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Pediatric Pancreatoblastoma: A Case Report

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Abstract

Background: Pancreatoblastoma (PB) is an exceedingly uncommon pancreatic tumor arising from pancreatic exocrine cells. It is the most common malignant pancreatic tumor in childhood.

Case presentation: We report a case of PB in a 5-year-old girl who presented to our institution with severe abdominal pain, anorexia, vomiting, and jaundice. Laboratory tests were compatible with cholestasis. Ultrasound imaging showed mild intra- and extrahepatic bile duct dilation as well as a pancreatic mass. A Computed Tomography (CT) scan confirmed a large mass in the head of the pancreas, which was associated with periportal lymphadenopathy as well as anterior and inward displacement of superior mesenteric vessels. Although the mass was unresectable at the time of admission to our center, an open biopsy of the tumor was performed, which revealed a diagnosis of PB. Following six months of neoadjuvant chemotherapy, the size of the tumor was dramatically decreased, allowing the complete resection of it.

Conclusion: When a child presents with a massive solid cystic tumor in the pancreas, the possibility of pancreatoblastoma must be considered. Surgery is utilized to completely remove the tumor, while pathology and immunohistochemistry are used to confirm the diagnosis. Patients with huge tumors or extensive lymphadenopathy typically need neoadjuvant chemotherapy before surgery to downstage their disease.

Key Words: Case report, Computed Tomography, pancreatic mass, Pancreatoblastoma.

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1- INTRODUCTION

Pancreatoblastoma (PB) is a rare tumor, mostly seen in children but occasionally affecting adults. Pancreatoblastomas are the most prevalent type of pancreatic tumor in children, although making up only 0.5% of all pancreatic non endocrine tumors. They arise from exocrine pancreatic cells (1). The course in infants and children is less aggressive compared to adults. Most of these tumors are located within the head of the pancreas and secrete Alpha-Fetoprotein (AFP) in up to 68% of cases. Ultrasound and Computed Tomography (CT) play a critical role in preoperative assessment, which is often challenging. The primary treatment is surgical resection of the pancreas (2). The role of adjuvant chemotherapy or radiotherapy is not clear, in part due to the small number of cases. Chemotherapy regimens consisting of Cyclophosphamide, Etoposide, Doxorubicin, and Cisplatin have been performed with some success. Poor prognostic factors include metastatic disease and unresectable primary tumors (3).

Clinical presentations and symptoms of pancreatoblastoma comprise a variety of non-specific symptoms, including palpable abdominal mass, abdominal pain, anorexia, vomiting, and weight loss. Jaundice occurs less commonly in children than in adults (2). The liver, lungs, and regional lymph nodes are the most common metastatic sites. Radical surgical resection is the treatment of choice, although many patients are unresectable at diagnosis and need chemotherapy.

2- CASE REPORT

A 5-year-old girl presented to our institution with severe abdominal pain from a few days ago with a 4-week history of anorexia, vomiting, and jaundice. Her vital signs were normal in the emergency department. Physical examination revealed icteric sclera as well as epigastric tenderness and abdominal guarding. A complete workup for her symptoms was done. Laboratory tests showed increased alkaline phosphatase levels and raised bilirubin levels with a cholestatic pattern. Blood/urine cultures were negative. Complete Blood Count (CBC), coagulation tests, renal function tests, thyroid function tests, serum electrolytes, bicarbonate, glucose, and albumin levels were in normal ranges. Abdominal ultrasonography was done, which showed mild dilation of intra- and extrahepatic bile ducts along with a large, heterogeneously hypoechoic pancreatic mass. Moreover, a CT scan was conducted showing a pancreatic mass measuring 23*28*50 mm in the head of the pancreas, along with periportal lymphadenopathy, dilation of intra- and extrahepatic bile ducts, encasement of the celiac trunk and anterior and inward displacement of the superior mesenteric artery and vein (**Fig. 1**).

A stenting procedure by Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed for the patient to relieve the incomplete biliary drainage. Tissue biopsy samples of the pancreatic mass were obtained via open surgery. Histologic examination reported irregular geographic areas of tumor fragments separated by fibrous tissue, composed of proliferating mildly atypical epithelial cells with hyperchromatic nuclei and abundant cytoplasm. Some areas with an acinar pattern of cell arrangement were present. There was no evidence of pseudopapillary architecture. There was diffuse immunoreactivity of all infiltrative-appearing small proliferating ducts as well as large normal ducts for CK7. All tumoral cells showed strong cytoplasmic immunoreactivity for β-catenin. There were multifocal areas of synaptophysin and a focal area of chromogranin immunoreaction.

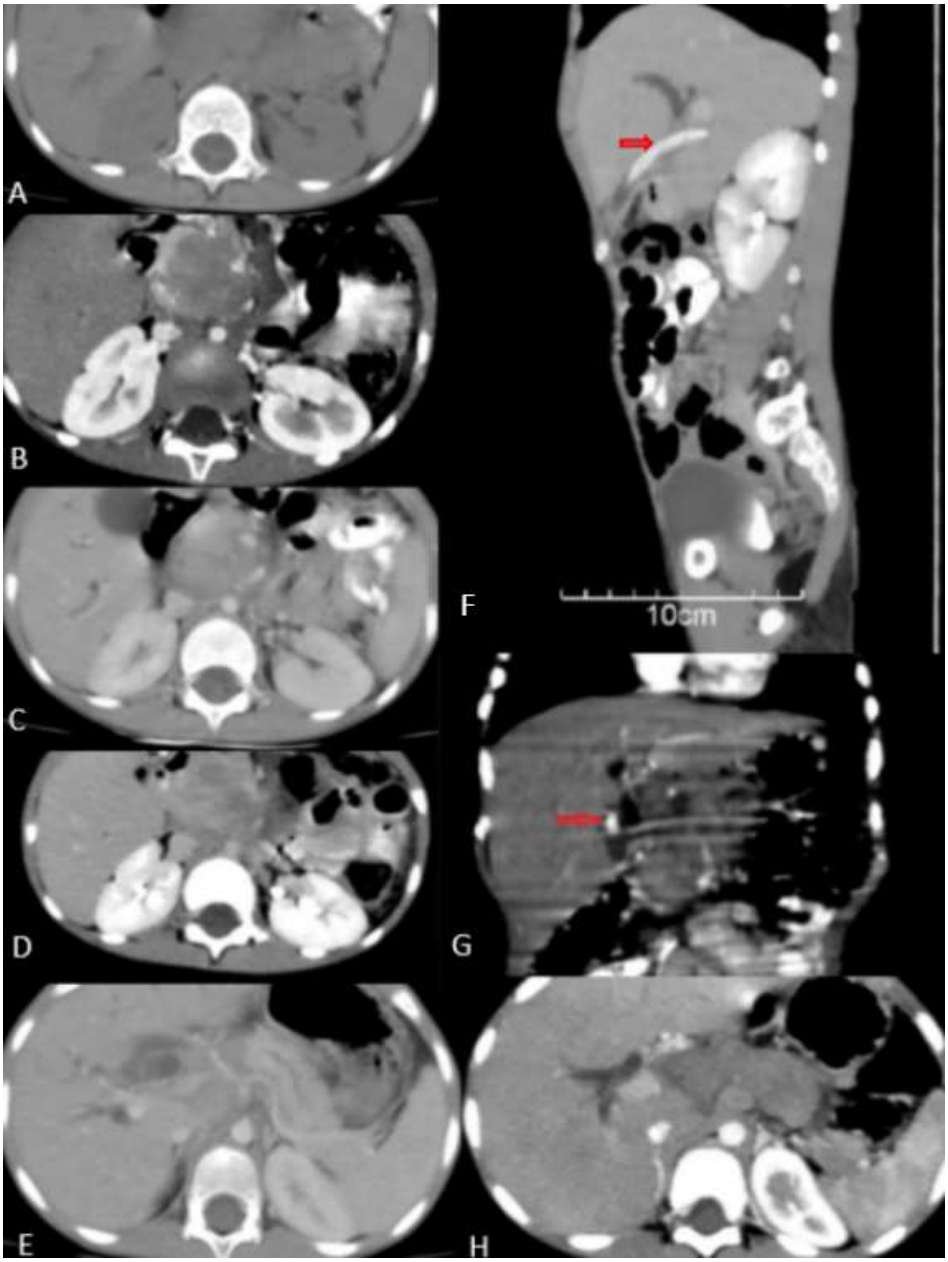

Fig. 1: pre-treatmentimaging findings

Axial planes of non-contrast (A), late arterial phase (B), portal phase (C), and delayed phase (D) CT scan show a large mass in the head of pancreas with mass effect on duodenum which has heterogeneous enhancement and has displaced superior mesenteric vessels to anterior and the left side. The compression effect of the mass and associated lymphadenopathies has caused dilation of the intra- and extrahepatic bile duct as well as the main pancreatic duct (E&H). Encasement of the celiac trunk by the soft tissue mass is also noted (E). Due to these findings, a stent (red arrow) was placed in the common bile duct, before starting chemotherapy (F&G). Multiple enlarged lymph nodes are seen adjacent to the celiac axis and in the periportal region (H)

Ki67 proliferative index measured approximately 5%. All cells tested negative for CEA, CD10, CD99, CK20, ER, and PR. The histopathologic and immunohistochemistry findings were consistent with pancreatoblastoma (**Fig. 2**).

Due to the large size of the tumor and the presence of extensive lymphadenopathies, surgical resection was not possible. Therefore, chemotherapy with Cisplatin and Adriamycin was administered. After six cycles of preoperative chemotherapy, the tumor size was reduced, and lymphadenopathies diminished (**Fig. 3**), allowing surgical resection. In follow-up, the patient was free of symptoms at 6 months and 1 year after surgery with no evidence of recurrence.

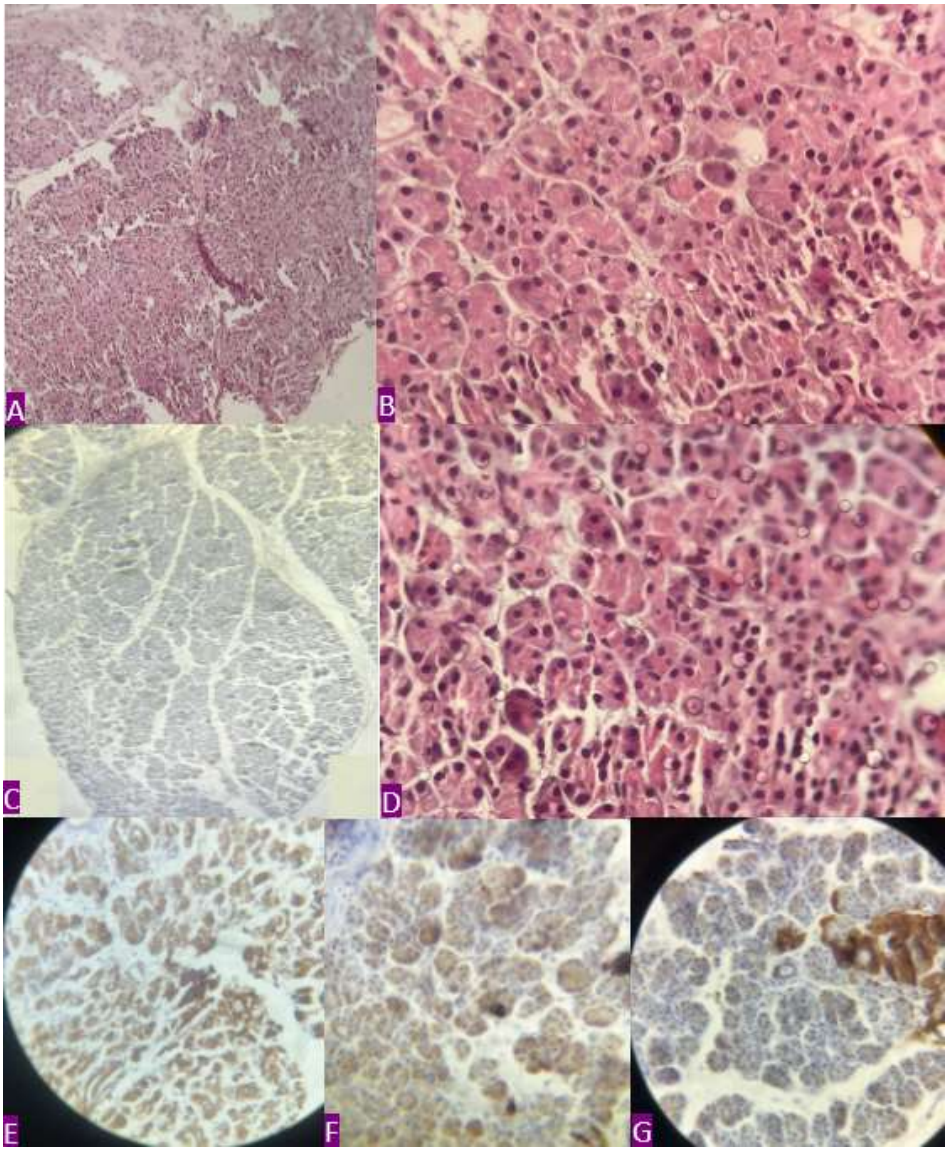

Fig. 2: Histopathology and Immunohistochemistry results

Mildly atypical polygonal cells with hyperchromatic nuclei and an abundant amount of cytoplasm separated by fibrotic bundles are seen in H&E stained slides (A, B&D), Negative CEA immunoreactivity (C). Strong immunoreaction of tumoral cells for β-catenin (E). Multifocal areas of immunoreaction for synaptophysin (F). The focal area of tumoral cells was weakly positive for chromogranin (G).

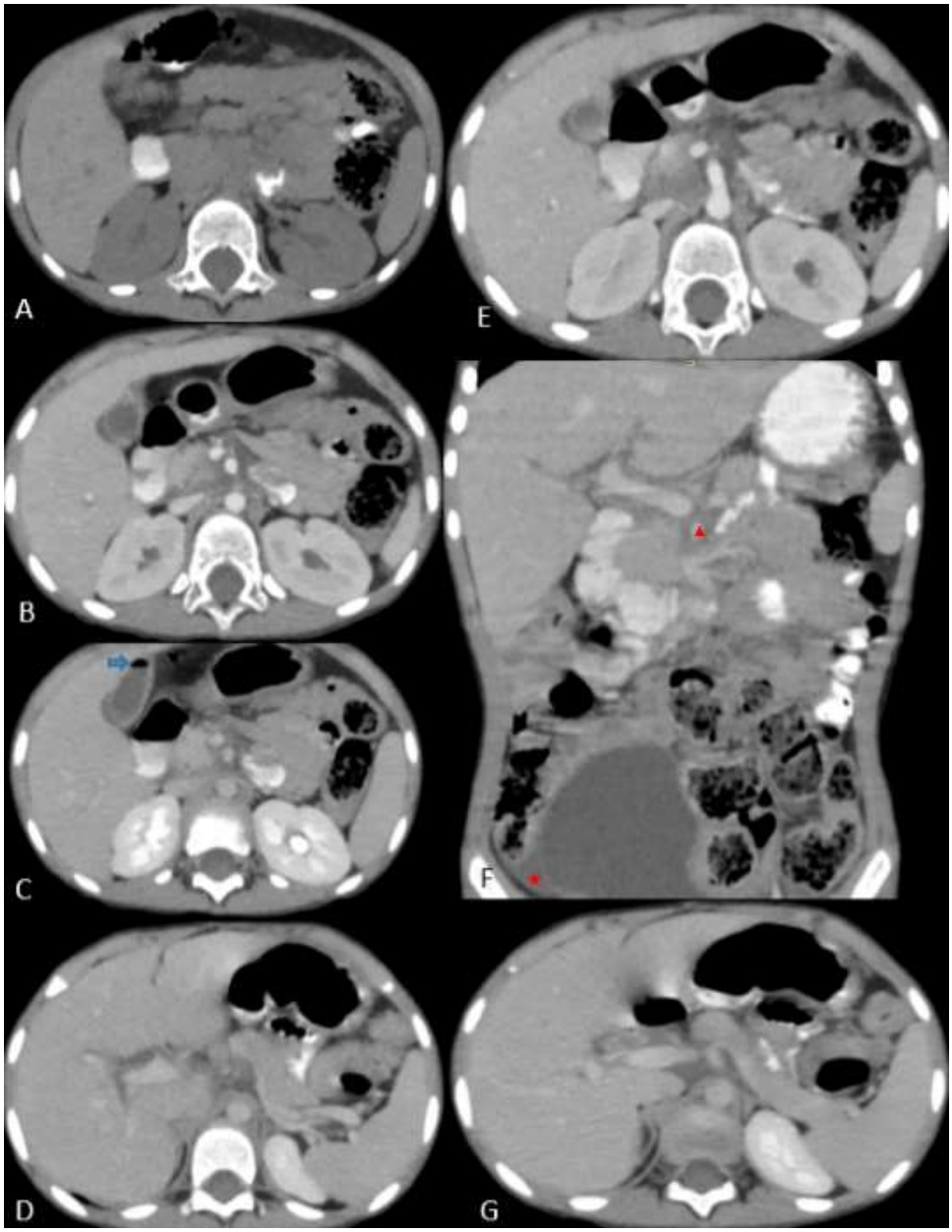

Fig. 3: Post-treatment imaging findings

Axial planes of non-contrast (A), portal phase (B & E), and delayed phase (C & G) CT scan show the dramatic response of the tumor to six cycles of the neoadjuvant chemotherapy regimen. There is only a small amount of hypo-dense soft tissue mass in the pancreatic head region (E), around the superior mesenteric vessels (B&C) as well as around the celiac trunk (G) which could be a residual tumor or fibrotic tissue. A small focus of air (blue arrow) is seen in the gallbladder due to prior stenting (C). In the coronal plane of the portal phase CT scan (F), there is no obvious evidence of mass in the head of the pancreas (compared to Figure 1G), and only a small hypo-dense area is seen around the superior mesenteric artery (red arrowhead). Mild free fluid is seen in the right side of the pelvic cavity (red star). The intensity of bile duct dilatation has been reduced compared to the previous CT scan and the main pancreatic duct is not dilated anymore (D). The amount of lymphadenopathies in the periportal region and near the celiac trunk (D & G respectively) has been significantly reduced in comparison to the pre-treatment CT scan (Fig. 1 E&H)

3- DISCUSSION

Pancreatoblastoma is a rare malignant nonendocrine pancreatic tumor. It is more common among Asians and in childhood. The mean age at presentation is 5 years old, with a male-to-female ratio of 1.14:1 (3). Although it may originate from any part of the pancreas, it most commonly arises from the head of the pancreas (39% of patients). Pancreatoblastoma are divided into two categories based on the site of origin: ventral analogy (right-sided) originating from the head of pancreas, and dorsal analogy (left-sided) tumors which originate from the body and tail of pancreas. Right-sided tumors, as in our case, are encapsulated and lack islet cells or calcifications, unlike left-sided tumors. Right-sided tumors have a better prognosis in comparison to left-sided tumors (2). According to the Surveillance, Epidemiology, and End Results (SEER) Program data (1972-2004), the median survival in PB is 193 months, with a 15-year survival rate of 75% (4).

The patient in our case presented with abdominal pain, anorexia, vomiting and obstructive jaundice. According to the literature, the clinical presentation of pancreatoblastoma includes various symptoms and signs. These include abdominal mass (47.6%), abdominal pain (44.4%), obstructive jaundice (7.9%), anorexia (4.8%), failure to thrive (1.6%), abdominal distension, vomiting or diarrhea (12.7%) and fever (3.2%) (5). Metastases are occasionally present at the time of diagnosis, with the liver being the most common site (6). As with hepatoblastoma, the tumor marker AFP levels increase in pancreatoblastoma proportionate to the tumor size. The level of AFP reduces with treatment and increases on relapse (7). In our case, the AFP level was not elevated. Also, the serum level of lactate dehydrogenase, alpha-1 antitrypsin, Carcinoembryonic Antigen (CEA), Cancer Antigen 19-9 (CA 19-9), and pancreatic enzymes such as trypsin and lipase may be elevated.

Preoperative diagnosis of pancreatoblastoma relies on ultrasound, CT, and Magnetic Resonance Imaging (MRI). On ultrasonography, PB usually presents as a large, sharply marginated mass with a heterogeneous hypoechoic appearance, often with internal cystic areas. The tumor is frequently well-circumscribed and hypodense on CT scans and may have a lobulated margin. Cystic foci with internal septation can be present in CT scans like ultrasonography. PB is usually hypo- to intermediate signal on T1 weighted sequence and hyper signal on T2 weighted sequence. MRI is the best imaging modality to visualize a tumor capsule. The capsule has an intermediate signal on T1 weighted sequence, a low signal on T2 weighted sequence, and shows rapid enhancement (8). Calcification, intratumoral vessels, and a feeding artery may be present in PB. Adenopathy and vascular invasion are possible. Anteromedial displacement of superior mesenteric vessels and lateral displacement of the D2 portion of the duodenum are typical for PB of the pancreatic head, as what happened in our case. Also, PB may have an exophytic growth pattern (9). Although biliary duct dilation is not common in PB, it can occur in a minority of cases (like in this case). The pattern of enhancement is variable in post-contrast CT scans, but usually, there is heterogenous and septal enhancement. Mild to moderate enhancement of PB on MRI with contrast study has been noted in previous studies (8, 10, 11). Progressive enhancement in dynamic-enhanced CT and MRI has been depicted in adult PBs indicating the hypovascular nature of this tumor (12). Although a similar pattern of enhancement can be seen in pediatric PB, this point should be considered that some foci with intense enhancement can be present, as well (9, 13).

Diagnosis of PB mainly depends on the pathology and immunohistochemistry. It usually presents as a hypercellular tumor consisting of primitive epithelial cells arranged in different lobules with intervening fibrous septa, which can show acinar, neuroendocrine, ductal, and squamous differentiation. Although the most characteristic histopathologic sign of PB is squamoid nests or corpuscles (1, 3, 13), it may be absent in rare cases (14, 15).

There are some differential diagnoses other than pancreatoblastoma in a young child with a pancreatic mass including neuroblastoma, Solid Pseudopapillary Neoplasm (SPN), neuroendocrine tumor, and less commonly non-Hodgkin lymphoma, Ewing sarcoma, acinar cell carcinoma, metastatic rhabdomyosarcoma, and Inflammatory Myofibroblastic Tumor (IMT) (11, 16).

Neuroblastoma arising from the retroperitoneum with pancreatic invasion and rarely primary pancreatic neuroblastoma may have the same radiologic presentation (13, 17). Neuroblastoma or its metastatic lymph nodes may have foci of calcification while it is uncommon in the pancreatic head PB (13, 17). Moreover, neuroblastomas may show neuroforaminal extension, and anterior displacement of the splenic artery, aorta, and celiac axis which were not present in our case (9). Furthermore, weak immunopositivity of synaptophysin and chromogranin and normal levels of catecholamines in our patient's serum and urine as well as the absence of neurological signs and symptoms were not consistent with the diagnosis of neuroblastoma in the presented case. If there are overlapping radiologic and histopathological findings, 123I-metaiodobenzylguanidine (MIBG) scanning could be used for further evaluation (17, 18).

Although SPN can present as a large well-circumscribed complex pancreatic mass in children associated with heterogeneous enhancement on postcontrast exam, internal necrotic/hemorrhagic areas as well as beta-catenin nuclear staining in IHC study, but absence of typical pseudopapillary structures, negative CD99 immunoreactivity and weak immunoreactivity of chromogranin were not consistent with this diagnosis (16). Additionally, our patient's age (≤ 5 years old) as well as the absence of hemorrhage in the mass and the presence of vascular encasement on CT scan were in favor of pancreatoblastoma rather than SPT (19).

Neuroendocrine tumors can arise in children in the setting of some inherited syndromes such as Multiple Endocrine Neoplasia type 1, von Hippel–Lindau syndrome, neurofibromatosis type 1, and tuberous sclerosis complex (TSC). Functional tumors cause symptoms and present as small hyper-enhancing tumors in the pancreas but non-functional tumors manifest as asymptomatic larger pancreatic masses with cystic degeneration. The absence of associated syndromes in this patient, the hypovascular pattern of enhancement of the pancreatic mass in our case (hypoattenuating relative to the pancreas parenchyma in the arterial phase with progressive enhancement in the portal and delayed phase) as well as weak immunoreactivity of chromogranin and synaptophysin and strong immunoreactivity of beta-catenin were inconsistent with the diagnosis of neuroendocrine tumor (13, 16).

Primary or secondary involvement of the pancreas by non-Hodgkin lymphoma is another rare differential diagnosis that usually presents with single or multiple homogeneously hypodense nodal masses with minimal enhancement in the pancreas. Diffuse involvement of the pancreas is also possible (11, 13). The heterogeneous pattern of enhancement in pre-chemotherapy CT scan as well as histopathology and IHC findings were not

in favor of this diagnosis. Although very rare, extraosseous pancreatic Ewing sarcoma has been reported in the pediatric population. It may show a heterogeneous appearance on cross-sectional imaging. These tumors do not show beta-catenin immunoreaction but do show strong CD-99 immunoreactivity (unlike this case) (16). Acinar cell carcinoma (ACC) can show similar imaging and histopathological findings but it is very rare in the pediatric population and occurs almost exclusively in older patients (13).

The treatment of choice is complete resection of the tumor. In patients with unresectable or metastatic tumors, as in our case, chemotherapy is recommended to reduce the tumor size. Unfortunately, there are no established chemotherapy regimens, but some studies show that vincristine, doxorubicin, etoposide, cyclophosphamide, Cisplatin, and adriamycin are effective. Although PLADO (cisplatin and doxorubicin) regimen can be used as the first-line chemotherapy regimen for patients with PB, some reports mention that the combination of Cisplatin and Adriamycin may be a better regimen. This patient responded dramatically to this combination (20, 21).

4- CONCLUSION

Pancreatoblastoma is the most common type of pancreatic tumor in children younger than 10 years old. All children with abdominal pains having a large, solid heterogeneous mass in the pancreas need to be checked for this diagnosis. Surgery is utilized to completely remove the tumor, while pathology and immunohistochemistry (IHC) are used to offer a definitive diagnosis. Patients with large tumors or extensive lymph node involvement typically undergo neoadjuvant chemotherapy before surgery to downstage their disease (like this case, which had an excellent response to neoadjuvant).

5- List of Abbreviations

AFP: Alpha-Fetoprotein

CA 19-9: Cancer Antigen 19-9

CBC: Complete Blood Count

CEA: Carcinoembryonic Antigen

CT: Computed Tomography

ER: Estrogen Receptors

ERCP: Endoscopic Retrograde Cholangiopancreatography

IHC: Immunohistochemistry

MRI: Magnetic Resonance Imaging

PB: Pancreatoblastoma

PR: Progesterone Receptor

SEER: Surveillance, Epidemiology, and End Results

6- CONSENT FOR PUBLICATION

Written informed consent for the publication of any accompanying images was obtained from the patient and her immediate family.

7- COMPETING INTERESTS

None.

8- AUTHORS' CONTRIBUTIONS

AJ, MG, RF, FR, and MF interpreted the patient's imaging, AR and GB interpreted the patient's clinical and laboratory examinations. MF and MG revised the manuscript. YS, RF, and GB prepared the first draft of the manuscript. AV prepared and interpreted the pathology slides.

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