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Case Report

Primary Pancreatic-Type Acinar Cell Carcinoma of Jejunum Arising from Ectopic Pancreas with Synchronous Metastasis to Left Adrenal Gland

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Abstract

Background: Pure pancreatic-type ACC outside the pancreas is extremely rare.

Methods: We presented a very rare case of primary ACC of the pancreatic-type involving jejunum with a synchronous metastasis to left adrenal gland arising in well-developed ectopic pancreas which had fully developed pancreatic acini, islets of Langerhans, ductal structures, pancreatic cancer precursor lesions and a well-formed minor papilla that opens to the mucosal surface of jejunum. We also reviewed all 21 cases of pure pancreatic-type ACC outside the pancreas in the literature.

Results: The pre-operative diagnosis of pancreatic-type ACC outside the pancreas is challenging and difficult based on imaging studies or on small biopsies. Only 2 of 14 cases, which reported a pre-operative diagnosis, were correctly diagnosed as pancreatic-type ACC on liver biopsy. Patients who presented with unresectable or stage IV disease had mean overall survival of 13.5 (standard deviation [SD], 4.2) months, which was shorter than those who underwent surgical resection with curative intent (mean: 54.3, [SD, 9.1] months, P = 0.008).

Conclusions: The pre-operative diagnosis of pancreatic-type ACC outside the pancreas is

challenging. Early detection and surgical resection may prolong survival in these patients.

Keywords
Pancreatic acinar cell carcinoma; ectopic pancreas; survival

1. Introduction

Pancreatic acinar cell carcinoma (ACC) is a rare neoplasm, accounting for only about 1%-2% of all exocrine tumors of the pancreas [1]. Pure pancreatic-type ACC outside the pancreas, arising from ectopic pancreatic tissue or pancreatic acinar cell metaplasia, is extremely rare. In the literature, only 21 cases of pure ACC of pancreatic-type have been reported: six in the stomach [2-7], nine in liver [8-13], one in the duodenum [14], one in the ampulla of Vater [15], two in the jejunum [16, 17], one in the sigmoid colon [18], and one in lesser omentum [19]. Among these reported cases, ectopic pancreatic tissue or pancreatic acinar cell metaplasia was present in only two cases [2, 16]. In this report, we presented an extremely rare case of pure pancreatic-type ACC of jejunum with a synchronous metastasis to left adrenal gland arising in well-developed ectopic pancreas which had fully developed pancreatic acini, islets of Langerhans, ductal structures, pancreatic intraepithelial neoplasia and a well-formed minor papilla that opens to the mucosal surface of jejunum. We also reviewed the clinicopathologic features and follow-up data of all 21 cases of pancreatic-type ACC arising from ectopic pancreas in the literature.

2. Case Presentation

The patient was a 64 year-old Caucasian gentleman with a long history of morbid obesity, type 2 diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, cardiac arrhythmias, and sleep apnea. The patient had no personal or family history of cancer. Even with adjustments to his blood pressure medications, control of his blood pressure could not be achieved, with baseline blood pressure of 180/105 mm Hg. Imaging studies showed a large mass measuring 7.0 cm in the left adrenal gland and bilateral multiple renal cysts, the largest measuring 3.3 cm in the upper pole of the left kidney. He was referred to our hospital for further evaluation and treatment. Extensive hormonal and laboratory work up was performed. He was found to have iron deficiency anemia (hemoglobin: 7.2 g/dl), which was treated with 4 units of blood transfusion followed by oral iron pills. No evidence of hormonal overproduction was found with normal levels of renin (<0.6 ng/ml/h), aldosterone (10 ng/dl), free normetanephrine (0.78 nmol/L), free metanephrine (<0.2 nmol/L), serum cortisol (4.3 mcg/dl), ACTH (10 pg/ml), dehydroepiandrosterone sulfate (<15 mcg/dl), and a negative low dose dexamethasone suppression test. He had no fever, changes in skin color, jaundice, abdominal pain, melena, bloody stool, hematuria, or any other bleeding. A colonoscopy as well as upper gastrointestinal endoscopy were performed by an outside gastroenterologist who reported diffuse gastritis and benign colon polyps, but otherwise unremarkable endoscopic findings. The follow-up abdominal computed tomography (CT) scan performed at our institution 3.5 months after the initial imaging study showed, in addition to the bilateral renal cysts, a slight increase in size of the left adrenal mass (7.2 cm) and areas of

calcification and fat necrosis in the omentum (Figure 1). There was no significant lymphadenopathy. The liver, pancreas, spleen, right adrenal gland and gallbladder were unremarkable. Chest CT scan showed calcified and non-calcified nodules up to 4 mm in size in the right lung, suggestive of granulomatous disease. The clinical and radiological findings favored the diagnosis of adrenal cortical carcinoma. Given the known potential for peritoneal seeding associated with biopsy of adrenocortical carcinoma, the decision was made to perform an open laparotomy and resection of the left adrenal mass. At the time of surgery, the patient was found to have areas of concern for metastasis in both lobes of the liver, spleen, and peritoneal surfaces, including the diaphragm, omentum, and pelvis. The planned left adrenalectomy was aborted. Upon examination of the small intestine and colon, a tumor within the jejunum was identified at approximately 10 inches distal to the ligament of Treitz that appeared to be partially obstructing the lumen. No other concerning lesions were identified. Segmental resection of the small bowel and resection of a 4 cm omental tumor were performed and sent for an intra-operative evaluation, which reported a frozen section diagnosis of neuroendocrine tumor in the small intestine and calcification, ossification and chronic inflammation in the omentum. Pathologic examination of the resected segment of small intestine (7 cm in length) revealed an ulcerated mass (4 x 3.5 x 1.8 cm) with a tan-white cut surface. Grossly, the tumor involved the muscular wall and extended into the subserosal soft tissue. The tumor was 2 cm from the closest small intestinal margin. In the subserosa and muscularis propria of small intestine adjacent to the tumor, there was a large area of tan-yellow lobulated tissue (4.0 x 3.5 x 1.2 cm), consistent with ectopic pancreas (Figure 2A). The rest of the small intestine was grossly unremarkable. Microscopically, the tumor invaded into, but not through, the muscularis propria. The tumor consisted of tumor cells forming solid sheets with an acinar pattern. The tumor cells had uniform nuclei, inconspicuous nucleoli, and purple granules in the cytoplasm. More than 10 mitotic figures per 10 high power fields were identified (Figure 3A-3C). Lymphovascular invasion was present. Immunohistochemical stains show that the tumor was positive for pancytokeratin and trypsin (Figure 3D-3E). The tumor cells were negative for chromogranin A (Figure 3F), synaptophysin, inhibin and HMB-45 (data not shown). Sections from the area of lobulated soft tissue showed an ectopic pancreas which had fully developed pancreatic acini, islets of Langerhans, ductal structures, a well-formed ductal complex mimicking pancreatic duct of Santorini, and minor papilla which opened to the mucosal surface of the jejunum and focal pancreatic intraepithelial neoplasia 1 and 2 (PanIN 1 and PanIN 2, Figure 2B-2D). The ectopic pancreas was predominately located in the muscularis propria and focally extended into the submucosa and subserosa. Therefore, the final diagnosis of primary acinar cell carcinoma of the pancreatic-type arising in ectopic pancreas of the jejunum was made. The frozen section diagnosis in the omentum was confirmed, and no carcinoma was identified. No lymph nodes were grossly or microscopically identified since there was only limited mesenteric adipose tissue present in the specimen. The pathologic stage was pT2,Nx,M1 (adrenal gland).

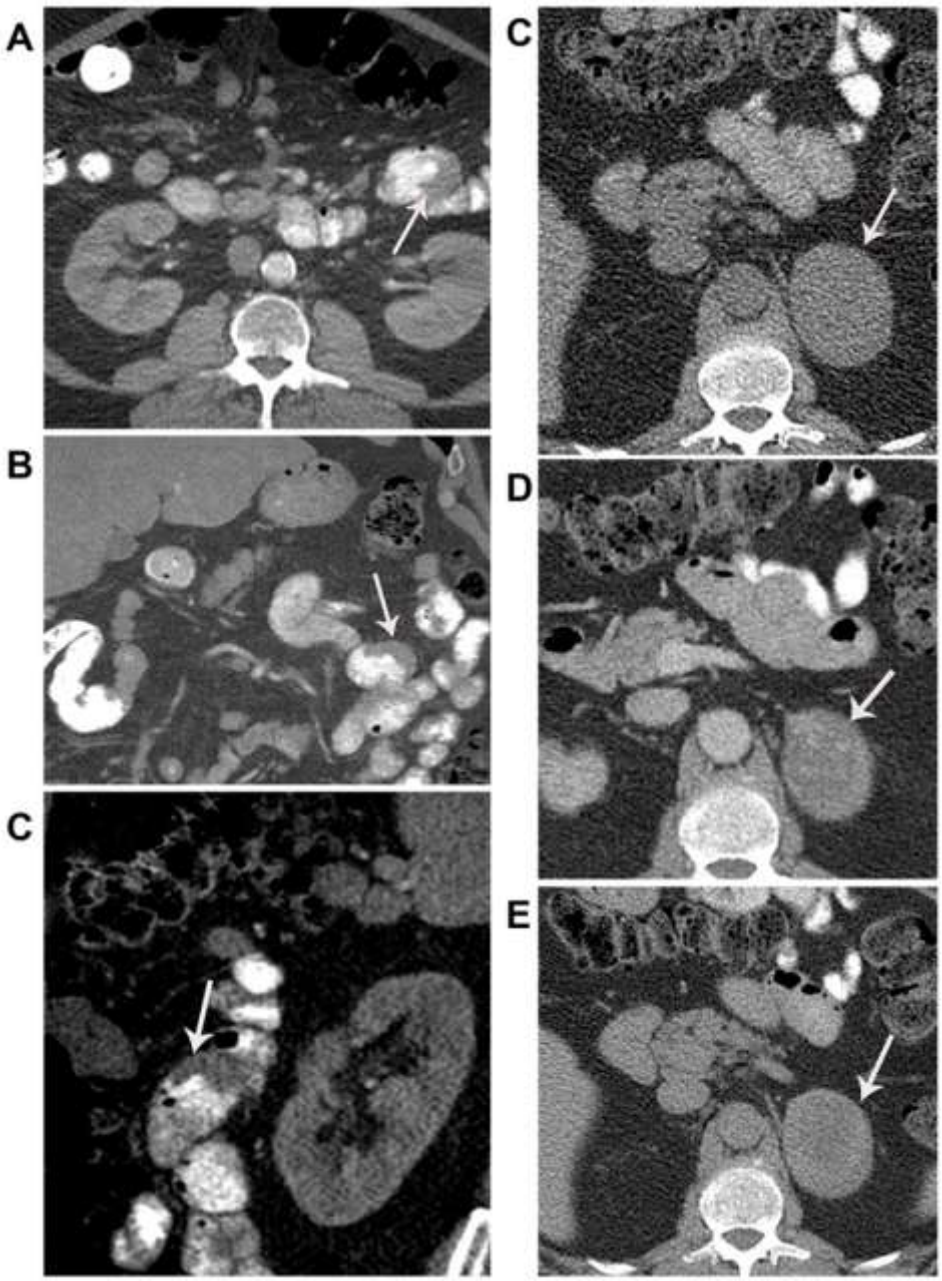

Figure 1 The axial (A), coronal (B) and sagittal (C) images show a mass (arrow) in the jejunal loop which is hypoattenutating to the contrast present in the bowel loops. The axial precontrast (C), portal venous phase (D) and delayed (E) images show a mass (arrow) in the left adrenal gland which demonstrates contrast enhancement and washout.

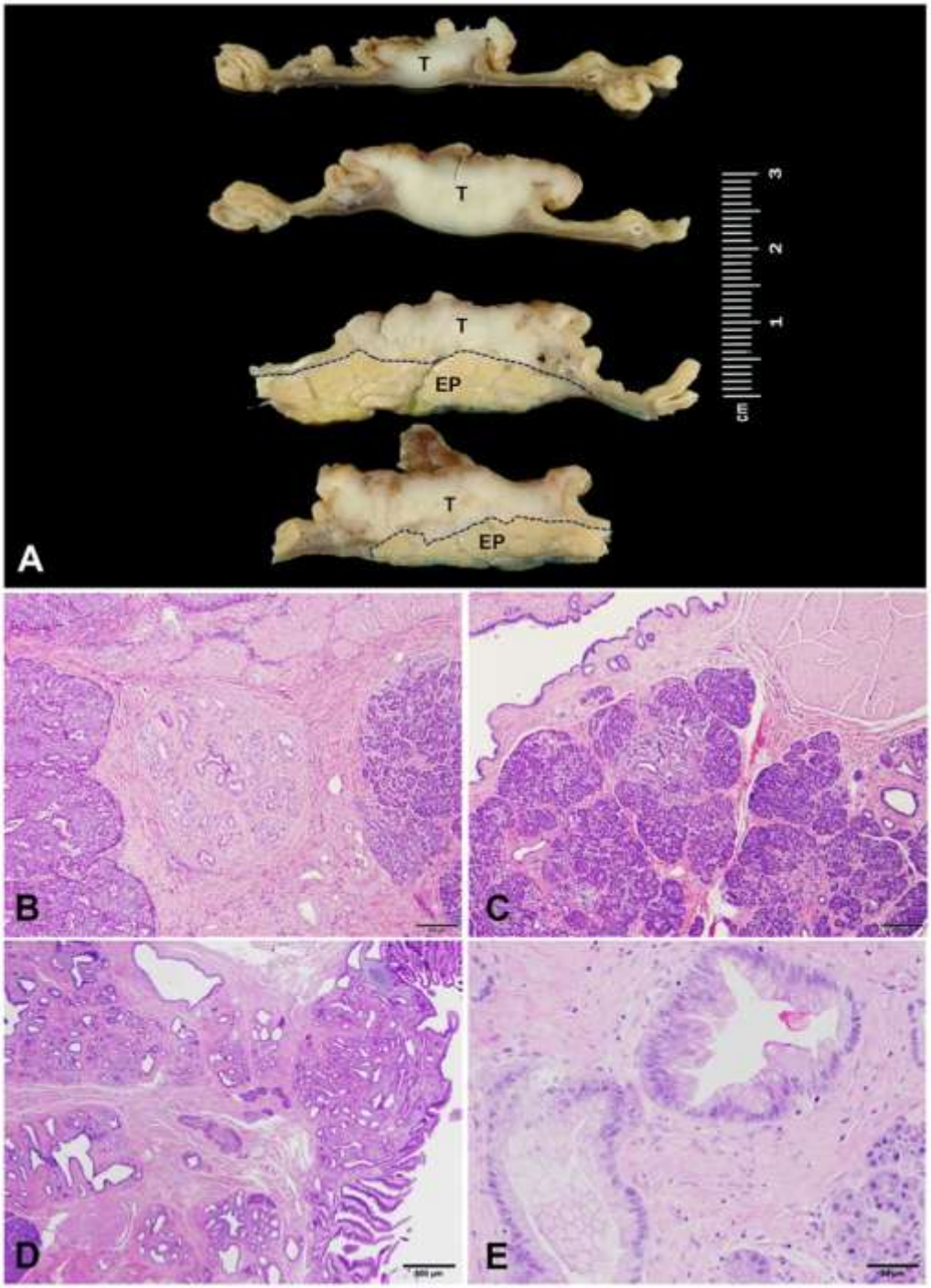

Figure 2 (A) Cross sections of tumor (T) with underlying ectopic pancreas (EP). (B) H&E-stained section of the interface between the tumor and non-neoplastic ectopic pancreas (40x). (C-E) H&E-stained sections of ectopic pancreas exhibiting fully developed pancreatic acini, islets of Langerhans, ductal structures (C, 40x), a well-formed ductal complex mimicking pancreatic duct of Santorini and minor papilla which opened to the mucosal surface of jejunum (D, 20x) and focal pancreatic intraepithelial neoplasia 1 and 2 (E, 100x).

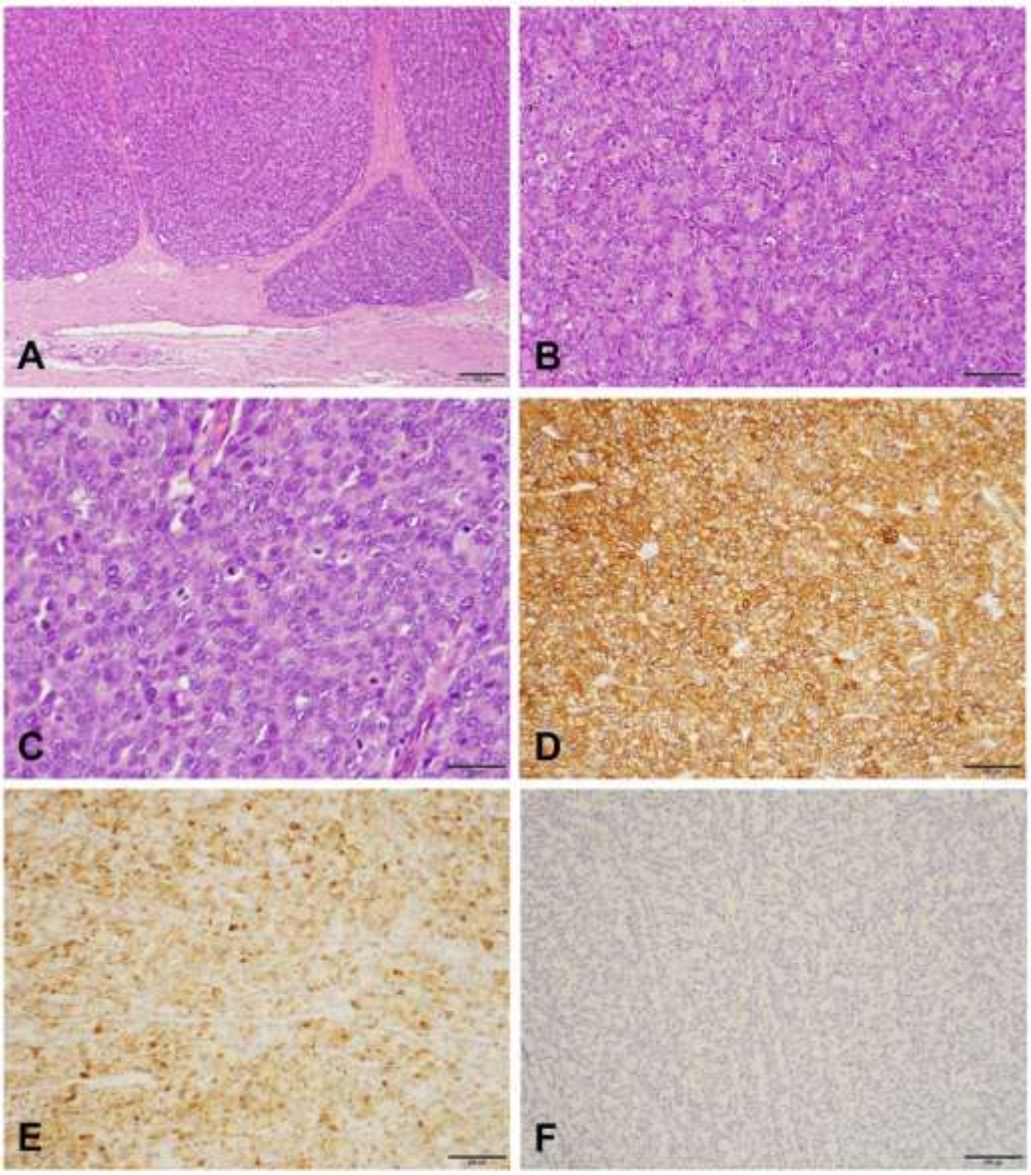

Figure 3 (A-C) H&E sections of tumor invading into the muscularis propria (A, 40x), exhibiting acinar pattern (B, 100x) and solid sheets with brisk mitosis (C, 200x). The tumor is positive for pancytokeratin (D, 100x) and trypsin (E, 100x), but negative for chromogranin A (F, 100x).

The patient tolerated the procedure well with no complications and fully recovered one month after surgery. Subsequent fine needle aspiration of the left adrenal mass confirmed the diagnosis of metastatic acinar cell carcinoma. Patient elected to receive no adjuvant chemotherapy. He was closely followed by multiple abdominal and thoracic CT or PET/CT scans every three months. The follow up scans showed a stable tumor in the left adrenal gland, normal pancreas, and no additional FDG-avid foci during the first eight months. However, 14 months post surgery, the patient developed bilobar hepatic metastases, recurrence in the mesentery adjacent to the site of jejunal resection, and progression of left adrenal tumor. The patient was then treated with Gemzar. The patient died of metastatic ACC, 18 months post surgery and 22 months from the initial imaging diagnosis.

3. Discussion

Malignant transformation of ectopic pancreas is extremely rare. The proposed criteria for carcinoma arising from ectopic pancreatic tissue include the following: (1) tumor is found within or near the ectopic pancreas; (2) a transition between non-neoplastic pancreatic tissue and carcinoma should be present, and (3) fully developed pancreatic acini and ductal structures should be present in the ectopic pancreatic tissue [20]. Our case fits all of the above criteria, with the ectopic pancreas exhibiting fully developed pancreatic acini, islets of Langerhans and ductal structures, a well-formed ductal complex mimicking pancreatic duct of Santorini, and a minor papilla that opens to the mucosal surface of the jejunum. Pancreatic intraepithelial neoplasia 1 and 2 (PanIN1 and PanIN2) were also present in the non-neoplastic pancreas in our case. In 19 of 21 previously reported cases, the ectopic pancreas was not identified, but operated with the assumption that the ACC arose from ectopic pancreas which was completely obliterated by the tumor.

Among the 22 reported cases, including our case, 12 were male and 10 were female with age ranging from 6 years to 86 years (median age: 64.5 years). The most common reported site is liver (9/22, 40.9%), followed by stomach (6/21, 27.3%), duodenum and jejunum (4/22, 18.2%, Table 1). Patients often presented with non-specific symptoms such as abdominal discomfort/pain, weight loss, anemia, etc. or the tumor was identified during workup for other causes. Given the rarity of this entity, the pre-operative diagnosis based on imaging studies or on small biopsies is challenging and difficult. Among the 14 cases which reported a pre-operative diagnosis, six were diagnosed as poorly differentiated adenocarcinoma/carcinoma on biopsy and six were diagnosed as hepatocellular carcinoma, gastrointestinal stromal tumor (GIST) vs lymphoma or cholangiocarcinoma based on imaging or endoscopic studies. Only two cases were correctly diagnosed as an ACC of the pancreatic-type on liver biopsy.

Treatment information, when available, varied among patients. Eighteen patients were treated with surgical resection, with three receiving adjuvant chemotherapy as well. One patient with gastric ACC of the pancreatic-type had synchronous pancreatic ductal adenocarcinoma with lymph node and liver metastases and was treated with up-front chemotherapy. The final diagnosis of gastric ACC of the pancreatic-type was only made on autopsy after the patient died, 5 months post diagnosis. One patient received steroid therapy for skin lesions secondary to lipase hypersecretion syndrome. Two patients with non-resectable liver tumors were treated with chemotherapy alone.

Table 1 The Clinical and pathologic features of 22 cases of pancreatic-type acinar cell carcinoma outside the pancreas.

Case	Age	Gender	Presenting symptom(s)	Tumor Site	Preoperative Diagnosis	Tumor Size and Characteristics	Treatment	Recurrence (months)	Outcome (months)	Author(s) [References]
1	52	M	Exacerbated dyspeptic symptoms	Gastric Antrum	Adenocarcinoma	4.0 cm, ulcerated tumor invading submucosa	Subtotal gastrectomy	No	NA	Ambrosini-Spaltro, et al [2]
2	86	F	Identified during work up for anemia	Gastric Antrum	Adenocarcinoma	5.0 cm, ulcerated tumor invading muscularis propria	Partial gastrectomy	No	NA	Sun and Wasserman [6]
3	73	M	Epigastralgia	Gastric Pylorus	GIST vs lymphoma	7.6 cm, submucosal mass invading pancreas with LN metastasis	Pancreaticoduodenectomy	Liver (7)	AWD (11)	Mizuno [5]
4	63	M	Abdominal pain, weight loss	Gastric Antrum	Adenocarcinoma	6.5 cm, ulcerated mass with liver metastasis	Chemotherapy	No	DOD (5)	Yonenaga [7]
5	77	F	Anemia	Gastric fundus	Poorly differentiated carcinoma	4.5 cm, polypoid and exophyitic mass invading MP	Partial gastrectomy	No	Died, complications (1)	Coyne [3]
6	54	M	Detected by endoscopy	Gastric cardia	GIST vs lymphoma	2.7 cm, well-circumscribed submucosal mass	Laparoscopic wedge resection	No	NED (33)	Kim [4]

7	35	F	Abdominal pain, weight loss	Liver, left	Hepatocellular carcinoma	4.0 cm, polycystic, unencapsulated mass	Left hepatectomy	No	NED (72)	Hervieu [9]
8	73	F	Painful cutaneous lesions	Liver, right and left	NA	1.0-6.0 cm, multiple liver masses	Steroid treatment for skin lesions	No	DOD (2.5)	Zundler [13]
9	68	F	Weight loss	Liver, left	Hepatocellular carcinoma	7.0 cm, well-circumscribed mass	Partial hepatectomy	No	NED (38)	Agaimy [8]
10	71	M	Abdominal pain	Liver, right	Hepatocellular carcinoma	Size not reported, mass	Right hemihepatectomy with hepaticojejunostomy	No	Died, unknown (3)	Agaimy [8]
11	72	M	Abdominal discomfort	Liver, right	Cholangiocarcinoma	Size not reported, large mass	Hepatectomy	Liver (18)	AWD (20)	Agaimy [8]
12	49	F	Abdominal discomfort	Liver, right	NA	Size not reported, multinodular mass	Right hepatectomy	No	NED (28)	Agaimy [8]
13	54	F	Early satiety, abdominal discomfort	Liver, right	NA	16.9 and 3.0 cm, 2 masses	Right hepatectomy plus chemotherapy	No	AWD (20)	Jordan [10]
14	48	M	Jaundice	Liver, right	Acinar cell carcinoma	15 cm, mass	Chemotherapy	No	AWD (13)	Laino [11]
15	31	M	Abdominal pain	Liver, right and left	Acinar cell carcinoma	Size not reported, large mass	Chemotherapy	Lung and LN	DOD (18)	Wildgruber [12]
16	58	M	Iron deficiency anemia	Duodenum, 2nd part	NA	2.7 cm, submucosal mass	Duodenectomy plus chemotherapy	No	NED (18)	Jharomi [14]

17	65	F	Jaundice and fatigue	Ampulla of Vater	Carcinoma of ampulla of Vater	1.2 cm, submucosal mass invading duodenal MP	Pancreaticoduodenectomy	No	NED (19)	Kawakami [15]
18	71	M	Incidental (during cholecystectomy)	Proximal jejunum	NA	3.5 cm, ulcerated mass invading subserosa	Segmental resection	Liver (12)	AWD (12)	Makhlouf [16]
19	78	F	Melena	Jejunum	Adenocarcinoma	8.5 cm, exophytic mass invading mesenteric tissue	Partial jejunectomy, partial pancreatectomy plus chemotherapy	No	NED (10)	Takagi [17]
20	65	F	Intestinal obstruction	Sigmoid colon	NA	4.0 cm, ulcerated tumor invading ipericolonic tissue with LN metastasis	Segmental resection	Femur (18)	DOD (24)	Chiaravalli [18]
21	6	M	Abdominal pain	Lesser omentum	NA	12 cm, mass with no involvement of pancreas	Omentectomy	No	NED (5)	Sharma [19]
22	64	M	Incidental (work up for blood pressure)	Jejunum	NA	4.0 cm, ulcerated mass with left adrenal gland metastasis	Segmental resection	Mesentery, liver (14)	DOD (22)	Our case

Follow-up information was available in 20 patients. During follow-up, one patient with gastric ACC and one patient with jejunal ACC developed liver metastasis after surgical resection at 7 and 12 months, respectively. One patient with liver ACC had liver recurrence at 18 months. One patient with ACC of the colon developed metastasis in the femur at 18 months after colectomy. Our patient developed bilobar hepatic metastases, recurrence in the mesentery adjacent to the site of jejunal resection, and progression of left adrenal tumor at 14 months after surgery. Five patients died of disease at 2.5, 5, 18, 22, and 24 months respectively, one patient died of surgical complications at 1 month and one patient died of unknown cause at 3 months. Five were alive with disease and eight were alive with no evidence of disease with a follow up of 5 to 72 months. The median overall survival was 24 months. Patients who presented with unresectable or stage IV disease had mean overall survival of 13.5 (standard deviation [SD], 4.2) months, which was shorter than those who underwent surgical resection with curative intent (mean: 54.3, [SD, 9.1] months, *P* = 0.008, Figure 4).

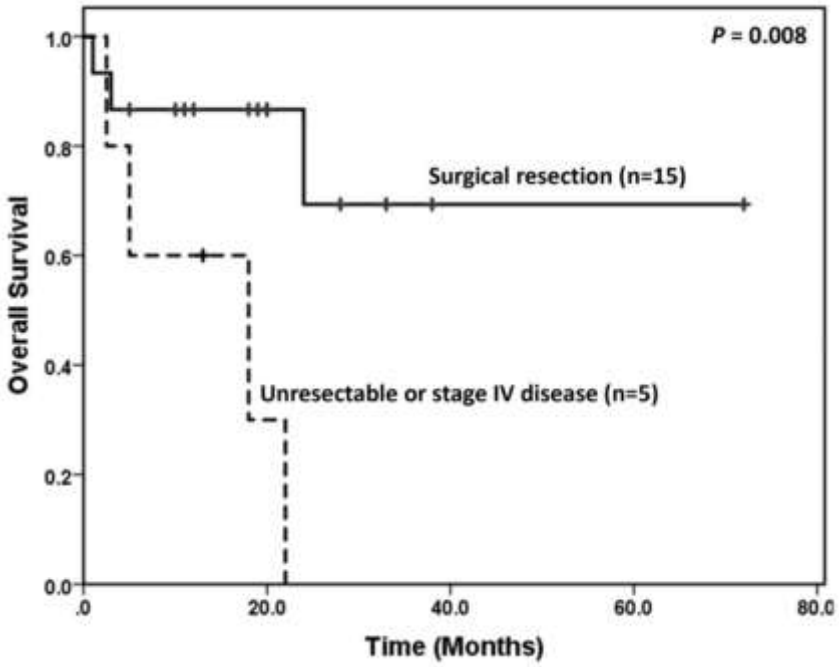

Figure 4 Kaplan–Meier survival curves showing patients with unresectable or stage IV disease had shorter overall survival than those who underwent surgical resection with curative intent (*P* = 0.008).

In this report, we presented a very rare case of primary ACC of the pancreatic-type involving jejunum with synchronous metastasis to left adrenal gland arising in well-developed ectopic pancreas which had fully developed pancreatic acini, islets of Langerhans, ductal structures, pancreatic precursor lesions, and a well-formed minor papilla that opens to the mucosal surface of jejunum. Given the rarity of this tumor, ACC of the pancreatic-type is difficult to diagnose in other organs outside of the pancreas, clinically and on small biopsy when ectopic pancreas is not sampled. Considering that patients who underwent resection with curative intent had better overall survival, based on a limited number of cases reports, early detection and surgical resection may prolong survival in these patients.

Author Contributions

OHW – writing and editing of manuscript, Figure 2 and Figure 3 construction; PRB – Figure 1 construction; JSE – writing and editing of manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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