Case Report/Series

Pancreatoblastoma in previously pancreatic pseudocysts in a 14-year-old female: a case report

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ABSTRACT

Pancreatoblastoma is a rare tumor characterized by uncontrolled growth of pancreatic epithelial cells with a mix of squamous nests and acinar differentiation. Diagnostic modalities include abnormal liver enzyme, pancreatic enzyme, and imaging findings. Treatment options include surgical resection, sometimes combined with chemotherapy, depending on the tumor's size and grade. We reported a pancreatoblastoma in a 14-year-old female with prior pancreatic pseudocysts. The transformation from pseudocysts to pancreatoblastoma is believed to be caused by the heterozygosity molecular loss on the 11p chromosome and several genetic mutations. Magnetic resonance cholangiopancreatography showed a well-defined, heterogeneous mass in the pancreatic head, with 70% of the mass composed of cysts. A partial pancreatectomy was performed because a complete pancreatectomy may harm the adjacent structures. However, a complete resection combined with chemoradiation may be the best option for long-term survival and complete remission. In this case, she was disease-free until 30 months after the chemotherapy protocol.

KEYWORDS pancreas, pancreatic neoplasm, pancreatic pseudocysts, pancreatoblastoma

Pancreatoblastoma is a rare and uncommon type of pancreatic cancer that can occur in children and is characterized by symptoms such as abdominal pain, abdominal mass, jaundice, diarrhea, or upper gastrointestinal (GI) bleeding. However, it is often asymptomatic.[1] Although only 74 cases were reported in adults with a median age of 41 years, it accounts for 25% of all pancreatic cancer in children with a mean age of 4 years.[2] Diagnosis of pancreatoblastoma can be established through imaging tests such as abdominal ultrasonography, multislice computed tomography (MSCT), or magnetic resonance imaging (MRI), which can help determine the location, shape, and surrounding structures. The head of the pancreas is the most commonly affected site, accounting for an estimated 33.3% of the reported cases.[3]

Total pancreatectomy is the primary treatment for pancreatoblastoma, which can result in a favorable outcome if the tumor is completely resected. Incomplete resection or the presence of metastasis can result in poor long-term survival.[4] Pancreatoblastoma can occur at any age, but it is more prevalent in female

children aged 1 to 8 years old; nonetheless, it is rare in fetuses and adults.[5] Although it is less aggressive, recurrence and metastasis are common.[6]

Pancreatic pseudocysts are an encapsulated homogenous fluid mass contained minimum necrotic tissue.[7] The rarity of pancreatoblastoma, combined with the lack of reported cases and pathognomonic symptoms, makes diagnosis a real challenge. To help shed more light on this underreported disease, we reported a case of pancreatoblastoma in a 14-year-old female with a prior history of pancreatic pseudocysts. The underlying cause of the disease transformation could be the loss of heterozygosity on the 11p chromosome and molecular changes in the β-catenin/adenomatous polyposis coli (APC) signaling pathway.[2,8] Despite a complete surgical resection, metastases might occur because it was located adjacent to suprapyloric, retropyloric, and subpyloric nodes.

CASE REPORT

A 14-year-old female patient presented at a pediatric surgery clinic with a 1-month history of jaundice, painless lump in the upper right abdomen, nausea, abdominal discomfort, and itching throughout the body. The lump had been growing recently. She had no symptoms of white stool or tea-colored urine. Her medical history included a cholecystojejunostomy Roux-en-Y laparotomy 2 years prior for a pancreatic cystic mass that was later confirmed as pancreatic pseudocysts through a postsurgical histopathological examination.

Physical examination revealed a body weight of 44 kg, height of 155 cm, and body surface area of 1.37 m^2. She had scleral icterus (Kramer 5) and a surgical scar on her abdomen. A palpable lump was found in the right upper quadrant, measuring 11 × 10 cm in size, with a firm and soft consistency. The liver was palpable 6 cm below the costal margin and 4 cm below the xiphoid process. No muscular defense signs were present.

Laboratory tests showed elevated levels of aspartate aminotransferase (AST) at 134 U/l, alanine aminotransferase (ALT) at 130 U/l, gamma-glutamyltransferase (GGT) at 726 U/l, alkaline phosphatase at 531 U/l, total bilirubin at 8.82 mg/dl, and direct bilirubin at 7.81 mg/dl. Furthermore, the amylase and lipase levels were within normal limits. Elevated levels of carbohydrate antigen 19-9 were at 471.3 U/ml (normal range: ≤37.0 U/ml). These abnormalities might have been caused by pancreaticobiliary.

An abdominal MRI showed a solid cystic mass in the entire pancreas, which pushed the right kidney to the posterior and caused abrupt extraluminal pressure on the common bile duct, resulting in dilatation of the proximal and middle common bile duct, cystic duct, common hepatic duct, bilateral intrahepatic bile duct, and gallbladder hydrops. The radiograph showed a pancreatic mass and pancreas-hepatosplenomegaly, leading to a suspicion of pancreatoblastoma. Magnetic resonance cholangiopancreatography further confirmed the presence of a 70% cystic form of a pancreatic mass and hepatosplenomegaly (Figure 1).

A pancreatic mass measuring 10 × 11 cm was surgically removed from the pancreatic head. The mass had invaded the pancreatic capsule and surrounding lymph nodes without significant adhesion between the diaphragm and the right liver portion. A laparoscopic exploration with a partial pancreatectomy of pancreatic head was performed, followed by a laparotomy biopsy and cyst drainage. The surgery was successful, and she was discharged on postoperative day 11. Pathological examination of the mass revealed an acinar cell carcinoma (ACC) pancreatoblastoma, as indicated by the presence of spindle to round, small, blast-like malignant tumor cells with back-to-back grouping, acini, ductal differentiation, and focal rosettes (Figure 2). Then, she received six cycles of chemotherapy, consisting of cisplatin 110 mg and doxorubicin 40 mg, as part of the treatments since the final staging was T1N0M1.

Three months following the partial pancreatectomy and chemotherapy, a contrast-enhanced MSCT revealed a recurrence of the mass in the head of the pancreas attached to the hepatic capsule, adjacent intestinal system, and peritoneum. Additionally, there were omental cake metastases in the left hypochondriac region and multiple lymphadenopathies in the paraaortic, bilateral paradisiacal, bilateral mesenteric, and bilateral inguinal regions (Figure 3). Based on the ACC subtype, additional adjuvant radiation therapy was added to these areas.

A psychiatrist provided behavioral counseling to the patient and her parents, focusing on coping skills and anxiety reduction. In addition, antioxidant supplements (vitamins A, C, and E) were administered, and a nutritional-dietary program was provided to reduce triglyceride levels. After a 9-month follow-

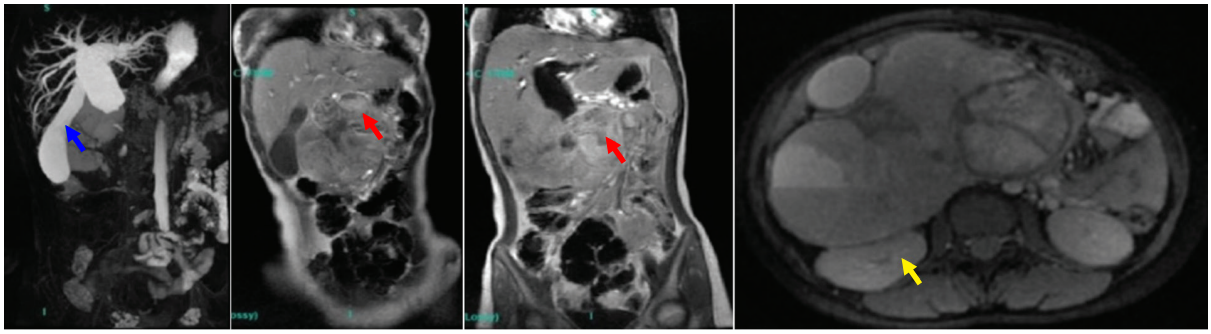

Figure 1. Magnetic resonance imaging (MRI) examination before surgery. Solid cystic mass (red arrows) in the pancreas compressing the right kidney (yellow arrow), dilatation of proximal and middle common bile duct, and gallbladder hydrops (blue arrow)

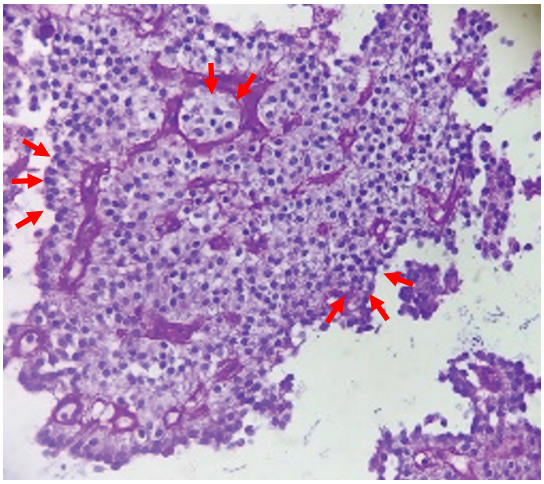

Figure 2. Histopathology of pancreatoblastoma showing roundish and pale areas of hypercellular neoplasm (squamoid nests) (red arrows)

up, there were no signs of recurrence or pancreatic insufficiency symptoms, such as abdominal pain, tenderness, loss of appetite, feelings of fullness, weight loss, and diarrhea. She was alive and disease-free 30 months after her partial pancreatectomy and chemotherapy, and no extra adjuvant therapies were required. She gave written informed consent for the publication of this study.

DISCUSSION

Pancreatoblastoma is a slow-growing, encrusted, large tumor that often presents with nonspecific symptoms.[2] Common complaints among patients include abdominal pain (45.2%), weight loss (29%), a palpable mass (19.3%), jaundice (19.3%), diarrhea (9.7%), GI

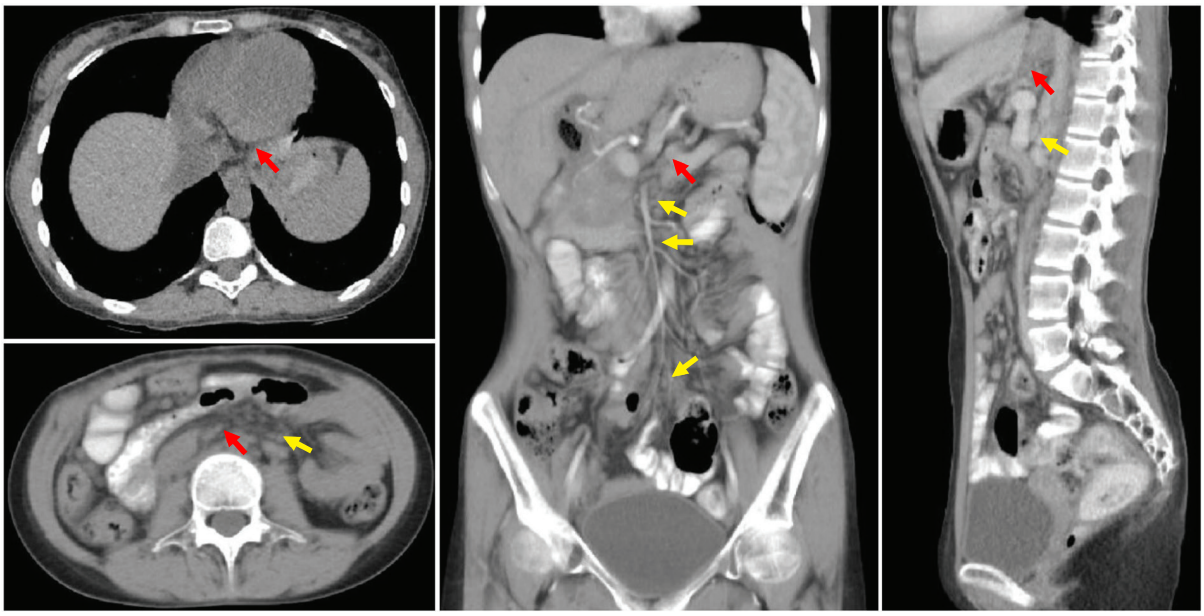

Figure 3. Postsurgical contrast-enhanced multislice computed tomography (MSCT) showing a recurrence of a pancreatic head mass (red arrows) attached to adjacent abdominal organs and several lymphadenopathies (yellow arrows)

bleeding (6.4%), splenomegaly (3.2%), and no symptoms at all (6.4%).[9] Those slight elevations of AST and ALT as well as significant elevation in GGT, conjugated, and total bilirubin indicated obstructive jaundice due to extrahepatic causes.[10] Unlike acute pancreatitis, normal to low serum level elevations of pancreatic enzyme are not specific to pancreatic cancer.[10] In this case, rupture and bleeding of the tumors were reported, and the pancreatoblastoma had spread throughout the entire pancreas instead of the head of the pancreas and had compressed the right kidney, obstructing the bile ducts.

Pancreatoblastoma has been linked to both Beckwith-Wiedemann syndrome (BWS) and familial adenomatous polyposis syndrome.[11] In this case, pancreatoblastoma was suggested to be associated with previous pancreatic pseudocysts. A study showed that the progression from pancreatic pseudocysts to pancreatoblastoma was caused by 11p chromosome heterozygosity loss. The β-catenin signaling pathway was also involved in 67% of pancreatoblastoma pathogenesis due to changes in the APC gene.[8] In some cases, biallelic APC gene mutation was found in pancreatoblastoma patients with a previous pancreatic familial adenomatous polyposis. Furthermore, the β-catenin/APC molecular signaling pathway abnormality has also been implicated in BWS-associated hepatoblastoma.[10] RNA sequencing studies have identified gene rearrangements in fibroblast growth factor receptor (FGFR) 2, FGFR1 mutation, and an upregulated FGFR1, -3, and -4 mRNA expressions along with their associated ligands, FGF3 and FGF4. These processes might lead to the development of malignancy in clinically benign cystic lesions.[12]

Radiological differential diagnoses for pancreatoblastoma include cystic pancreatic neoplasms, ductal adenocarcinoma, salt cell carcinoma, malfunctioning pancreatic endocrine tumors, solid pseudopapillary tumors, peripancreatic lesions, and pancreatic lesions including pancreatic tuberculosis and autoimmune pancreatitis.[13] In this case, the patient's initial issue was pancreatic pseudocysts that progressed into pancreatoblastoma 2 years later. Any cystic pancreatic lesions may develop into a pancreatic malignancy.[14,15]

Standard of care for pancreatoblastoma is limited due to its rarity. Preoperative chemotherapy has been used in some cases, including inoperable, large tumors, or metastases.[16] There are ongoing controversies surrounding laparoscopic pancreatectomy. In most cases of metastases, the best approach is either anterior or posterior radical antegrade modular pancreatosplenectomy. The surgical approach is based on the tumor's location, with a pancreaticoduodenectomy (Whipple procedure) performed for tumors in the head and neck of the pancreas.[16] To prevent tumor spread, common steps include dissection of the pancreatic inferior margin, splenic flexure mobilization, and division of the gastrocolic ligament close to splenic inferior pole.[17] Compromised lymph node dissection also increases the risk of postsurgical infection.

Postoperative adjuvant radiotherapy has been preferred over adjuvant chemotherapy in some cases, and small-sized pancreatoblastoma without metastases should be resected without pre- or postoperative chemotherapy for complete remission.[18] In this case, both chemotherapy and radiotherapy were used due to their role in the treatment of residual, recurrent, unresectable, and metastatic diseases.[2] Long-term follow-up and monitoring for metastasis and recurrence are essential. Following pancreatectomy, comprehensive care is important to improve the patient's quality of life, including supportive care, pain relief, chemotherapy and radiotherapy, endoscopic interventions for secondary duodenal-biliary obstruction, dietary management, and psychiatric support for patients and their families dealing with anxiety and depression.[19]

Diagnosis of pancreatoblastoma is challenging due to its nonspecific symptoms. In this case, there was a lack of established treatment guidelines for pancreatoblastoma. The limitation was the absence of postsurgical MRI. Treatment of pancreatoblastoma typically involves total surgical resection with or without chemotherapy, depending on the stage and size of the tumor.[20] In this case, an early partial pancreatectomy of the pancreatic head was performed and continued with chemoradiation. Comprehensive postsurgical supportive care should be addressed to optimize the patient's recovery and quality of life.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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