CASE REPORT

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Gruber–Frantz tumor: a very rare pathological condition in children

RADU-IULIAN SPĂTARU[1)], AUGUSTINA ENCULESCU[2)], MARIUS CĂLIN POPOIU[3)]

[1)]*Department of Pediatric Surgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; "Maria Skłodowska Curie" Emergency Clinical Hospital for Children, Bucharest, Romania*

[2)]*Department of Pathology, "Maria Skłodowska Curie" Emergency Clinical Hospital for Children, Bucharest, Romania*

[3)]*Department of Pediatric Surgery, "Louis Ţurcanu" Emergency Clinical Hospital for Children, Timisoara, Romania; "Victor Babeş" University of Medicine and Pharmacy, Timisoara, Romania*

Abstract

Solid pseudopapillary tumor of the pancreas or Gruber–Frantz tumor is a rare pathological entity. Its incidence is even lower in children. This neoplasm has low malignant potential and with adequate surgical treatment has a very good prognosis. We present the case of a 15-year-old girl admitted in our department for an intra-abdominal tumor, diagnosed incidentally on ultrasonography after a minor trauma. The CT scan revealed an important mass, apparently localized in the liver. Intraoperative assessment found the tumor originating from the pancreatic head (12 cm in diameter), well defined, with reddish-brown color, well-vascularized and heterogeneous consistency. It was completely removed without sacrificing other tissues. The postoperative evolution was uneventful. The microscopic feature of the tumor, using Hematoxylin and Eosin staining was characteristic. Immunohistochemistry confirmed the diagnosis. Four years postoperative follow-up showed no recurrence. Only several hundred solid pseudopapillary tumors of the pancreas are described in the literature. In children, the incidence of this tumor is extremely rare. Some investigators believe it is originated from pluripotent primordial stem cells. The clinical picture is non-specific. Despite its rarity, this type of tumor should be taken into account in the differential diagnosis of abdominal masses in children, especially in girls. The diagnosis is made only histologically. Complete surgical excision is curative.

Keywords: solid pseudopapillary tumor, Gruber–Frantz tumor, children.

Introduction

Gruber–Frantz tumor is a very rare pathological condition of the pancreas, firstly described by Frantz, in 1959 [1]. In 1996, the *World Health Organization* renamed this entity as solid pseudopapillary tumor (SPPT) for the international histological classification of the tumors of the exocrine pancreas [2]. The incidence of this condition varies in different papers between 0.2% and 2.7% of all primary pancreatic tumors [3]. More than 90% occur in young woman [4]. Only 7% of cases are men, usually they are 10 years older than affected women [5]. They occur even more rare during childhood. In 2004, Raffel reviewed the data from the literature and concluded that there are 111 pediatric cases published so far [6].

It was found that the incidence of SPPT is higher in individuals of Asian descent [7]. It is noted a constant apparent growth of the incidence of this tumor in this last decades, but this is probably due to a better knowledge of this condition [8]. The pathogenesis of this tumor remains unclear, some authors claiming that it has an endocrine origin, while others say that it arises from ductal cells, acinar pancreatic cells, or primitive cells [4, 7]. Characteristically, the majority of patients suffering from SPPT show minor symptoms or none at all, despite the fact that these tumors are often large [9].

The clinical picture of these patients is not specific: abdominal pain, anorexia, weight loss, jaundice, vomiting, or abdominal mass [5]. In 85% of cases, the tumor only interests the pancreas, while the other 15% may present peritoneal, hepatic, lymph nodes, spleen, colon metastases or even generalized carcinomatosis [5, 9]. The metastases incidence in pediatric patients is quite uncommon [7]. This tumor is known to have a low malignant potential, total resection of the tumor offering a good prognosis.

Patient, Methods and Results

A 15-year-old female presented with upper abdominal pain, apparently due to a minor abdominal trauma. Clinical examination of the patient revealed minor tenderness in the epigastrium. It was noted a palpable mass in the lower abdomen. The patient claims a minor abdominal pain history and occasional nausea for the past six months. Jaundice was absent. Routine laboratory tests (blood count, liver and renal function tests) were within normal range. CRP was 1.30 mg/dL. CEA and AFP were in the normal range. Ultrasound examination showed a well-defined mass lesion, apparently developed from the inferior aspect of the liver, being in contact with the head of the pancreas. Computer tomography revealed a heterogeneous, well-delineated, large mass (10/12 cm), apparently developed from the liver (Figure 1). No images of local invasion or intra-abdominal metastases were found. Also, the CT examination did not reveal any dilatation of the hepatic or pancreatic ducts.

Per-operative examination showed a 12/12 cm well-capsulated retroperitoneal mass, developed from the postero-lateral aspect of the pancreatic head, with a

clear delimitation from the visceral surface of the liver, with the preservation of Glisson's capsule. There was not found any local invasion or any intra-abdominal metastases. The tumor was removed without sacrificing pancreatic tissue (Figure 2). Macroscopically, the cut surface showed fleshy, pale-tan aspect with papillary excrescences and no cystic components (Figure 3).

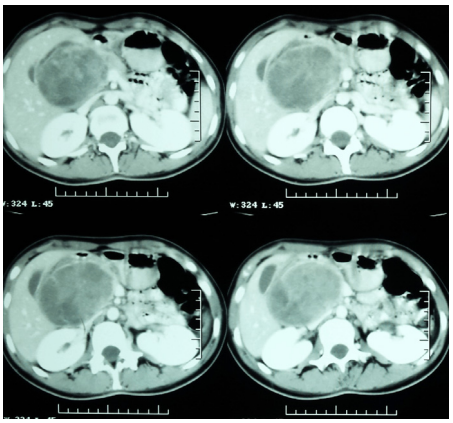

Figure 1 – ***CT: heterogeneous, large mass, apparently developed from the liver. No images of local invasion or intra-abdominal metastases were found. Also, the CT examination did not reveal any dilatation of the hepatic or pancreatic ducts.***

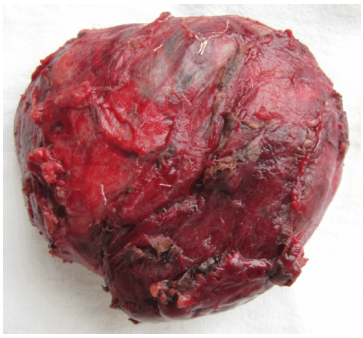

Figure 2 – ***Heterogeneous, large mass, well capsulated, entirely removed.***

Figure 3 – ***Cut surface of the tumor: fleshy, pale-tan aspect with papillary excrescences and no cystic components.***

The surgical specimen was fixed in 10% buffered formalin for 24 hours, then multiple tissue fragments were processed manually, embedded in paraffin and the 4 µm thick-sections were stained routinely with Hematoxylin–Eosin (HE).

Microscopically, the tumor was composed of solid, papillary and cystic areas, with compact sheets of neoplastic small round-to-oval cells with bland nuclei and eosinophilic cytoplasm, delicate papillae with fibrovascular cores lined by neoplastic cells and cystic spaces containing blood and necrotic debris.

For the immunohistochemistry, 4 µm thick sections were incubated with the following monoclonal antibodies: vimentin (rabbit monoclonal, SP20 clone, RTU), beta-catenin (14 clone, 1:50 dilution), progesterone (rabbit monoclonal, SP42 clone, 1:500 dilution), CD10 (56C6 clone, 1:50 dilution) with HiDef Detection HRP Polymer System, DAB chromogen and NSE cocktail (mouse monoclonal, DT01+BC100 clone, 1:80 dilution, MACH4 detection, DAB chromogen).

On immunohistochemistry, the tumor cells were consistently positive for vimentin, CD10 and progesterone receptors (PR); as for neuroendocrine markers, we found positivity for neuron specific enolase (NSE) in most tumor cells; beta-catenin expression was both cytoplasmic and nuclear in neoplastic cells.

The microscopic features, together with the immunophenotype were consistent with the diagnosis of solid pseudopapillary tumor [10] (Figures 4–11).

The postoperative evolution was uneventful. The patient was discharged on the 8th postoperative day. Four years follow-up period showed no recurrence.

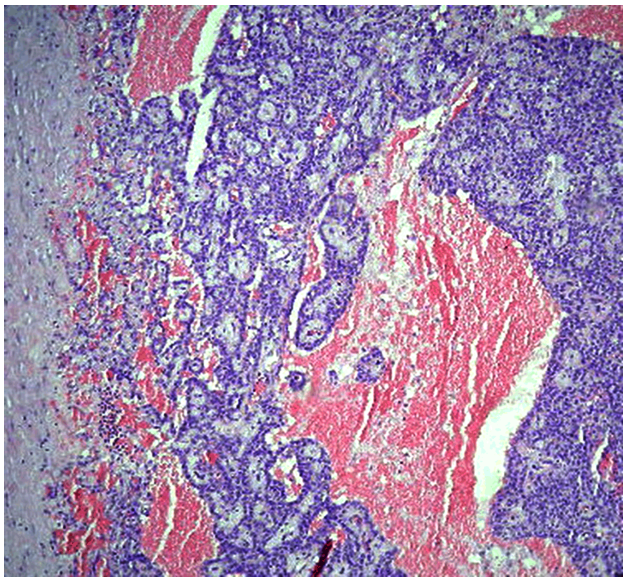

Figure 4 – ***Compact sheets of neoplastic small cells and cystic features with pseudopapillae. HE staining, ×100.***

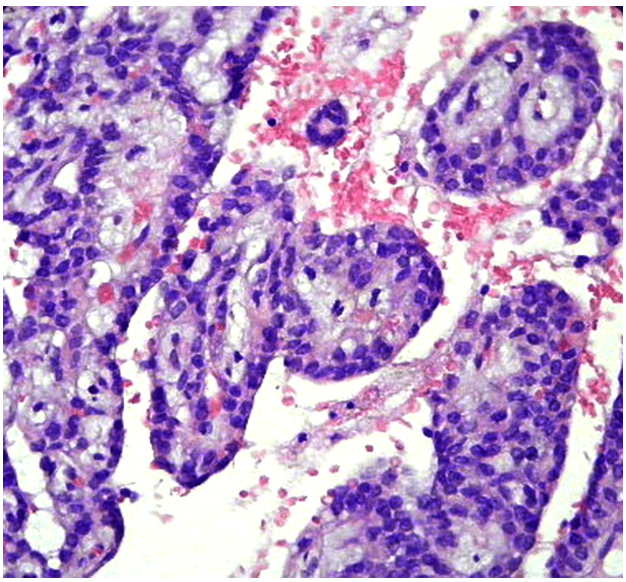

Figure 5 – ***Several layers of epithelial cells covering the papillae, with fibrovascular core and mucinous changes. HE staining, ×200.***

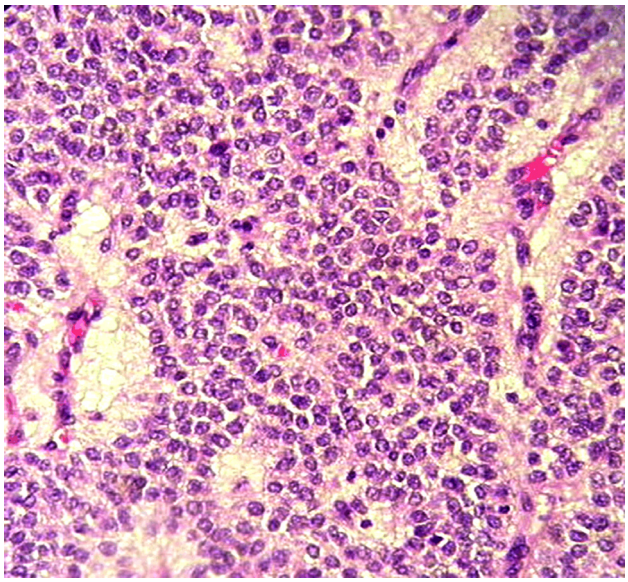

Figure 6 – ***Solid sheets of small cells and perivascular mucinous changes. HE staining, ×200.***

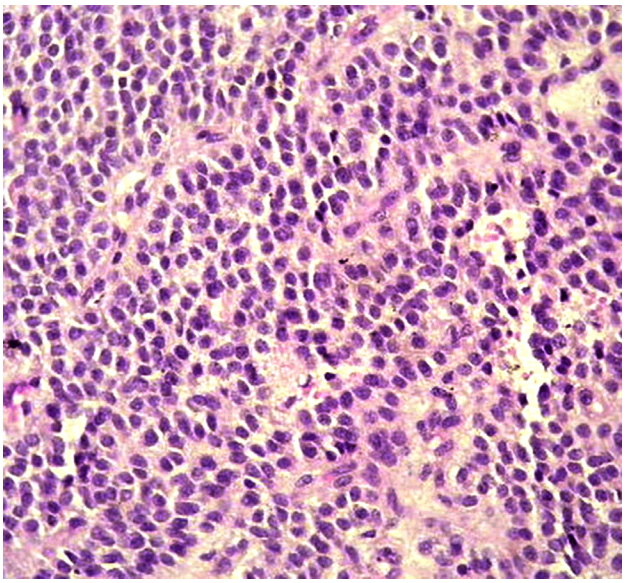

Figure 7 – ***Closely packed small cells and delicate fibrovascular stroma. HE staining, ×200.***

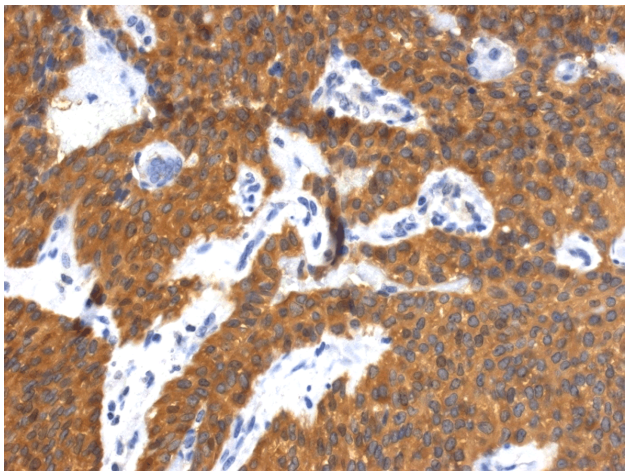

Figure 8 – ***Immunoreactivity to NSE in most tumor cells. NSE immunohistochemistry, ×200.***

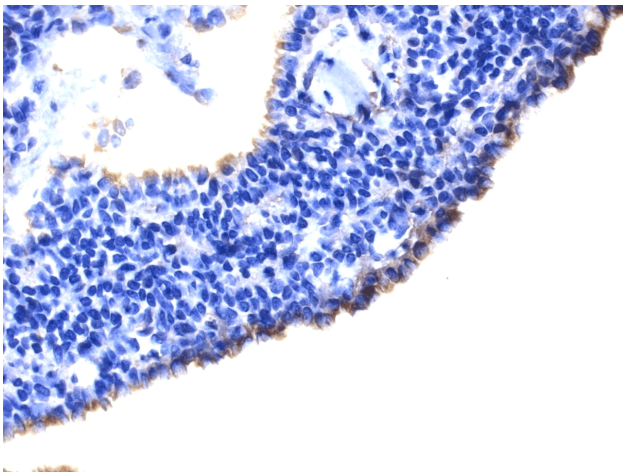

Figure 9 – ***CD10 positive cells. CD10 immunohistochemistry, ×200.***

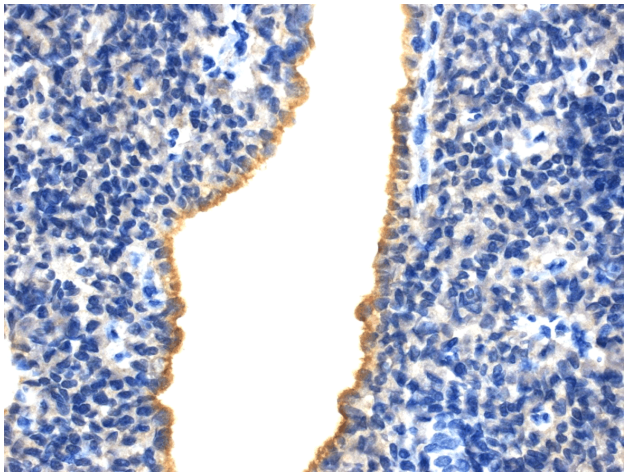

Figure 10 – ***Beta-catenin expression in tumor cells. Beta-catenin immunohistochemistry, ×200.***

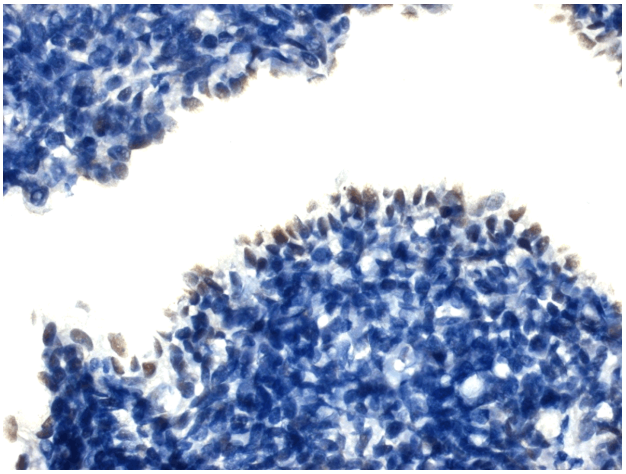

Figure 11 – ***Positivity for progesterone receptors. PR immunohistochemistry, ×200.***

Discussion

SPTT is a rare possibly malignant tumor of the pancreas. It occurs mainly in young women and girls and it accounts for only 1 to 2% of exocrine pancreatic tumors [5]. Some investigators [3, 4] have indicated a race, sex and age tendency for SPTTs of the pancreas in African-Americans and Asians, with a predilection for young women (mean age 27 years). Aydiner *et al.* believe

that this tumor have origin from a pluripotent primordial stem cell [11].

The pathogenesis of SPT of the pancreas remains uncertain although it has been suggested to be associated with a mutation of beta-catenin [9]. It was also suggested that the preference for females could be related to hormonal factors [12, 13]. Clinical picture is not relevant. Some patients are asymptotic and present with large tumors located in epigastrium, and sometimes patients experience chronic abdominal pain. Rarely, the patients had acute abdominal pain due to the rupture of a cyst [14]. Exocrine or endocrine insufficiencies have not so far been described and there are no specific tumor markers known [6].

SPTT can occur anywhere in the pancreas, but it was found that in children the predominant localization is in the pancreatic head [6, 15]. However, in other studies, Martin *et al.* reported 33.3% in the head, 25% in the body and 42% in the tail [16], while de Castro *et al.* reported 42% in the head, 50% in the corpus/tail and central in 8.3% [17].

Metastases can be found in about 15% of the cases and involve lymph nodes, liver, spleen, colon and mesocolon [5].

Aydiner *et al.* concluded in an article that immunohistochemistry does not offer additional information for the diagnosis of solid pseudopapillary tumor due to different lines of differentiation of tumor cells. Macroscopic and microscopic features (using HE staining) are mandatory for the diagnosis and differential diagnosis of this tumor [11], but careful correlation with the immunophenotype allows differential diagnosis with many entities like well differentiated pancreatic endocrine neoplasm, acinar cell carcinoma and pancreatic pseudocyst.

In another study, Raffel *et al.* emphasized that immunohistochemistry examinations of gastrin, insulin, glucagon, p53 and somatostatin varied considerably in different PCSN and do not allow general conclusions to be made for these tumors [6].

Differential diagnosis includes: inflammatory pseudocyst, mucinous cystic tumors, mucus secreting tumors, microcystic adenoma, islet cell tumor, acinar cell carcinoma, cystadenocarcinoma, pancreaticoblastoma and vascular tumors (hemangioma, lymphangioma, and angiosarcoma) [5].

After total resection of the tumor, most patients can survive for years but there is a risk of recurrence and hepatic metastasis [7, 8].

The various surgical procedures used in this disease are: Whipple's intervention, pylorus preserving pancreaticoduodenectomia, distal pancreatectomy with or without splenectomy, enucleation and excision. Also, liver metastasis should be treated with resection [5].

Recognition of this entity, especially in children is important because treatment differs from that of other pancreatic malignancies. Tumor resection without large safety margins is adequate for treatment. Therefore, preservation of pancreatic tissue and the spleen should be attempted in every child [18].

In our case, the tumor was revealed by chance, following a minor abdominal trauma. Preoperatory imagistic findings were not consistent with the tumor origin. We succeeded to remove only the tumor, leaving the pancreatic normal tissue intact. The diagnosis was established on histopathological examination and certified by immunohistochemistry. Four years follow-up period showed excellent results.

Conclusions

SPPT occurs extremely rare in children. Clinical picture and imagistic findings are not suggestive, only histopathological examination establishing the diagnosis. As it has a low malignant potential, in the absence of metastasis children can show positive evolution after tumor excision only, with the possibility of preserving surrounding tissues and organs.

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Corresponding author
Radu-Iulian Spătaru, Assistant Professor, MD, PhD, Department of Pediatric Surgery, "Carol Davila" University of Medicine and Pharmacy, "Maria Skłodowska Curie" Emergency Clinical Hospital for Children, 20 Constantin Brâncoveanu Avenue, 041434 Bucharest, Romania; Phone +40788–372 478, e-mail: radu_spataru@yahoo.com

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