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Case Report

Aggressive Adult Pancreatoblastoma with Early Recurrence: A Case Report

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ABSTRACT

Background: Pancreatoblastoma (PB) is a rare malignant epithelial tumor of the pancreas, mainly occurring in pediatric population. Pancreatoblastoma of the adult is extremely rare and usually shows a more aggressive biological behavior and a worse prognosis.

Case Presentation: The patient was a 54-year-old man admitted for abdominal pain and weight loss. A computed tomography (CT) scan showed a 12 cm heterogeneous hypoattenuating mass in the pancreatic head. An endoscopic ultrasound-guided biopsy suggested the diagnosis of pancreatoblastoma (PB). The patient underwent a pancreaticoduodenectomy (PD) combined with limited liver resections for intraoperative finding of multiple liver metastasis. Pathological findings confirmed the diagnosis of PB metastatic to the liver. The tumor recurred in the liver 5 months after surgery and the patient succumbed due to tumor dissemination 8 months after initial diagnosis.

Conclusion: Adult pancreatoblastoma is a rare pancreatic neoplasm with malignant behavior. The aim of this manuscript is to report our experience with pancreatoblastoma in the adult and to contribute improving knowledge about the clinical behavior of this rare and aggressive malignancy.

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Introduction

Pancreatoblastoma (PB) is a rare malignant epithelial tumor of the pancreas, accounting for less than 1% of pancreatic neoplasms and with an annual incidence of approximately 0.004 per 100,000 people [1, 2]. First described by Becker *et al.* in 1957, as “infantile pancreatic carcinoma”, was subsequently renamed “pancreatoblastoma” by Horie *et al.* in 1977 for its morphologic similarity to fetal pancreatic tissue [3, 4]. Pancreatoblastoma mainly affects pediatric population, accounting for 25% of pancreatic neoplasms occurring in the first decade of life [5]. In contrast, adult pancreatoblastoma is extremely rare and usually more aggressive. Since Palosaari *et al.* described the first case of adult pancreatoblastoma in 1986, only 74 cases have been reported in literature so far [6]. Surgical resection is the treatment of choice, but there is no consensus on the best management of adult patients with

pancreatoblastoma, since, because of its rarity, the clinical practice mainly relies on isolated case reports or small series reported in literature.

Here we report the case of a 54-year-old man diagnosed with pancreatoblastoma who underwent surgical resection, with intraoperative finding of multiple liver metastasis and recurred to the liver 5 months after surgery. The present report aims to contribute improving the existing clinical knowledge about the management of adult pancreatoblastoma.

Case Presentation

A 54-year-old man was admitted to our hospital due to abdominal pain and progressive weight loss (10 kgs in 2 months). His past medical history included no relevant information other than a previous surgery

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for varicocele repair in the childhood. A chest- abdomen computed tomography scan (CT- scan) showed a heterogeneous hypoattenuating mass measuring approximately 12 cm in the head of the pancreas with partially ill-defined and lobulated margins. The lesion shaped the confluence of the splenic and superior mesenteric veins but without signs

of infiltration. The pancreatic contour blended with the lesion, causing dilatation of the main pancreatic duct (Figure 1). The laboratory workup, including tumor markers, was unremarkable, alfa- fetoprotein (AFP) was 276 (ng/mL).

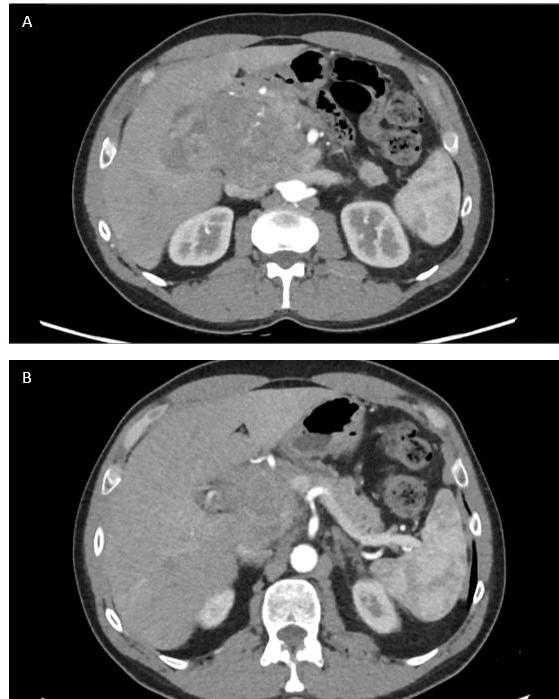


Figure 1: A & B) CT- scan showed a heterogeneous hypoattenuating mass measuring approximately 12 cm in the head of the pancreas with partially ill-defined and lobulated margins. The lesion shaped the confluence of the splenic and superior mesenteric veins but without signs of infiltration.

An endoscopic ultrasound (EUS) was performed, confirming the presence of a heterogeneous hypoechoic mass without a clear cleavage plan from the pancreas, and a core- biopsy was taken (Figure 2). Histological examination revealed sheets of neoplastic cells with rare acinar formation and focal swirling of the cells suggestive of squamoid nests. A panel of immunohistochemical stains was performed and the

neoplastic cells focally labeled with cytoke­ratin 19 (CK19), alfa- fetoprotein (AFP) and beta-catenin. Immunolabeling with trypsin and chymotrypsin highlighted the areas with acinar differentiation. The morphology and immunohistochemical labeling pattern suggested the diagnosis of pancreatoblastoma.

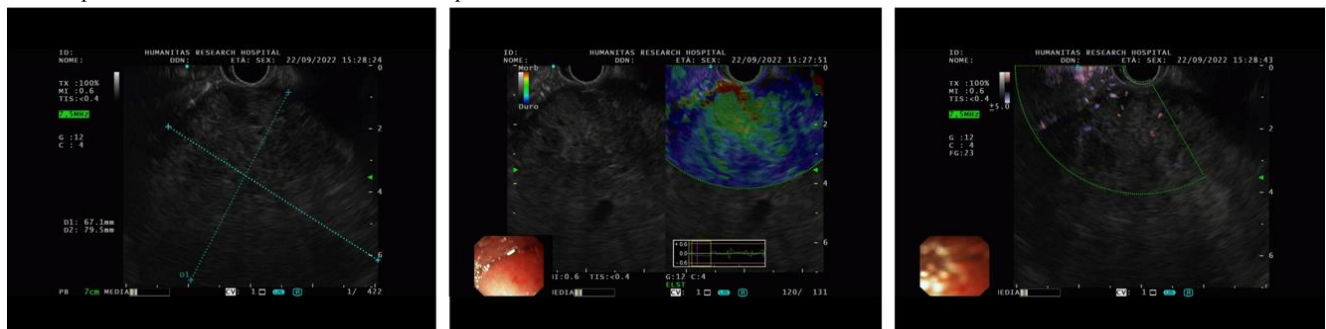


Figure 2: An endoscopic ultrasound (EUS) was performed, confirming the presence of a heterogeneous hypoechoic mass without a clear cleavage plan from the pancreas.

The case was discussed in the multidisciplinary tumor board meeting and the patient was scheduled for a pancreaticoduodenectomy (PD). Pre-operative laboratory workup showed an alfa- fetoprotein (AFP) of 689 ng/mL. Intraoperatively, a liver lesion on the Glissonian's surface highly suspicious for metastasis was detected in segment 2 (S 2). An intra-operative liver ultrasound (IOUS) with contrast enhancement was carried out for staging, confirming the presence of an isoechoic

heterogeneous lesion in S 2 and two additional subcentric lesions in segment 3 (S 3). Considering the resectability of the liver lesions, a pilorus- preserving pancreaticoduodenectomy combined with IOUS- guided S 2 resection and a limited resection of S 3 was performed (Figure 3). The post- operative course was uneventful, and the patient was discharge on post- operative day 9.

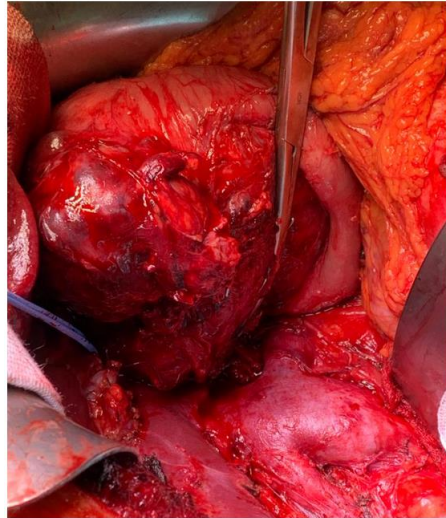


Figure 3: The intraoperative findings showed that the tumor was capsular and was in contact with the confluence of the splenic and superior mesenteric veins; however, obvious infiltration of these vessels was not observed.



Figure 4: A & B) CT- scan 5 months after surgery showed multiple liver lesions consistent with liver metastases.

Final pathology showed a 15 cm tumor of the head of the pancreas with negative margins and 12 lymph nodes negative for tumor involvement with vascular but no perineural invasion. Both histology and immunohistochemical labeling (CK AE1/AE3, CK5/6, CK19, EMA - Epithelial membrane antigen, sinaptofisin, cromogranin, INSM1 - Insulinoma-associated protein 1, c110- Anti-Folate receptor beta, AFP, Hepatocyte, beta-catenin) confirmed the diagnosis of pancreatoblastoma. The pathology examination also confirmed the presence of three liver metastases measuring, respectively, 1.4, 1.1 and 0.8 cm. Final pathological staging was pT3 N0 M+ (liver). The patient

did not undergo adjuvant chemotherapy and started the follow-up. At the first follow-up 5 months after surgery, the CT- scan showed multiple large liver lesions consistent with metastases (Figure 4).

The patient was then scheduled to start systemic treatment with Doxorubicin and Cisplatin but his conditions rapidly deteriorated and two weeks later he was admitted for bowel obstruction, treated conservatively. A new CT- scan showed disease progression in the liver and peritoneal carcinosis. The patient was then referred to palliative care and died 8 months after surgery.

Discussion

Pancreatoblastoma (PB) is a rare malignant epithelial tumor of the pancreas, mainly occurring in pediatric population. Pancreatoblastoma of the adult is extremely rare and usually shows a more aggressive biological behavior and a worse prognosis. To the best of our knowledge, since first described by Palosaari *et al.* in 1986, only 74 cases of adult PB have been reported in literature [6]. The etiology is unknown and even if most cases are sporadic, few adult pancreatoblastomas have been described in the setting of familial adenomatous polyposis (FAP) and associated with Beckwith-Wiedemann syndrome [2, 7-9].

Adult pancreatoblastoma more frequently occurs in the head of the pancreas, followed by tail and body [10]. The diagnosis might be challenging because of its resemblance with other pancreatic neoplasms and non-specific symptoms at presentation, more frequently represented by abdominal pain and weight loss [10]. At imaging PB usually presents as large and well-defined heterogeneous mass and there are no significant differences in the imaging findings of adult versus pediatric patients [10, 11].

Enhancement is a common feature on contrast-enhanced computed tomography images and might be present on magnetic resonance imaging (MRI). At MRI, PB shows low to intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images [12]. Tumor markers, including Ca 19.9 and CEA, are usually in the normal range and AFP is rarely elevated in adult pancreatoblastoma [7]. Microscopically, pancreatoblastomas are composed of cellular well-delineated lobules separated by dense fibrous band. PB predominantly show acinar differentiation; other cell lines like ductal, neuroendocrine and mesenchymal differentiation are less commonly identified but may be present [13]. The characteristic histological feature of pancreatoblastoma is the squamoid nests, which can help in distinguishing PB tumor cells with acinar differentiation from acinar cell carcinoma or solid-pseudopapillary neoplasm [14].

Pancreatoblastomas typically express trypsin, chymotrypsin, lipase, and BCL10. Squamoid nests may be positive for EMA, AE1/AE3 or CD10 and nuclear and cytoplasmic expression of β -catenin may be present [1, 7]. To date, the staging of pancreatoblastoma follows the TNM classification of carcinoma of the exocrine pancreas [15]. Surgical resection is usually treatment of choice, but there is no consensus on the best management of adult patients with pancreatoblastoma and the role of adjuvant chemotherapy or radiotherapy is not clear yet, based on the very small number of patients treated. Here we reported the case of an aggressive adult pancreatoblastoma in 54-year-old man who underwent surgical resection, with intraoperative finding of multiple liver metastases. The patient had liver recurrence 5 months after surgery and succumbed due to tumor dissemination 8 months after initial diagnosis.

Of the 74 cases of adult pancreatoblastoma reported in the literature, outcome information is available for 57 patients. The median overall survival for adult patients with pancreatoblastoma reported in literature is 15 months (range, 1–108 months) [10]. Among the cases described in literature, metastasis and/or local invasion was found at diagnosis or operation, in 59 % of patients [1]. Liver is usually the most common site of metastasis, followed by lymph nodes and lungs [1, 2, 7, 10, 17, 18].

Chest wall, breast, bone, and brain metastases are described in literature, but they are exceptionally rare [1, 7, 19].

The biological reasons of this aggressive behavior in the adults are still unclear. Recently, molecular aberration in the fibroblast growth factor receptor (FGFR) signalling pathway, including somatic FGFR1 mutation, FGFR2 gene rearrangement, have been identified with RNA sequencing [20]. Further studies are needed to better understand the biological features of this rare tumor and to identify potential molecular targets to select patients that might benefit from systemic treatment strategies.

Conclusion

Adult pancreatoblastoma is a rare pancreatic neoplasm with malignant behavior. The prognosis is dismal due to advanced stage at presentation and disease recurrence. Diagnosis might be challenging because of its resemblance with other pancreatic neoplasms and non-specific symptoms at presentation. Surgical resection is usually the treatment of choice, but there is no consensus on the best management of adult patients with pancreatoblastoma and the current clinical management mostly relies on case report and small case series. Further data are needed to improve the knowledge about the clinical behavior of this rare and aggressive malignancy.

Disclosures

None.

Informed Consent

Written informed consent was obtained by the patient, and no IRB was required since all patient information was removed and de-identified.

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