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Complete Surgical Resection and Aggressive Treatment for Liver Metastasis May Be Beneficial to Adult Patients With Pancreatoblastoma: A Case Report and Review of Literature

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Introduction: Pancreatoblastoma (PB) is a rare pancreatic neoplasm that occurs most in pediatric patients. Here, we report a rare case of adult PB with liver metastasis and review the literature in order to assist clinicians in the management of the disease.

Case Presentation: A 27-year-old female patient suffered from postprandial fullness, anorexia, and weight loss in the past 3 months. An abdominal ultrasound and contrast-enhanced computed tomography scans confirmed right abdominal mass with compression of major liver vessels, as well as the P-duct and biliary ducts and causing mild dilatation. Pancreatoduodenectomy was performed and pathologic findings showed typical squamoid corpuscles, which confirmed the diagnosis of PB. The patient was alive and disease-free for 1 year and 10 months until a new metastatic lesion was found. Radiofrequency ablation was arranged as a curative treatment, and no viable tumor or sign of recurrence was found until this paper was submitted. Based on a review of previous case reports, we found adult PB

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patients with only liver metastasis presented with a smaller tumor size ($P = 0.031$), more frequent pancreatic head origin ($P = 0.043$), and decreased 1-year mortality ($P = 0.009$) compared with patients with other distal metastases. Therefore, we assumed that PB with liver metastasis might present favorable outcome by complete surgical resection or other curative treatment.

Conclusion: PB patients with liver metastasis are more likely to show a pancreatic head origin, smaller tumor size, and more favorable outcomes compared with other sites of metastasis. PB should be treated aggressively with surgical resection or other curative treatment as opposed to chemotherapy alone.

Key words: Adult pancreatoblastoma – Pancreatoduodenectomy – Liver metastasis

Pancreatoblastoma (PB) is a rare epithelial malignant neoplasm of the pancreas that typically occurs in the pediatric population. The annual incidence of PB is around 0.004 new cases per 100,000 individuals of all ages,[1] and there have been only 42 cases of adult PB reported in the literature to date since Palosaari *et al*[2] reported the first case of adult PB in 1986.

Adult PB typically presents with nonspecific symptoms mostly related to tumor mass effects, which are predominantly abdominal pain, palpable mass, weight loss, obstructive jaundice, and abdominal distention.[3] Compared with pediatric patients, adult patients with PB have a poor prognosis, and it usually exhibits a malignant behavior with high rates of local invasion, recurrence, and occasionally distant metastasis.[4] Surgical resection is considered the chief treatment strategy and the only potentially curative therapy. Because of the rarity of PB, there are currently no management guidelines, and preoperative diagnosis in adults with PB remains challenging.

The current study presents the case of a 27-year-old female PB patient treated with pancreatoduodenectomy who developed liver metastasis. This article includes a brief review of the clinicopathologic features and management outcomes as well as the predictive factors for and prognosis of PB with liver metastasis.

Case Report

A 27-year-old female patient was admitted to the Department of General Surgery, Kaohsiung Chang Gang Memorial Hospital, in March 2017. She experienced postprandial fullness, anorexia, and weight loss in the past 3 months. Physical examination revealed mild tenderness over the epigastrium. Laboratory tests identified elevated serum levels of aspartate aminotransferase (143 IU/L; normal range, 10–37 IU/L), alanine aminotransferase (201 IU/L; normal range, 0–40 IU/L), alkaline phosphatase (567 IU/L; normal range, 28–94 IU/L), amylase (186 IU/L; normal range, 27–137 IU/L), and lipase (239.1 IU/L; normal range, 22–51 IU/L). Cancer antigen 19-9, α-fetoprotein, and carcinoembryonic antigen levels were within the normal ranges.

An abdominal ultrasound performed at a local medical clinic revealed an encapsulated and well-defined right abdominal mass. Contrast-enhanced computed tomography (CT) scans confirmed a large, heterogeneous, right abdominal mass about $12 \times 14 \times 19$ cm in size with a mass effect on the main portal vein, hepatic artery, and biliary ducts, as well as mild dilatation of the P-duct and biliary ducts (Fig. 1). Furthermore, contrast-enhanced magnetic resonance imaging (MRI) showed a retroperitoneal tumor arising from the pancreatic head, with mixed hemorrhagic, cystic, and solid components and some calcification, as well as displacement of and compression to adjacent organs and vessels, which are findings compatible with a solid and pseudopapillary neoplasm of the pancreas (Fig. 2). Ultrasound-guided fine-needle biopsy was done and revealed a solid pseudopapillary neoplasm of the pancreas. Therefore, surgical resection was arranged for further treatment and diagnosis.

The patient initially underwent exploratory laparotomy, which revealed a palpable mass measuring $18 \times 11 \times 10$ cm located at the pancreatic head, without ascites, vascular invasion, or distant metastasis. Therefore, a classic pancreatoduodenectomy (Whipple operation) for the pancreatic lesion with duct-to-mucosa reconstruction was performed. The cut surface of the pancreatic tumor grossly revealed a well-demarcated, soft, tan-yellow mass with focal hemorrhage. Microscopy showed tumor cells with

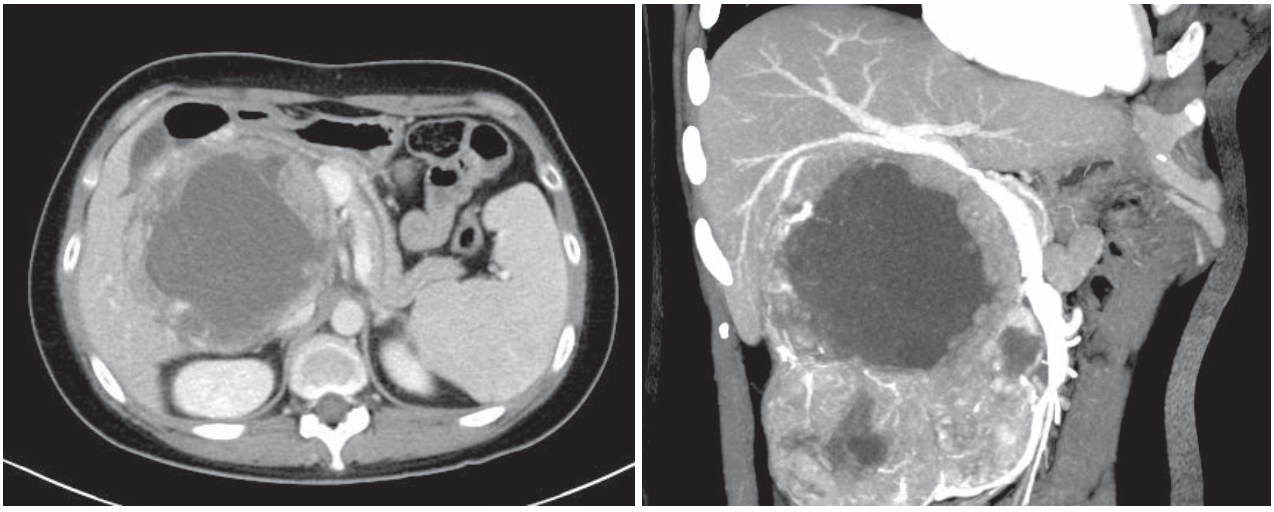

Fig. 1 Preoperative contrast-enhanced CT. (a) Multiloculated intra-abdominal mass with enhancing septa, measuring 12 × 14 × 19 cm with mild dilatation of the main pancreatic duct, and (b) mass effect to main portal vein, hepatic artery, and biliary ducts.

acinar differentiation polarized around small lumina. Squamoid corpuscles were demonstrated by multiple foci of light-staining spindle-shaped cells with an epithelioid appearance and nests of squamoid cells among round primitive cells (Fig. 3). Immunohistochemical staining showed CD10 positivity in squamoid nests and diffuse positivity for CK7, trypsin, and chymotrypsin.

The postoperative course was uneventful, and the patient was discharged on postoperative day 14. The patient was alive and disease-free for 1 year and 10 months until a new metastatic lesion was found during a regular sonographic follow-up. Biopsy confirmed metastatic PB, and radiofrequency ablation was arranged as a curative treatment. At the time this paper was written, the patient is receiving further chemotherapy with cisplatin/doxorubicin as an adjuvant treatment. No other viable tumor or metastatic lesion is detected (Fig. 4), and all tumor makers are all within normal range.

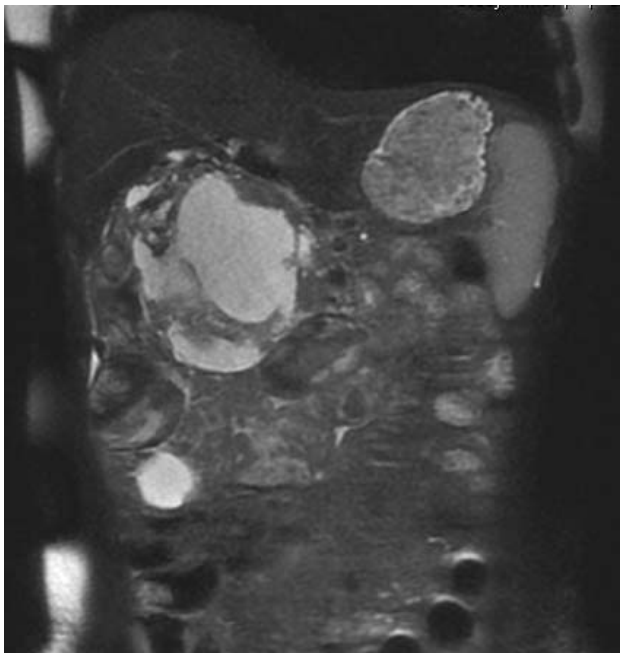

Fig. 2 High signal intensity on T2-weighted MRI. An encapsulated heterogeneous mass arises from retroperitoneum with mixed solid and cystic component, indicating tumor necrosis or internal hemorrhage.

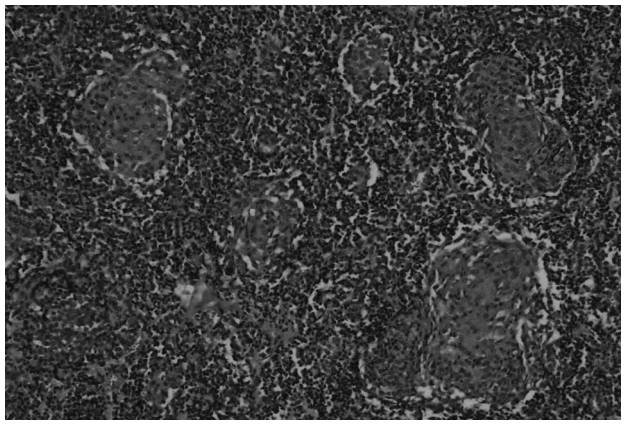

Fig. 3 Histologic analyses. The tumor cells exhibit epithelioid appearance with nests of squamoid cells among round primitive cells (hematoxylin-eosin, original magnification ×200), showing the typical presentation of squamoid corpuscles.

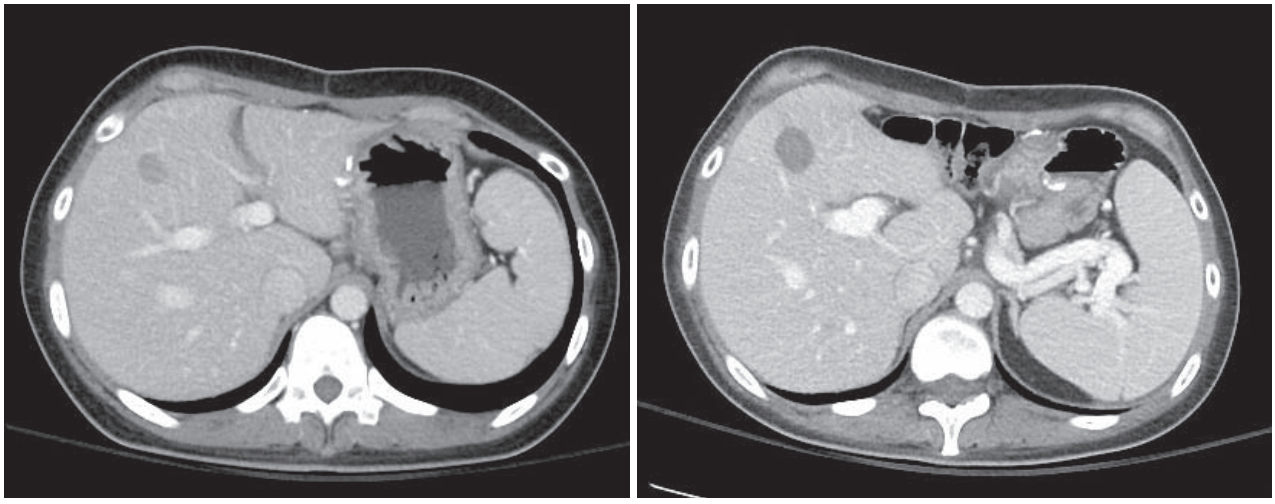

Fig. 4 Liver metastasis. (a) New-onset liver metastasis with biopsy proof was found over S4 at 1 year 10 months after surgery. (b) No viable tumor noted after radiofrequency ablation after 6 months' follow-up.

Discussion

PB is an extremely rare tumor of the pancreas that accounts for less than 1% of pancreas neoplasms and usually occurs in pediatric patients. To date, only 44 cases have been published in the literature since Palosaari *et al*[2] published the first case of adult PB in 1986. In our retrospective review, a total of 44 adult cases with pathologically proven PB reported from 1986 to 2018 were included. A literature search of PubMed using the key words "adult pancreatoblastoma," "pancreatoblastoma," and "pancreatic neoplasm" was performed, and data pertaining to the clinical features, diagnosis confirmations, imaging and pathologic findings, treatments, and follow-up were recorded.

The demographic characteristics and clinical and imaging findings of the adult PB patients are summarized in Table 1. The median age of the patients was 40.4 years (range, 18–78 years), and a total of 24 male (53.33%) and 21 female (46.67%) patients were included. The most frequent presenting symptom and sign was abdominal pain (17 of 45; 37.78%), followed by weight loss (13 of 45; 28.89%), obstructive jaundice (8 of 45; 17.78%), and palpable abdominal mass (7 of 45; 15.56%). Other atypical clinical symptoms, such as persistent diarrhea[5] and urinary occult blood,[6] were also reported.

Radiographic features of PB in adults have been infrequently reported, and no significant differences between adult and pediatric patients have been established. The typical findings in PB are large, well-circumscribed, multiloculated masses with rim-shaped and enhancing septa on CT imaging.[7,8] Cystic or intratumoral hemorrhage or necrotic components with calcification have also been reported. On MRI, PB is most commonly described as having low to intermediate signal intensity on T1-weighted images and high T2 intensity.[9] In our literature review, the average tumor size was 8 cm (range, 2.7–20 cm), and the tumor origin was the pancreatic head in nearly half of the patients (22 of 45; 48.89%), followed by the tail (10 of 45; 22.22%) and the body (8 of 45; 17.78%). According to the

Table 1 Features characterizing PB presentation in adults[a]

	No. (%)
Sex	
Male	24 (53.33)
Female	21 (46.67)
Symptoms	0
Abdominal pain	17 (37.78)
Abdominal mass	7 (15.56)
Weight loss	13 (28.89)
Obstructive jaundice	8 (17.78)
Age	40.4 (89.78)
Site	0
Head	22 (48.89)
Body	8 (17.78)
Tail	10 (22.22)
Vater	1 (2.22)
Metastasis or direct organ invasion	25 (55.56)
Liver	15 (33.33)
Lymph node	8 (17.78)
Lung	3 (6.67)
Size, cm	8.11 (2.7–20)

[a]Four cases no data for site. Six cases no data for size.

Table 2 Demographic and clinical findings of PB without metastasis, with liver metastasis only, and patients with other metastasis or direct invasion to other organs[a]

	No metastasis	Liver metastasis	Other metastasis	*P* value
Sex, n (%)				0.98
Male	5 (33.3)	10 (66.7)	7 (70.0)	
Female	10 (66.7)	5 (33.3)	3 (30.0)	
Age, y	45.8 ± 19.1	32.4 ± 7.5	42.9 ± 21.0	0.07
Size, n (%)				0.031
Tumor >8 cm	4 (28.6)	4 (30.8)	7 (78.8)	
Tumor <8 cm	10 (71.4)	9 (69.2)	2 (22.2)	
Site, n (%)				0.043
Head	3 (20.0)	11 (73.3)	5 (55.5)	
Other	12 (80.0)	4 (26.7)	4 (44.4)	
Mortality within 1 y, n (%)	2 (15.4)	3 (25)	7 (70)	0.009

[a]Four cases no data for site. Six cases no data for size. Five cases no data for metastasis or not.

review by Chen *et al*,[10] tumor size and location are not associated with the patients' sex or metastatic status in PB.

Preoperative pathologic diagnosis is difficult because of sampling errors from fine-needle aspiration, and only 3 cases with adult patients have been reported.[11–14] Microscopically, PB tumors often demonstrate a combination of acinar, endocrine, ductal, and islet cell components.[15] The presence of squamoid corpuscles, which is characterized by the squamous appearance of plump epithelioid cells and variably sized foci of staining, flattened cells with a whorled nested pattern, is the most distinguishing feature of PB.[16,17] Immunohistochemical staining may identify tumor cells with acinar differentiation, which are highlighted with trypsin, chymotrypsin, lipase, and esterase.[3,4,11] The ductal components stain with CK7 and CK19, and neuroendocrine differentiation with expression of chromogranin and synaptophysin is also a crucial element of a PB diagnosis.

To date, there are no specific international guidelines regarding the treatment of PB. Surgical resection may be the potentially curative therapy that is associated with the longest survival compared with chemotherapy and radiation.[4] PB is an aggressive malignant neoplasm with a poor prognosis. In our literature review of previous cases, PB metastasis and/or local invasion was found in 25 of 45 adult patients (55.56%). The liver (33.33%) and lung (6.67%) were the most common sites of distal metastasis (Table 1). We further compared the patients with liver metastasis only to those without metastasis, with multiple metastases, and/or with local invasion to other organs. In contrast to patients with other organ invasions or multiple metastases, patients with only liver metastasis present with a smaller tumor size ($P = 0.031$), more frequent pancreatic head origin ($P = 0.043$), and decreased 1-year mortality ($P = 0.009$; Table 2). Although the role of systemic treatment in PB remains controversial because of the limited number of patients treated, several case reports showed favorable long-term survival after aggressive surgical intervention and adjuvant therapy in PB patients with liver metastasis.[16,18,19]

In summary, PB is an extremely rare pancreatic neoplasm in adults that presents clinical challenges in terms of both diagnosis and management. It should be considered as a diagnosis in the context of large pancreatic tumors presenting with well-circumscribed and heterogeneous components. Histopathologic presentation of squamoid corpuscles and immunohistochemical staining are necessary for an accurate diagnosis.

According to our review, in comparison to metastases to other sites, patients with liver metastasis are more likely to have pancreatic head origin, a smaller tumor size, and more favorable outcomes. Complete surgical resection of the primary tumor and aggressive treatment for liver metastasis followed by adjuvant therapy may yield better long-term clinical outcomes compared with systemic chemotherapy alone. Further larger, prospective, randomized studies are required to determine whether surgical resection or adjuvant chemotherapy represents the optimal treatment protocol in PB.

Acknowledgment

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