

## Acinar Cell Carcinoma (ACC) in a Patient with Hypoglycemia: A Case Report

### Hipoglisemili Bir Hastada Asiner Hücreli Karsinomu (ACC): Bir Olgu Sunumu

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#### ABSTRACT

Pancreatic acinar cell carcinoma is one of the rare conditions of the gastrointestinal tract. Here we report Acinar Cell Carcinoma (ACC) in an old man with Hypoglycemia. The patient was a 79-year-old man with history of seizure. In lab data, Blood Sugar was 40 mg/dl and Brain problems were ruled out. For the last 2 to 3 months, he had spells shaky, sweaty, and weak; past medical history (PMH): Low grade Transitional cell carcinoma (TCC) and Diabetes mellitus (DM): negative. The prognosis for patients with mixed acinar–neuroendocrine carcinoma did not differ from that for those with histologically pure pancreatic ACC.

**Key Words:** Acinar cell carcinoma, seizure

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#### ÖZET

Pankreas asiner hücreli karsinom, gastrointestinal sistemin nadir durumlarından biridir. Burada hipoglisemili yaşlı bir erkekte Asiner Hücreli Karsinomunu (ACC) sunuyoruz. Hasta, 79 yaşında, nöbet öyküsü olan bir erkekti. Laboratuvar verilerinde kan Şekeri 40 mg / dl idi ve beyin sorunları ekarte edildi. Son 2-3 ay boyunca, titrek, terli ve zayıf nöbetleri vardı; öyküsünde düşük dereceli transizyonel hücreli kanser, Diabetes mellitus ise negatifti. Miks asiner–nöroendokrin karsinoması olan hastalar için prognoz, histolojik olarak saf pankreas ACC'si olanlardan farklı değildir.

**Anahtar Sözcükler:** Asiner hücreli karsinom, nöbet

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#### INTRODUCTION

Pancreatic acinar cell carcinoma is one of the rare conditions of the gastrointestinal tract (1, 2). Although acinar cells predominate in the normal pancreas, their malignant transformation is rare, representing 1–2% of malignant pancreatic tumors (3). Although considered as a single tumor entity, acinar cell carcinomas (ACCs) vary in their morphological and clinicopathological characteristics (4).

Presenting signs and symptoms are usually nonspecific and may include abdominal pain, weight loss, nausea, and vomiting. Jaundice is an uncommon presenting sign in 0-21% of Patients (5-7). Acute pancreatitis is the presentation in about 13% of cases (5), but is less frequently acknowledged in retrospective case series. Lipase hypersecretion syndrome, a paraneoplastic syndrome of panniculitis and polyarthralgia secondary to hyperlipasemia, is one of the rarest disease presentations described in 0-16% of cases (4, 5, 8). Metastasis is detected in about 50% of cases at the time of diagnosis and is most commonly found in the liver and regional lymph nodes (2, 4, 5). Endogenous hyper insulinism can occur in some conditions, including; a beta cell secretion stimulant, such as a sulfonylurea, a beta cell tumor, a functional beta cell disorder, Insulin autoimmune hypoglycemia (9). But as far as we know, hypoglycemia is a rare presentation of ACC. So, here we report Acinar Cell Carcinoma (ACC) in old man with Hypoglycemia.

#### CASE REPORT

The patient was a 79-year-old man with history of seizure. In lab data, Blood Sugar was 40 mg/dl. Brain problems were ruled out. For the last 2 to 3 months, he had spells shaky, sweaty, and weak; In Past medical history, he had Low grade TCC, DM and DH were not detected. None of the family members had DM.

Physical examination in this case including BMI=27 Kg/m<sup>2</sup> (no changes in body weight changes), BP=130/70 mmHg, PR=85 beats/min, revealed as normal. Regarding the fasting test, patient showed neuroglycopenic signs and symptoms within 2 hours.

Laboratory findings showed that Urine sulfonylureas was negative and in abdominal CT scan, No mass was found. Pancreatic tissue was atrophic with normal contour. There was a 5mm round hypoechoic mass lesion with rim around it in mid body of pancreas without any regional LAP. PD was about 3.3, 1.9 and 1 mm in head, body and tail respectively. Common bile duct (CBD) was about 6 and 5mm in mid and distal parts respectively and contained no sludge or stone.

Ampulla, Celiac trunk, Left liver lobe and Cystic duct was Normal. Also gallbladder had normal wall thickness and contained multiple small stones and sludge. The patient's blood sugar is then controlled after surgery and did not sign and symptom of hypoglycemia. In the case of established laboratory criteria, this lesion is mostly Insulinoma. Pathological examinations were performed in this study.

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1- Mac: Specimen consists 4 fragments of creamy tissue 1.5\*1.5\*1 cm in size (totally submitted in 2 blocks). 2- Mic: histologic examination shows pancreatic tissue with tumoral involvement of acinar cell carcinoma. The tumoral cells formed sheets and few acini. The cells are rather large with eosinophilic cytoplasm and round nuclei. All resected biopsies shows tumoral invasion with invasion to fatty tissue. 3- Dx: Acinar cell carcinoma.

Also, in this patient, the amount of insulin, C.peptid, Blood Sugar 120 minutes after fasting, Cortisol, TSH, Hemoglobin, Creatinine, Sodium and Potassium were measured, as shown in Table 1.

**Table 1-** Some laboratory findings in patient

Variable	Level
Insulin	25 lu/ml
C.peptid	5.93 ng/ml
Blood Sugar(120 minutes after fasting)	20 mg/dl
Cortisol	198 ng/ml
TSH	1.89 mIU/L
Hemoglobin	13 g/dl
Creatinine	1.4 mg/dl
Sodium	140 mEq/l
Potassium (K)	3.7 mEq/l

## DISCUSSION

Pancreatic acinar cell carcinoma (ACC) is a very rare pancreatic exocrine cancer. It accrue in 1% of pancreatic tumors in adults and 15% in pediatric subjects. They may show different clinical symptoms at presentation, morphological features, outcomes, and molecular alteration. The average age 59 years old (range 20–88 years). Male/female ratio of 2:1. ACC may arise in any portion of the pancreas. Average tumor diameter of 8–10 cm, well circumscribed, and at least partially encapsulated. Invasion through the capsule is a common finding and in about 50% of cases infiltration of the duodenum, large vessels, stomach, kidney, peritoneum, or spleen. Endocrine manifestations of ACC are Hypoglycemia secondary to tumor secretion of insulin and insulin-like growth factors. The diagnostic hallmark of ACC is IHC of acinar-specific products such as: trypsin, chymotrypsin, lipase, amylase, and carboxyl ester lipase (CEL). Histological Variant of ACC are Mixed acinar-neuroendocrine carcinomas, Acinar cell cystadenocarcinoma, Mixed acinar-neuroendocrine-ductal carcinoma, Mixed acinar-ductal adenocarcinoma. It's extremely difficult to distinguish pure acinar cell neoplasm from mixed acinar-endocrine neoplasms based on morphology alone. Neoplasms exhibiting >25% of both cell types should be designated mixed acinar- endocrine neoplasms (10-12).

The molecular mechanisms involved in ACC pathogenesis and progression are largely unknown. Unlike ductal adenocarcinomas, typical mutations in KRAS, DPC4, p16, and TP53 genes are absent or very rare in ACCs. Pathogenesis mechanism includes abnormalities in the APC/ $\beta$ -catenin pathway. There is some morphological similarities between ACCs and NETs, so the differential diagnosis with NETs may be difficult. High-mitotic index, abundant necrosis, clearly evident nucleoli in apparently well to moderately differentiated cells, abundant eosinophilic cytoplasm, should give rise to the suspicion of an ACC. IHC must be used with caution. The use of general NET markers, chromogranin A and synaptophysin alone may be risky because ACCs show at least scattered NE cells, in 30% of cases, are particularly abundant (12-16).

Treatment includes Surgery which has median survival (36 months for resected ones and 4 months survival for those without any resection) and Adjuvant therapy has not been established for patients with resected pancreatic ACC because prospective randomized trials are lacking. ACC is sensitive to adjuvant therapy remains a controversial issue. A recent case report from Johns Hopkins: preoperative neoadjuvant therapy effectively down staged four patients. Distant metastasis is the most common pattern of recurrence. Poor overall survival is more common in Elevation of CA19-9, LN metastasis, neural invasion. In these cases 5-year survival rate is 36–72%.

We observed a high recurrence rate of 56.3 % in resected ones, including both local and distant metastases despite the well-circumscribed local confinement, ACC remains aggressive in nature overall median survival of 19 months. Factors related to a poor prognosis in pancreatic ACC in patients with resected tumor are Elder age, Large tumor size (>6.5 cm), Lymph node metastasis, Positive resection margin, Poorly differentiated tumors, Advanced tumor stage. (The prognosis for patients with mixed acinar–neuroendocrine carcinoma did not differ from that for those with histologically pure pancreatic ACC) (12-14, 17).

## Conflict of interest

No conflict of interest was declared by the authors.

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