Thorner P, Wesson DK, Filler RM, Shandling B. A 20-year review of pediatric pancreatic tumors. J Pediatr Surg 1992; 27:1315–7.

[8] Sclafani LM, Reuter VE, Coit DG, Brennan MF. The malignant nature of papillary and cystic neoplasm of the pancreas. Cancer 1991;68: 153–8.
[9] Todani T, Shimada K, Watanabe Y, Toki A, Fujii T, Urushihara N. Frantz tumor: a papillary and cystic tumor of the pancreas in girls. J Pediatr Surg 1988;23:116–21.
[10] Liu X, Rauch TM, Siegal GP, Jhala N. Solid-pseudopapillary neoplasm of the pancreas. Three cases with a literature review. Appl Immunohistochem Mol Morphol 2006;14:445–53.
[11] Poustchi-Amin M, Leonidas JC, Valderrama E, Shende A, Paley C, Lanzkowsky P, Kutin N. Papillary–cystic neoplasm of the pancreas. Pediatr Radiol 1995;25:509–11.
[12] 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;199:707–11.
[13] Raffel A, Cupisti K, Krausch M, Kreuz H, Schulte KM. Therapeutic strategy of papillary cystic and solid neoplasm (PCSN): a rare non-endocrine tumor of the pancreas in children. Surg Oncol 2004;13:1–6.
[14] Nishihara K, Nagoshi M, Tsuneyoshi M, Yamaguchi K, Hayashi I. Papillary cystic tumors of the pancreas: assessment of their malignant potential. Cancer 1993;71(1):82–92.
[15] Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. J Am Coll Surg 2005;2:965–72.