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CASE REPORT

Acinar Cell Carcinoma in the Background of Chronic Calcific Pancreatitis

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Background

Acinar cell carcinoma (ACC) is a rare malignancy of pancreas. It represents around 1% of pancreatic exocrine tumors. Chronic pancreatitis is a predisposing factor for pancreatic adenocarcinoma (PAC). Locally advanced pancreatic tumors often require multivisceral resection. The present report describes a rare combination of ACC in a patient with chronic calcific pancreatitis (CCP).

Case Report

A 48-year-old gentleman presented with intermittent upper abdominal pain radiating to back for 5 years, which had increased in severity recently. He was a diabetic and had steatorrhoea. Anorexia, weight loss, or jaundice were absent. His serum amylase and tumor markers were normal.

A contrast-enhanced computed tomography (CECT) revealed dilated main pancreatic duct with multiple intraductal calculi and atrophic pancreatic parenchyma suggestive of CCP. A 5.7 × 5.5 × 4.5-cm solid mass with central necrosis was present in distal body and tail of pancreas, which enhanced in the periphery and along the papillary like projections radially. Splenic vein was thrombosed proximal to the mass. There was no apparent lymphadenopathy or adjacent organ involvement (Fig. 1). These features suggested that the tumor could be solid pseudo papillary tumor. He was planned for distal pancreatosplenectomy with coring of pancreatic head and pancreatojejunostomy.

Intraoperatively, a hard tumor was found in the distal body and tail of pancreas, fixed to splenic hilum infiltrating superior pole of the left kidney and the adjacent mesocolon. Rest of the pancreas was firm with multiple intraductal calculi. Hence, multivisceral resection was contemplated with curative intent. Patient underwent distal pancreatosplenectomy with en bloc left nephrectomy, left adrenalectomy, segmental colon resection and anastomosis, coring of pancreatic head, and pancreatojejunostomy. He had an uneventful postoperative recovery.

Pathological examination of specimen revealed a solid, circumscribed tumor measuring 5 × 4.5 × 3.8 cm occupying the tail of pancreas infiltrating the splenic hilar tissue and adherent to renal capsule. The mesocolon showed fibrosis and was tumor-free (Fig. 1). Tumor cells were arranged in acinar pattern with mild atypia. Cytoplasm stained positively for diastase resistant periodic acid Schiff (d-PAS). Ductal structures were absent. Immunohistochemistry demonstrated positive staining for Pan CK, alpha-1 anti-trypsin and negatively for neuroendocrine markers: chromogranin-A, synaptophysin, and progesterone receptor (Fig. 2). None of the four lymph nodes identified were involved by tumor. The final diagnosis was locally advanced acinar cell carcinoma-stage pT3N0M0.

Patient received eight cycles of adjuvant gemcitabine. He was healthy 10 months following surgery without recurrence.

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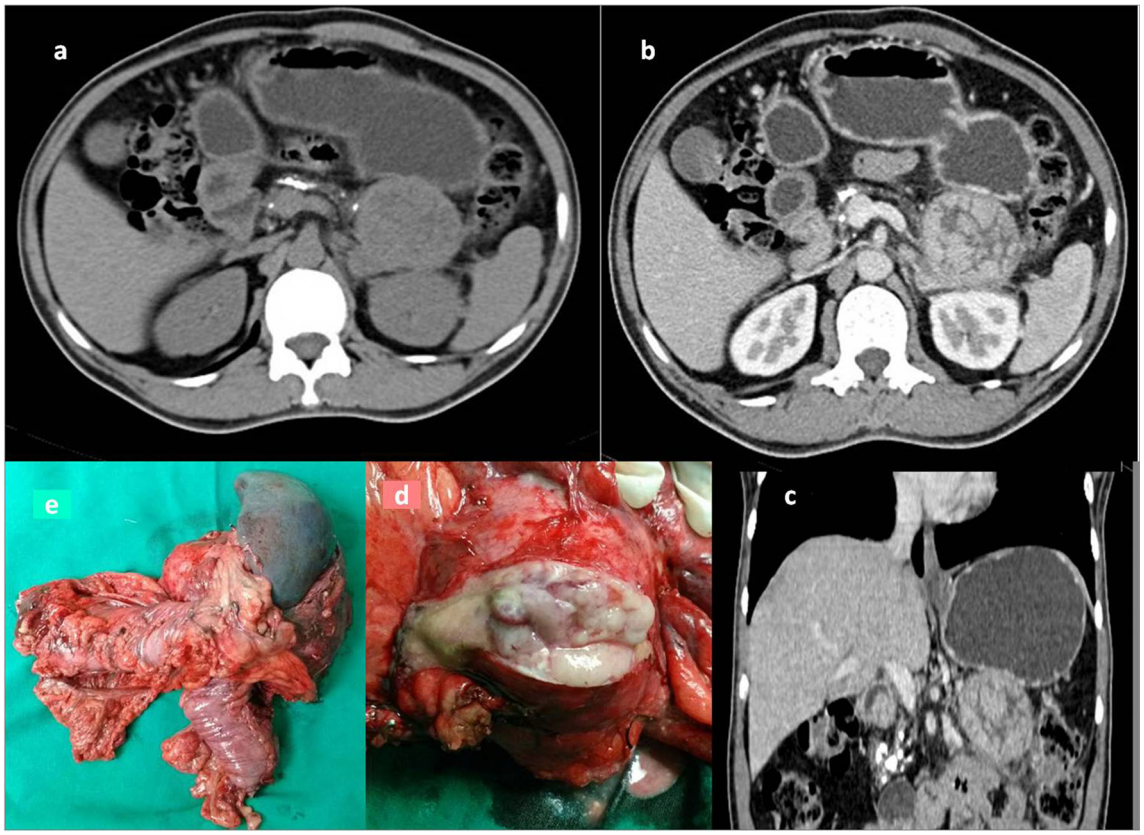

Fig. 1 **a** Noncontrast CT image, white arrow showing multiple radio opaque calculi in main pancreatic duct. **b** Contrast-enhanced CT image showing a solid enhancing mass in the distal body and tail of pancreas with central and radial areas of non enhancement. Splenic vein thrombosis seen. Planes with the left kidney and the adrenal appeared clear. **c** Contrast-enhanced CT images sagittal view showing pancreatic tail mass having clear planes with the stomach and colon. **d** Cut open specimens showing a solid tumor with lobulation and minimal hemorrhage. **e** Gross specimen-tumor in the tail of pancreas resected along with the spleen, left kidney, adrenal gland and adjacent segment of colon

Discussion

ACC contributes for 1% of pancreatic exocrine malignancy. It has male predilection presenting mostly in sixth-seventh decade. ACC usually involves the pancreatic head (56%), followed by the tail (36%) and the body (8%). Unlike PAC, ACC does not present with jaundice [1]. They are often found incidentally. Symptoms are nonspecific including weight loss (50%), abdominal pain (32%), and nausea and vomiting (20%). Schmidt triad comprising of subcutaneous fat necrosis, polyarthralgia, and eosinophilia [1, 2] is seen in 16% of ACC when there is excessive lipase secretion from tumor. Our patient presented with abdominal pain, which was attributed to acute on chronic pancreatitis. Imaging done subsequently revealed a mass in pancreas incidentally.

ACC can occasionally present as recurrent acute pancreatitis, where diagnosis is often delayed as symptoms are attributed to pancreatitis [3]. ACC in the presence of chronic pancreatitis have been reported only once in literature. In that report, patient underwent Frey's procedure. Histopathology examination of the cored head tissue revealed ACC and was subjected to pancreatoduodenectomy later [4]. In our report, the patient also had chronic pancreatitis with suspected pancreatic malignancy preoperatively and was subjected to curative resection.

Classically, ACC are huge tumors with intensely enhancing capsule and areas of necrosis in cross-sectional imaging. Mangafodipir trisodium-enhanced magnetic resonance imaging may be superior to CT in case of functional tumors. Endoscopic ultrasound is non-characteristic. Differentiating ACC from solid pseudo papillary tumor radiologically is difficult, which happened in our case [3].

ACC is usually large, multilobulated with areas of hemorrhage and necrosis. They are encapsulated, however mostly have finger like projections infiltrating the surrounding pancreatic parenchyma. Microscopically, the tumor cells can have four pattern of growth: acinar, cellular, glandular, and trabecular, with first two patterns occurring commonly. Vascular invasion occurs in two thirds and perineural invasion in one third of cases.

Immunohistochemistry is diagnostic for ACC. Acinar cells stain positively for butyrate esterase and d-PAS. They also stain intensely for pancreatic enzymes. Positive trypsin staining is seen in 100%, positive lipase in 77%, while

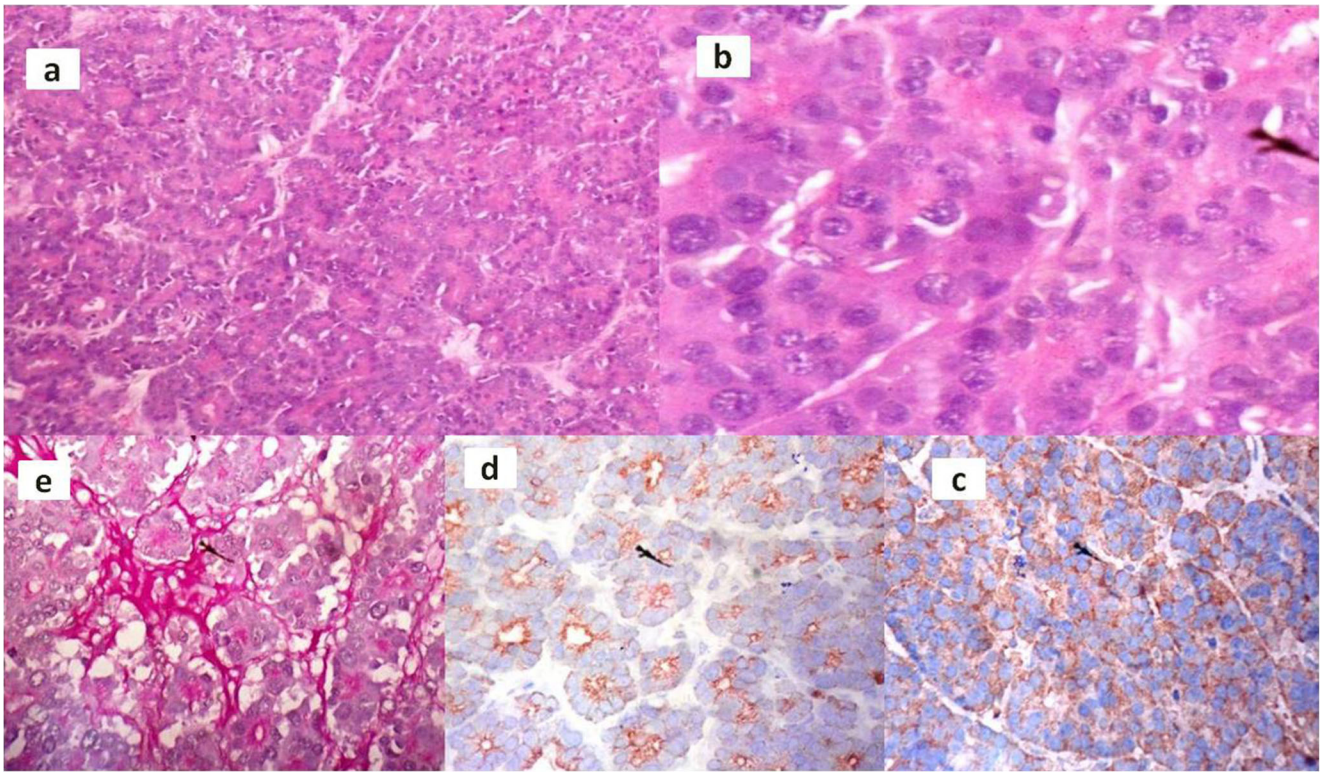

Fig. 2 Histopathological examination: **a** H/E staining at ×100 shows acinar pattern of arrangement of cells. **b** H/E staining at ×400 shows acini with small lumina surrounded by cells with eosinophilic granular cytoplasm. **c** Immunohistochemistry-alpha 1 antitrypsin stain showing intense cytoplasmic positivity. **d** Immunohistochemistry-Pan CK stain showing cytoplasmic positivity. **e** Diastase resistant periodic acid Schiff stain showing luminal magenta colored zymogen granules, delicate vascular channels coursing through tumor

chymotrypsin and amylase are positive in around 30% of cases. About one third of ACC have > 30% of neuroendocrine component and are classified as mixed acinar-neuroendocrine carcinomas, which stain for neuroendocrine markers too [5].

Surgery is the treatment of choice in absence of distant metastasis. En bloc resection with tumor-free resection margins is advocated for locally advanced tumors. The resectability rate of ACC is 64%, much higher than that of PAC (10–20%) [6]. No definitive consensus exists regarding role of adjuvant chemotherapy. Various chemotherapeutic agents have been administered in individual basis; however, gemcitabine was most commonly used. Recent studies have showed possibility of neoadjuvant chemotherapy and surgical resection after downstaging the tumor [7, 8]. Our case was treated with en bloc resection followed by adjuvant chemotherapy as the tumor was locally advanced.

Almost half of ACC patients present initially with metastasis. Subsequently, additional one fourth develop metastases, usually restricted to the regional lymph nodes and liver [1]. ACC had better survival than PAC. In a large study, comparing 672 ACC patients with PAC, they found that the overall 5-year survival was 42.8% for ACC (median 47 months) and 3.8% for PAC (median 4 months, $P < .0001$) [9]. Surgical resection improved survival significantly. The 5-year survival was 72% in ACC and 16.3% in PAC following resection ($P < .0001$) [8]. Studies have suggested that ACC presenting with age above 60 years, symptoms of lipase secretion and size > 10 cm have poor prognosis [6].

Our case had some unique features. The patient had symptomatic CCP for 5 years. An acute exacerbation helped revealing the tumor incidentally. He was promptly managed with en bloc resection and adjuvant chemotherapy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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