

Hypoglycemia, a rare presentation of a solid pseudopapillary neoplasm of the pancreas: A case report

Maha ARAFAH, Hala KFOURY, Shaesta NASEEM

Department of Pathology, King Saud University, King Khalid University Hospital, Riyadh, Saudi Arabia

A solid pseudopapillary neoplasm of the pancreas is an uncommon and “enigmatic” pancreatic neoplasm of low malignant potential generally occurring in young women. The pathologic features of this tumor are characteristic, and adequate surgical intervention is associated with an excellent prognosis. We report the first case of combined solid pseudopapillary neoplasm and islet cell hyperplasia of the pancreas in the pediatric age group. A 16-year-old Saudi female presented to the Emergency Room with a history of frequent attacks of hypoglycemia. Radiologically, a mass in the tail of the pancreas was identified. The pre-operative diagnosis of insulinoma was suggested, and en bloc distal pancreatectomy with splenectomy was performed. A solid pseudopapillary neoplasm and islet cell hyperplasia of the tail of the pancreas was diagnosed by routine histology and by immunohistochemistry. The patient was treated successfully and is now in good health with regular follow-up for the last 13 months. In the pediatric age group, these tumors are very rare and can present as repeated episodes of hypoglycemia. This association sheds light on the histogenesis of solid pseudopapillary neoplasm of the pancreas and also allows appropriate and prompt management to be undertaken by the clinicians.

Key words: Solid pseudopapillary tumor, benign neoplasm of pancreas, hypoglycemia

Hipoglisemi, pankreasın solid pseudopapiller tümörünün nadir bir prezentasyonu – Vaka sunumu

Pankreasın solid pseudopapiller neoplazisi, nadir görülen, anlaşılması güç, malign potansiyeli düşük olan ve genelde genç kadınlarda tespit edilen tümördür. Bu tümörün patolojik özellikleri karakteristiktir ve uygun cerrahi ile oldukça iyi prognoz sağlanabilmektedir. Burada, pediatrik hastada solid pseudopapiller tümör ile adacık hücresi hiperplazisinin birlikte olduğu literatürdeki ilk vaka sunulmuştur. Onaltı yaşında Sudi kadın hasta acil servise sık tekrarlayan hipoglisemi ile başvurdu. Radyolojik incelemesinde pankreas kuyruğunda kitle tespit edildi. Preoperatif ön tanısı insulinoma olan hastaya enblok distal pankreatektomi ve splenektomi uygulandı. Rutin histolojik ve immunhistokimyasal inceleme sonucunda pseudopapiller neoplazi ve adacık hücresi hiperplazisi tanısı konuldu. Hastanın tedavisi başarılı oldu ve postoperatif 13. ayda sağlıklı olarak takip edilmektedir. Pediatrik yaş grubunda, bu tümörler oldukça nadir görülürler ve tekrarlayan hipoglisemi atakları ile prezente olabilirler. Bu ilişki pankreasın pseudopapiller tümörünün histogenezine ışık tutmakta ve klinisyenlerin doğru tanı ve erken tedavi uygulamalarına imkan tanımaktadır.

Anahtar kelimeler: Solid pseudopapiller tümör, pankreasın benign neoplazisi, hipoglisemi

INTRODUCTION

Solid pseudopapillary neoplasm of the pancreas is a rare tumor accounting for approximately 1-2% of exocrine pancreatic tumors (1) and approximately 13% of surgically resected cystic lesions of the pan-

creas. Frantz (2) first described this tumor in 1959 as a “papillary tumor of the pancreas, benign or malignant”. It was not until 1996 when the World Health Organization assigned its current term ‘so-

lid pseudopapillary tumor (SPT)' in the international histological classification of tumors of the exocrine pancreas (3).

The tumor is exclusively encountered in young females with a mean age of 27.2 years (1). It is frequently asymptomatic and found incidentally in 15% of cases (4). Although a low-grade malignant potential is recognized, about 14.7% of cases demonstrate malignant behavior with recurrence and metastases (5).

Solid pseudopapillary neoplasm appears to be unique to the pancreas, but its origin is unclear, as it lacks clear evidence of ductal, acinar or endocrine differentiation. Because of the prolonged natural history and the relative rarity of the tumor, it has been difficult to establish histopathologic criteria predictive of aggressive behavior with metastatic dissemination, possibly leading to death. The accurate diagnosis of this entity is important as the tumor generally carries a much better prognosis than the typical adenocarcinoma of the pancreas, and complete surgical resection is usually curative in more than 90% of cases (6). Patients rarely die as a direct result of this neoplasm.

CASE REPORT

The patient, a 16-year-old girl, a known case of bronchial asthma on Symbicort and Ventolin inhaler, presented to the Emergency Department with dizziness, drowsiness, nervousness, sweating, and tremors. The patient had experienced similar attacks intermittently for the past month, which were aggravated by stress and relieved by drinking

fruit juice. At the time of admission, her temperature and vital signs were normal. All her routine laboratory parameters were within range except for low blood glucose level of 1.5 mmol/L. She was further investigated to determine the cause of the hypoglycemia. Her insulin level was 74.81 micro unit/ml (high) and C-peptide was 2.22 ng/ml (high). Computerized tomography (CT) of the abdomen showed a large multi-cystic mass with an irregular low-density pattern measuring 7.5 x 6.5 x 3 cm in the tail of the pancreas, suggesting a neuroendocrine tumor of the pancreas. Considering her repeated hypoglycemic attacks and her laboratory and radiological findings, the provisional diagnosis of insulinoma of the pancreas was made, and laparoscopic distal pancreatectomy with splenectomy was performed. There were no signs of local invasion or distant dissemination perioperatively. The postoperative course was uneventful, and no adjuvant therapy was given except for pneumococcal and *Haemophilus influenzae* vaccines before she was discharged a week later.

On gross examination, a nodular, friable, partly hemorrhagic and cystic tan mass measuring 7.5x6.5x3 cm, with an adjacent pancreatic tissue measuring 2 cm, was noted. The light microscopic study demonstrated solid areas composed of uniform small-to-medium, round-to-oval eosinophilic cells with folded nuclei and indistinct nucleoli arranged around delicate fibrovascular septae (Figure 1A, 1B). In non-cohesive areas, the creation of spaces between the cells resulted in a rare papillary pattern. Frequent periodic acid-Schiff (PAS)-

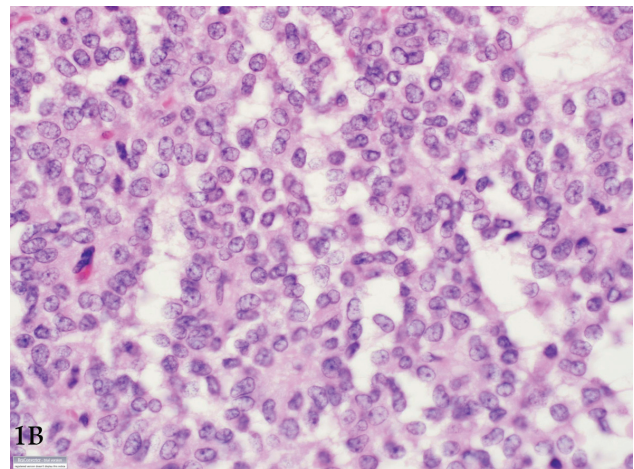
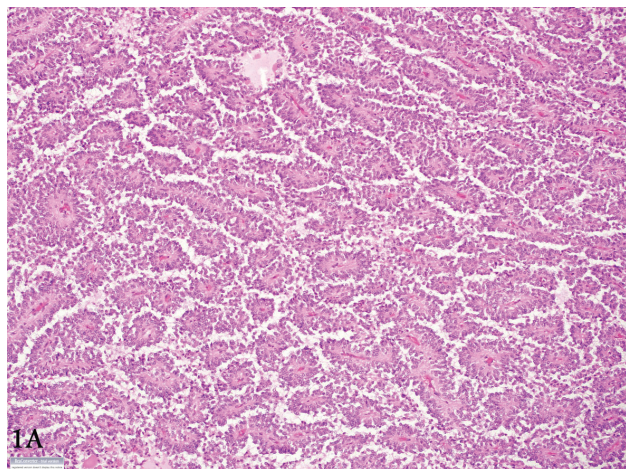


Figure 1. (A): Characteristic pseudopapillary formations consisting of irregular cuffs of cells clinging to the central fibrovascular cores (Hematoxylin and eosin x100). **(B):** At high power, the solid areas showing polygonal tumor cells exhibiting relative uniformity and round-to-oval nuclei with nuclear grooves (Hematoxylin and eosin x600).

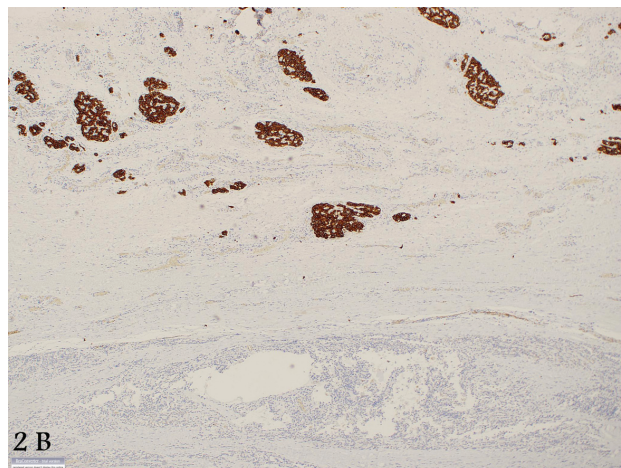
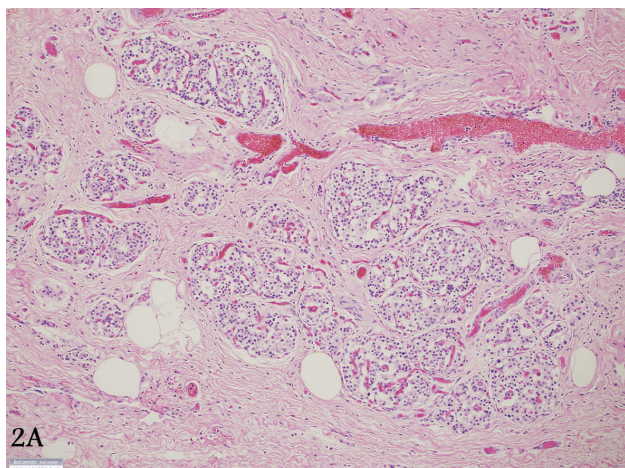


Figure 2. Multiple foci of hyperplastic islet cells (A) (Hematoxylin and eosin x100), which are positive for synaptophysin. (B): The adjacent tumor cells are negative (x40).

positive globules were seen. The neoplasm was not encapsulated, and although the interface between the mass and the uninvolved pancreas was irregular on histology, no invasion of the pancreatic parenchyma was noted. Perineural invasion was noted. Multiple foci of hyperplastic islet cells were seen outside the neoplasm and in the peripancreatic fat (Figure 2A, 2B). Six lymph nodes were identified and were negative for metastases.

By immunohistochemistry, the tumor cells were positive for CD56 and vimentin, and focally positive for CD10, cyclin-D1 and progesterone receptor. The cells were negative for synaptophysin, chromogranin and B-catenin. On the basis of the characteristic morphologic and immunohistochemical findings, the diagnosis of SPT of the pancreas with islet cell hyperplasia was made. At the last follow-up 13 months after the operation, the patient was well without any complaints.

DISCUSSION

Recently, SPTs of the pancreas are being recognized with increasing frequency and have become a more common finding in clinical practice because of the greater awareness of this disease, better understanding of its diagnosis and widespread use of advanced imaging modalities. It is the tumor of young females in their second or third decades of life and is rarely seen in children. A review of the literature revealed 31 cases reported in the pediatric age group (7-12). When searching the national literature, we were able to find only two reported cases of SPT in the pediatric age group in the Saudi population (10,13).

In spite of their possibly histological findings of malignancy, SPT typically shows a benign clinical course and a low malignant potential. These tumors are detected incidentally in most cases; however, abdominal pain may be the sole and important sign of this tumor (7). In addition, anorexia, weight loss, abdominal mass, and pressure symptoms in adjacent organs can also be present. Very rarely, the patient can present with acute pancreatitis (14) or hematemesis (15). Our patient presented with hypoglycemia, which is usually not seen with this type of tumor, as this tumor is non-functional. SPT was identified incidentally in our case. The presence of hypoglycemia was explained by the presence of multiple foci of hyperplastic islets cells outside the neoplasm and in the peripancreatic fat.

Solid pseudopapillary tumor (SPT) of the pancreas has distinct pathological features. The mass may occur anywhere in the pancreas but is found most frequently in the head or tail. Grossly, the tumor is large, usually encapsulated. The cut section is typically soft with degenerative cystic foci, hemorrhage and necrosis. On light microscopy, the hallmark histologic pattern occurs when the tumor cells form papillary configurations composed of a fibrovascular stalk surrounded by several layers of epithelial cells.

Immunohistochemical studies have shown that SPT is reactive for CD10, CD56, and estrogen and progesterone receptors. Markers of acinar (trypsin and chymotrypsin) and ductal (glycoproteins) differentiation are consistently absent (16). Flow cytometry shows aneuploidy. Laboratory values

are not contributory, although few cases do show a raised level of CA19-9 (17).

Solid pseudopapillary tumors (SPTs) are able to metastasize to the liver in 5.6% of cases mainly through blood vessels via the superior mesenteric vein and portal veins (18). Since the malignant potential of these tumors is low, the prognosis is excellent when complete resection is achieved, even in the presence of metastatic disease.

Surgery is the therapy of choice. Complete surgical excision should always be attempted in a suspected case of SPT, even if it implies major resection has to be performed (i.e. pancreaticoduodenectomy along with adjacent organ resection). Although the treatment of metastasis is not standardized, there is general agreement that surgical debulking should be performed (19). Even in the reported cases with malignant behavior, the survival of the patient is prolonged after surgical resection.

In conclusion, the awareness of both the pathologist and surgeon of this entity when assessing solid or partially cystic pancreatic mass in the pediatric age group plays an important role in the correct diagnosis and treatment of this neoplasm. The complete removal of the tumor irrespective of the magnitude of resection involved is the only effective but highly successful treatment option, and is associated with long-term survival even in the presence of metastatic disease. However, regular follow-up is mandatory for all patients who undergo potentially curative resection. The association of this entity with hypoglycemia, to our knowledge, has not been reported previously in the literature. This association could be a coincidental finding, or it can shed a light on the histogenesis of SPT of the pancreas, which may be related to neuroendocrine cells. The possibility that SPT produces a factor that induces hyperplasia of the adjacent neuroendocrine cells is an aspect requiring further investigation and study.

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