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Case Report

A Rare Tumor in Adulthood: Extrapancreatic Pancreatoblastoma

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Abstract

Pancreatoblastoma is a rare malignant epithelial neoplasm of the pancreas. It primarily occurs in the pediatric population and is extremely uncommon in adults. A 64-year-old male patient with no known systemic disease presented to our clinic with abdominal pain and dyspeptic complaints. On physical examination, a tender epigastric mass was palpated. The patient was operated on with a preliminary diagnosis of gastrointestinal stromal tumor. En-bloc resection of the mass was performed. The transverse colon was segmentally resected with wedge resection of the gastric corpus. A stapled side-to-side anastomosis was performed. The macroscopic examination of the case revealed a tumoral lesion of approximately 16x13.5x10m, located in the submucosal area between the gastric corpus and the transverse colon. The microscopic examination showed acini, which have a highly cellular appearance, contain areas of necrosis, and form nested structures in places, stratification in places. The immunohistochemical examination demonstrated positive Trypsin expression, while focal positive expression of neuroendocrine markers such as Synaptophysin, Chromogranin, and Insulinoma-associated protein 1 (INSM-1) was observed. In beta-catenin staining, aberrant nuclear and cytoplasmic positive expression was observed, and this staining pattern and morphology confirmed the diagnosis of pancreatoblastoma. Pathological Stage: PT3,N0,Mx the patient had an uneventful postoperative period and was referred to the oncology department for adjuvant chemotherapy. Pancreatoblastoma is an extremely rare type of pancreatic cancer and there are no established guidelines for the treatment of this aggressive disease. Surgical resection is recommended if anatomically possible. Pancreatoblastoma should be considered in the differential diagnosis of asymptomatic masses containing cystic–solid components and reaching very large sizes.

Key words: Pancreas, Rare tumor, Pancreatoblastoma

Introduction

Pancreatoblastoma (PB) is a rare epithelial neoplasm of the pancreas that is very rarely diagnosed in the adult, typically occurring in the pediatric population. Since the first report of PB in 1957, less than 200 cases have been reported in the literature, of which about 50 were found in the adult age population (1,2,3).

Clinical presentation is often nonspecific; it presents with nonspecific symptoms such as abdominal pain, abdominal mass, jaundice, and weight loss. Although definitive diagnosis is only possible with histopathological analysis, imaging techniques seem to be the most useful approach to detect and stage these tumors. On computed tomography (CT) and Magnetic Resonance Imaging (MRI), it usually appears as an exophytic, irregular, and hypovascular mass with well-defined margins and progressive enhancement (1,4). Endoscopic ultrasound may be a useful tool allowing tissue sample collection.

Due to its rarity, there are currently no guidelines on management protocols for PB. Surgical resection is the only potential curative treatment of choice for this tumor type. However, surgical treatment is not always possible, as most cases are detected in the advanced, unresectable stage. The poorer prognosis of PB in adults is considered to be related to its faster growth and spread and more aggressive biological behavior in this age group (5).
Extrapancreatic Pancreatoblastoma, Ugur Topal, et. al.

In current literature reviews, PB originated in the head of the pancreas in (53%) of the patients, other common sites were the tail and body of the pancreas, respectively (6). It has been reported that it may develop in the extra-pancreatic pancreatic tissue in childhood as in other pancreatic tumors (7), however, extra-pancreatic PB in adulthood has not been identified in the literature.

In this study, we aimed to present a 64-year-old male patient diagnosed with extrapancreatic pancreatoblastoma located in the stomach, in the light of the literature.

Case Presentation

A 64-year-old male patient with no known systemic disease presented to our clinic with abdominal pain and dyspeptic complaints. On physical examination, a tender epigastric mass was palpated. Lab results were unremarkable except for anemia: hemoglobin (HGB) 9.1 g/dL, hematocrit (HCT) 29.3%, tumor markers were normal, carcinoembryonic antigen (CEA) 3.03 ug/mL Carbohydrate Antigen (CA–19–9) 3.42 U/mL.

Computed tomography revealed a tumoral mass suspicious for pancreatic invasion originating from the gastric corpus.

The patient was operated on with a preliminary diagnosis of gastrointestinal stromal tumor. The patient had a mass surrounded by the omentum invading the transverse colon originating from the gastric corpus. En-bloc resection of the tumor was performed. The transverse colon was segmentally resected with wedge resection of the gastric corpus. The stapled anastomosis was performed.

The macroscopic examination of the case showed a tumoral lesion of approximately 16x13.5x10 cm, located in the submucosal area between the gastric corpus and the transverse colon. Although the tumor contained dense brown necrotic areas, it also had off–white lobulated areas. The microscopic examination showed acini, which have a highly cellular appearance, contain areas of necrosis, and form nested structures in places, stratification in places (Figure 1). Squamoid corpuscle–like structures accompanying these structures were also noted in focal areas (Figure 2). A neuroendocrine–like pattern was present forming rosette–like structures in some areas (Figure 3). Significant pleomorphism, atypia, increased mitotic figure were observed in the cells (Figure 4). The tumor formed lymphovascular invasion (Figure–5) and perineural invasion. The tumor has reached the gastric and colon mucosa and ulceration was present in these areas. Neuroendocrine tumor, acinar cell carcinoma, and pancreatoblastoma were included in the differential diagnosis with these histomorphological findings, and immunohistochemical staining was performed accordingly. The immunohistochemical examination revealed positive Trypsin expression (Figure 6), while

Figure–1: Formation of acini–like structures by infiltrative tumoral formation, accompanying necrosis areas at the bottom of the figure (x40).

Figure–2: Squamoid structures prominent centrally between the acini (x10).

Figure–3: Uniform appearance of acini forming neuroendocrine–like rosette–like areas in places (x20).
focal positive expression of neuroendocrine markers such as Synaptophysin, Chromogranin, and INSM-1 was observed. In beta-catenin staining, aberrant nuclear and cytoplasmic positive expression was observed, and this staining pattern and morphology confirmed the diagnosis of pancreatoblastoma (Figure 7). Lymph Nodes: Reactive hyperplasia in 9 lymph nodes. Pathological Stage: pT3, N0, Mx (AJCC 8). Immunohistochemical Findings: – Trypsin: Positive – B-Catenin: Nuclear and cytoplasmic positive – INSM-1: Weakly positive – Synaptophysin: Positive – CK7: Negative – CK20: Focal positive – CDX2: Positive – CD56: Negative – Chromogranin: Negative – MLH 1: Intact nuclear staining – PMS2: Intact nuclear staining – MLH6: Intact nuclear staining – MSH2: Intact nuclear staining (Figure 4).

The patient had an uneventful postoperative period and was referred to the oncology department for adjuvant chemotherapy. The patient received a cisplatin and doxorubicin–based chemotherapy regimen. No progression or systemic metastasis developed in the follow-ups. He died due to cerebrovascular failure in the 20th postoperative month.

Discussion

Adult PB is a rare neoplasm of epithelial origin, accounting for <0.5% of exocrine pancreatic tumors in adulthood. PB was initially described by Becker(3) in 1957 as infantile pancreatic carcinoma, Horie et al coined the term pancreatoblastoma in 1977(8). Palosaari et al. presented the first case of PB in a 37–year–old patient in 1986(9).

The etiology and molecular pathogenesis of PB are unknown. The tumor mostly occurs sporadically, but its association with genetic syndromes such as familial adenomatous polyposis syndrome and Beckwith–Weidemann syndrome has been documented. Unlike pancreatic ductal adenocarcinoma, PB does not seem to exhibit K–ras oncogene or p53 tumor mutations(6,10). Abraham et al. demonstrated that allelic loss on chromosome 11p is the most common genetic alteration in pancreatoblastoma, present in 86% of the patients(11). In our case, there was a sporadic developing tumor.

In the review of 41 adult pancreatoblastoma cases in the literature, the mean age at diagnosis was 41.4 ± 17.4 (18–75) years. Tumor diameter was found to be greater than 8 cm at the time of diagnosis in 39.0% of the cases. Patient age and tumor size were similar between men and women (P = 0.59; P = 0.32, respectively)(3). In the same literature review, abdominal pain was the most common symptom (41.5%), followed by weight loss (29.2%), jaundice (21.9%), abdominal mass (17.1%), and diarrhea (7.3%)(3). The age of our case was higher than the mean age in the literature, and the presenting complaint was similar to the literature.


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In pediatric PB patients, elevated alpha fetoprotein (AFP)
and CEA levels are the most common abnormal serological markers, and increased AFP expression has been reported in ≤ 68% of cases. In contrast, these tumor markers typically remained within the normal range in adult patients. In addition, serum AFP levels may be used to monitor clinical response to therapy or to monitor for relapses(6). It was also within normal limits in our case.

Imaging features of pancreatoblastoma have been described in the literature. There are no significant differences in imaging findings of adult and pediatric patients. Adult pancreatoblastoma is usually a large, well-circumscribed, heterogeneous mass(10). PB is observed as a well-circumscribed lesion with a heterogeneous architecture consisting of solid and cystic components at US. Internal septa are common in cystic components. Rarely, it is seen as a hypoechoic solid mass. Color Doppler US may show increased vascularization within the mass. Most PB tumors are well-defined, large, heterogeneous on cross-sectional imaging, and have a mixed solid-cystic appearance. On magnetic resonance imaging, tumors are usually identified to be heterogeneous with low-to-moderate signal intensity on T1-weighted images and high signal on T2-weighted images(6,10).

Pathological criteria of pancreatoblastoma include a calcified mass containing solid and cystic elements, necrosis, the presence of acinar cells, and a distinct organoid pattern containing lobular structures with squamoid corpuscles in the pancreas region. Immunohistochemistry may facilitate the characterization of various components of the tumor. PB tumors often contain multiple cell types and demonstrate variable combinations of ductal, acinar, and neuroendocrine components. In immunohistochemical examinations, pancreatoblastoma had pancreatic enzymes such as lipase, tyrosine, chymotrypsin, α-1-antitrypsin, and glucose–6–phosphatase, AFP, carcinoembryonic antigen, cancer-associated antigen 19–9. Seldom, endocrine marker-like chromogranin, neuron-specific enolase, and synaptophysin have also been positive(7). In our case, the positivity of trypsin, β–catenin, insm–1, and synaptophysin was observed. We can attribute this condition to the fact that the tumor contained different components in our patient.

PB invades adjacent structures such as the spleen, colon, duodenum, mesenteric vascular structures, and peripancreatic soft tissue. Metastasis and/or invasion of adjacent structures accounted for 35–58% of adult PB. The liver is the most common site of metastasis. However, metastases to the lymph nodes, lungs, bone, and peritoneum have also been reported(4,10). In our case, there was no distant organ metastasis. The tumor originating from the stomach invaded the colon, and no metastasis was detected in the dissected lymph nodes.

Surgical resection is the mainstay of treatment and complete resection has been associated with long-term survival. There are no specific National Comprehensive Cancer Network guidelines regarding the treatment of pancreatoblastoma. However, in the 2000s, Italian Tumori Rari in Età’ Pediatrica project developed chemotherapy guidelines consisting of cisplatin at 80 mg/m2 for a continuous 24 h followed by doxorubicin at 60 mg/m2 for a continuous 48 h(13). Although the benefits of neoadjuvant chemotherapy have yet to be studied in randomized trials, it has demonstrated a survival benefit in a small pediatric series(13). A certain degree of response to chemotherapy with long-term survival was reported in locally unresectable, metastatic, or recurrent diseases. Radiotherapy is recommended together with chemotherapy in unresectable tumors(14). In the literature, the best prognosis has been reported in patients who had no metastasis and had a total resection(4,8).

**Conclusions**

Pancreatoblastoma is an extremely rare type of pancreatic cancer and there are no established guidelines for the management of this aggressive disease. Surgical resection is advised if anatomically possible, and the role of chemoradiotherapy is unclear. It has worse outcomes in adults than in children. Pancreatoblastoma should be considered in the differential diagnosis of asymptomatic masses containing cystic–solid components and reaching very large sizes.

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None

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**Authors’ contributions:**

Author Uğur Topal and author Begüm Çalıım Gürbüz have given substantial contributions to the conception or the design of the manuscript, author Hasan Bektaş to acquisition, analysis and interpretation of the data. All authors have participated to drafting the manuscript, author A revised it critically. All authors read and approved the final version of the manuscript.
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