Clinical Case Report

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# Undifferentiated carcinoma with osteoclast-like giant cells of pancreas

## A case report with review of the computed tomography findings

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**Abstract**

**Rationale:** Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGCs) of the pancreas is an extremely rare and aggressive pancreatic malignancy. To our knowledge, the computed tomography (CT) findings of this disease have rarely been analyzed.

**Patient concerns:** A 65-year-old man who experienced weight loss of about 4 kg over 3 months presented to our clinic. The abdominal ultrasound (US) detected a 5.8 × 5.5 cm well-defined, cystic-solid mass in the head of the pancreas, which had been present for 1 month.

**Diagnosis:** A benign pancreatic tumor was initially suspected on the basis of the US findings. The patient then received serum tumor markers and CT examinations for further diagnosis, including carbohydrate antigen 199 (CA199), carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), contrast-enhanced CT (CECT) and CT angiography (CTA). His CA199, CEA, and CA125 marker levels were normal, which supported the diagnosis of a benign tumor. CECT showed a well-defined cystic-solid mass in the head of the pancreas, with a slightly enhanced solid portion and pancreatic ductal dilatation, which led us to consider the possibility of a malignant tumor. CTA revealed that the tumor nourishing arteries emitted from the pancreaticoduodenal superior and inferior arteries into the mass. Then, the patient underwent a pancreaticoduodenectomy. Finally, postoperative pathology and immunohistochemistry confirmed UC-OGC of the pancreas.

**Interventions:** The patient has been treated by a pancreaticoduodenectomy alone.

**Outcomes:** The operation had no complications, and the patient recovered well after surgery. Ten months after surgery, the patient reviewed the CECT, and no recurrence or metastasis was noted.

**Lessons:** Old patients with cystic-solid lesions in the pancreas should be aware of UC-OGC. CT findings usually show a clear boundary and a slightly enhanced mass with pancreatic duct expansion.

**Abbreviations:** CA199 = carbohydrate antigen 199, CEA = carcinoembryonic antigen, CECT = contrast-enhanced computed tomography, CT = computed tomography, CTA = computed tomography angiography, IPMN = intraductal papillary mucinous neoplasm, MCT = mucinous cystic tumor, OGCC = osteoclast-like giant cell carcinoma, PGCC = pleomorphic giant cell carcinoma, SPN = solid pseudopapillary neoplasm, UC-OGC = undifferentiated carcinoma with osteoclast-like giant cells, US = ultrasound.

**Keywords:** giant cell, osteoclast like, pancreas, undifferentiated carcinoma

## 1. Introduction

Pancreatic undifferentiated carcinoma is a rare and aggressive pancreatic malignancy that is divided into 2 categories by the WHO: osteoclast-like giant cell carcinoma (OGCC) and pleomorphic giant cell carcinoma (PGCC); of these, OGCC is more rare.[1] Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGCs) of the pancreas was first described by Rosai in 1968.[2] Less than 100 cases have been reported in English papers so far. The neoplasm is mainly composed of 2 cellular components: osteoclast-like giant cells (OGCs) and ovoid-to-spindle-shaped mononuclear tumor cells.[3] Due to the lack of typical clinical symptoms and the manifestation of a large cystic-solid mass, these tumors are easily misdiagnosed as mucinous cystic tumors (MCTs) or solid pseudopapillary neoplasms (SPNs). Most existing reports in the literature discuss pathologic findings, while imaging findings have been rarely reviewed. In this article, we reported the case of a patient with pancreatic UC-OGC and review clinical and computed tomography (CT) data from prior articles.

## 2. Case report

Written informed consent was obtained from the patient, and the data had been de-identified. The case report was approved by the

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A 65-year-old man with weight loss of about 4 kg over 3 months presented to our clinic. A pancreatic mass was discovered by abdominal ultrasound (US), which had been present 1 month. He denied any other discomfort, including abdominal pain, bloating, nausea, vomiting, diarrhea, constipation, and fever. He had a medical history of diabetes, was treated with insulin, and his glycemia was well controlled. The physical examination found no jaundice of the skin and sclera, mild tenderness in upper abdomen without rebound pain, and a palpable mass. The tumor markers, including carbohydrate antigen 199 (CA199), carcinoembryonic antigen (CEA), and carbohydrate antigen 125 (CA125) were normal.

The abdominal US showed a $5.8 \times 5.5$ cm well-defined, round-like, mixed cystic and solid mass in the head of the pancreas. Numerous capsules of varying sizes, thick spacers, and solid ingredients were observed in the mass. Color Doppler flow imaging showed no significant flow signal (Fig. 1). US findings were indicative of a benign tumor.

The upper abdominal CT revealed a $6.0 \times 5.9$ cm heterogeneous mass lesion that arose from the head of the pancreas, with a clear margin and regular form. Contrast-enhanced CT (CECT) showed a peripheral and internal solid portion that was slightly enhanced at the arterial phase and continuously enhanced at the portal venous and delayed phases. The pancreatic duct was dilated, which supported a malignant tumor. While the biliary dilatation was not observed, the pancreatic head tumor compressed the inferior vena cava and caused local stenosis, but the boundary was still clear (Fig. 2). The CT angiography (CTA) showed that the tumor nourishing arteries emitted from the pancreaticoduodenal superior and inferior arteries into the mass. In the 3-dimensional revascularization, the mass was poorly developed (Fig. 3). There were no significantly enlarged local lymph nodes, and other metastases were not observed.

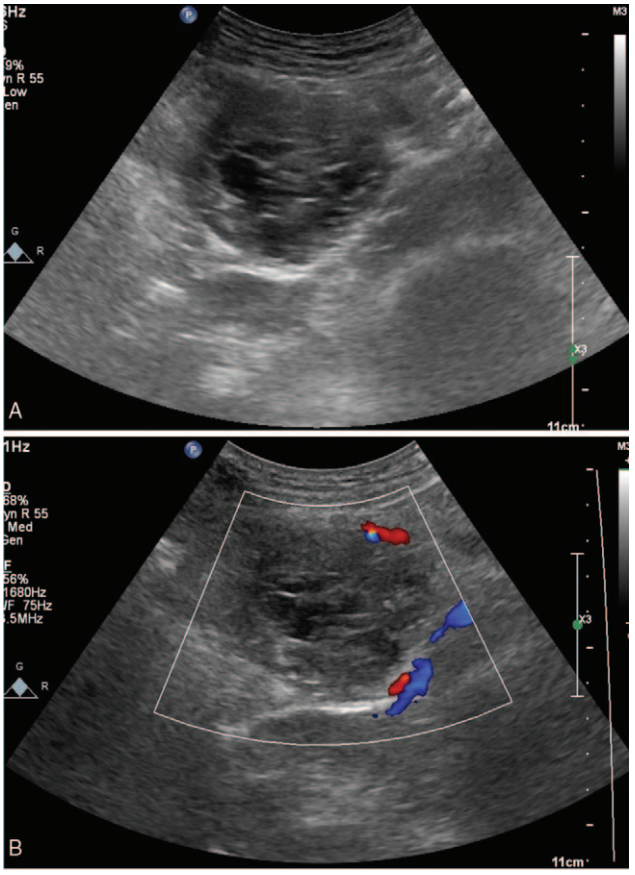


**Figure 1.** The ultrasound revealed a $5.8 \times 5.5$ cm mixed cystic and solid mass in the head of pancreas. Color Doppler flow imaging showed no significant flow signal.

To confirm the diagnosis, a laparotomy was performed. In the laparotomy, a hard mass of about 5 cm in diameter that involved the uncinate of the pancreatic head was confirmed. The head of the pancreas could be lifted. The mass was clearly demarcated from the surrounding tissues and vessels and had no adhesion to the inferior vena cava. The intraoperative rapid frozen pathologic section showed "undifferentiated carcinoma of the pancreas." Therefore, a pancreaticoduodenectomy was performed, and the operation proceeded smoothly. The patient recovered and was discharged 13 days after surgery.

The gross specimen presented as a $6 \times 6 \times 4$ cm brittle mass with a clear boundary and dark red and light-yellow exterior. Hematoxylin and eosin staining revealed OGCs that contained multiple small regular nuclei scattered in the ovoid to fusiform mononuclear tumor cell background (Fig. 4). Immunostaining showed that epithelial-derived markers including cytokeratin (CK) and epithelial membrane antigen (EMA) were focally positive. The mesenchymal-derived marker vimentin (Vim) was positive, and CD68 was focal positive. CA199 and gastrointestinal stromal tumor markers, including CD117 and Dog-1, were negative. B-cell lymphoma-2 (Bcl-2) gene mutation was positive, P53 gene mutation was suspected to be positive, and cell proliferation index Ki67 increased (+30%). The final diagnosis was "undifferentiated carcinoma with OGCs of the pancreas" that invaded the entire intestinal wall of the duodenal papilla region. One of the 2 peripancreatic lymph nodes metastasized.

The patient refused radiotherapy and chemotherapy. He received an upper abdomen CECT due to shiver and fever 3 months after surgery, which revealed a potential liver abscess. He was hospitalized again and underwent liver puncture drainage and antibiotic therapy. The patient's condition improved, and he was discharged after 20 days. Ten months following surgery, the patient was generally in good condition and the chest and abdomen CECT revealed that the abscess had been absorbed and no recurrence or metastases were observed.

## 3. Discussion

Undifferentiated carcinoma of the pancreas is a tumor that contains large eosinophilic pleomorphic cells and/or ovoid-to-spindle-shaped cells. The WHO divided this cancer into 2 types, OGCC and PGCC,[1] of which OGCC is rare and comprises <1% of exocrine pancreatic tumors.[4] The survival of patients with OGCC is generally considered to be better than those with PGCC.[5,6] OGCC consists of oval- or spindle-shaped mononuclear cells and scattered OGCs with multiple small regular nuclei. Its histogenesis is complicated and sometimes coexists with MCN and PGCC. Monocytes are tumor cells that constitute a sarcomatoid carcinoma background, express EMA, and are focally positive for CK, which suggest epithelial origin.[7,10] While scattered OGCs are nonneoplastic phagocytic cells that secrete osteoids, CD68 (a glycoprotein that binds to low-density lipoprotein), and vimentin are positive, which suggest a mesenchymal source.[3,9]

We reviewed the English literature for reports with clear CT images and descriptions from inception to July 31, 2018, and a

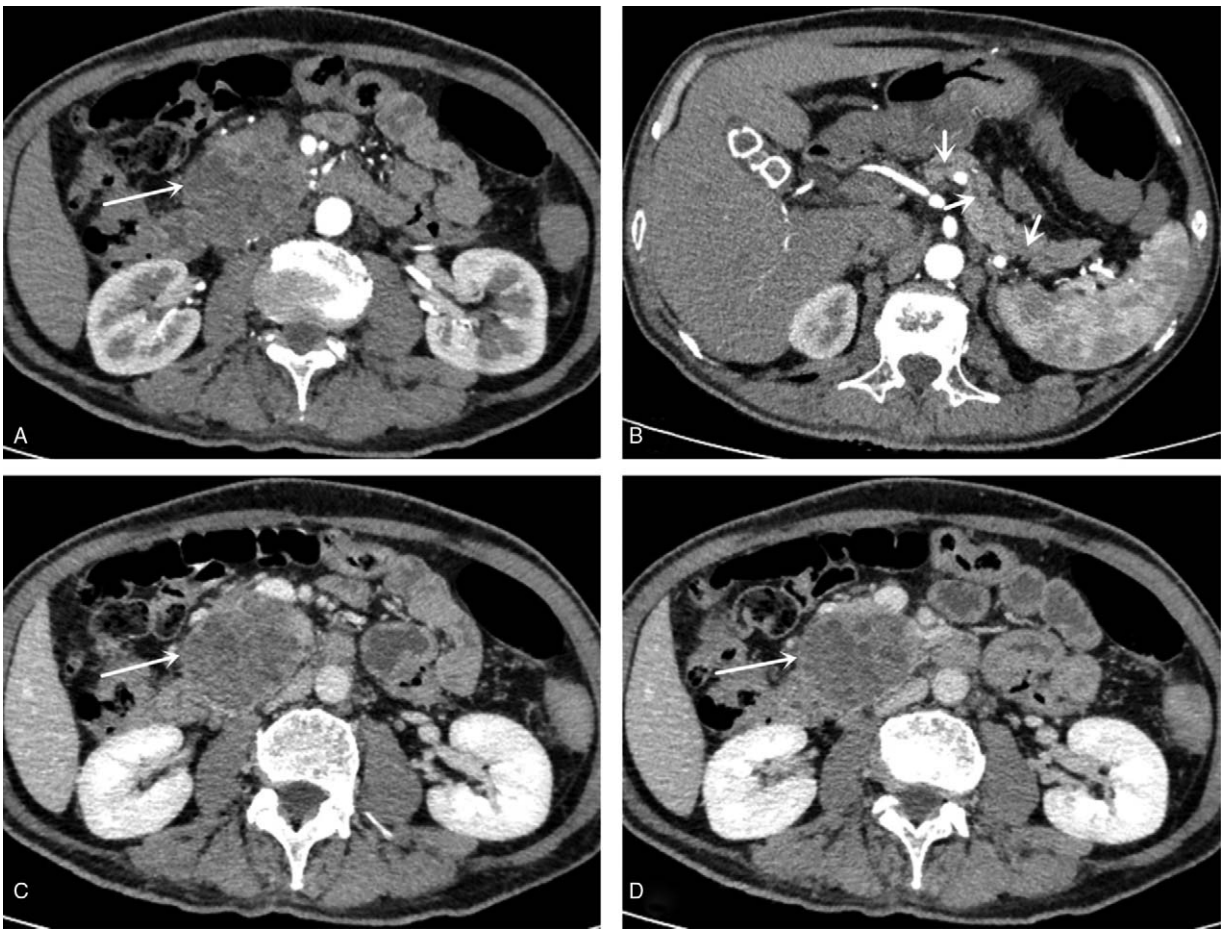


**Figure 2.** The computed tomography (CT) showed a 6.0 × 5.9 cm heterogeneous mass in the head of the pancreas (long arrow). The contrast-enhanced CT revealed a solid portion with a slightly enhanced arterial phase and continuously enhanced portal venous and delayed phases (A, C, D). The pancreatic duct was dilated (B, short arrows).

total of 17 cases were included (including our case).[6,8,10–23] We focused on clinical features and imaging findings. Two researchers analyzed the CT images and descriptions independently. When the opinions were inconsistent, a 3rd radiologist intervened; and finally, a consensus was achieved. A tumor with complete pseudo-envelope or clear demarcation from the surrounding tissues was defined as a clear margin. A round or oval shape was defined as regular form. Otherwise, the tumor

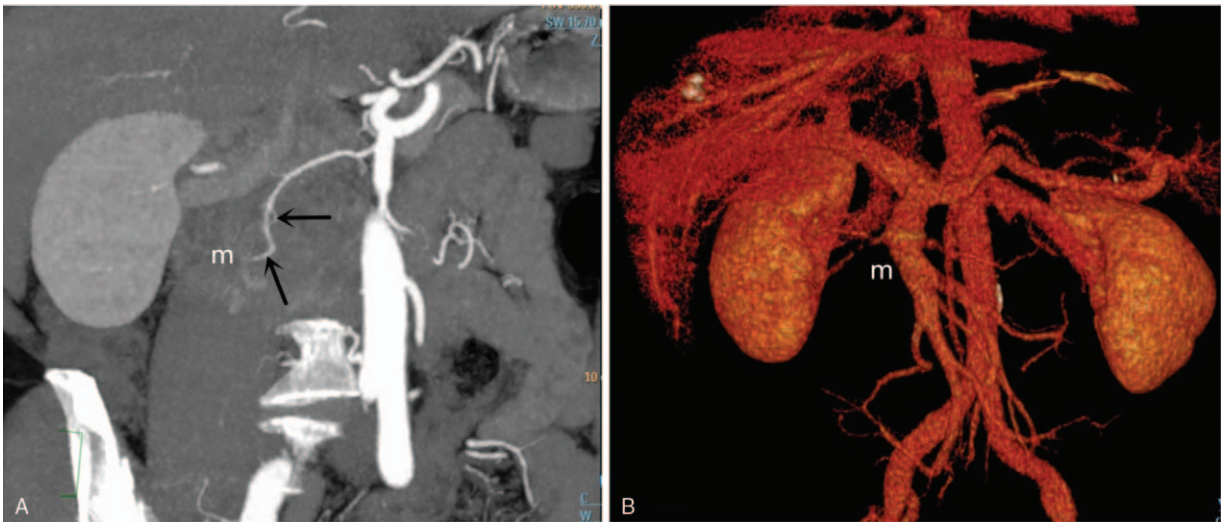


**Figure 3.** The computed tomography angiography revealed that nourishing arteries emitted from the superior and inferior pancreaticoduodenal arteries into the mass (A, arrows). In the 3-dimensional revascularization, the mass was poorly developed (B). m = mass.

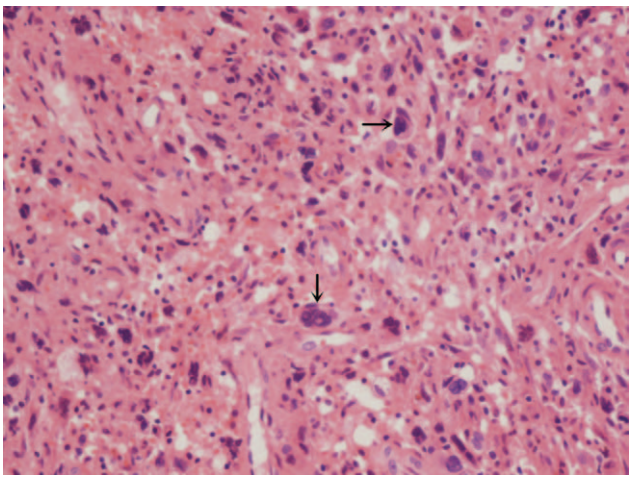

**Figure 4.** The histopathology revealed osteoclast-like giant cells (arrows) scattered on the background of ovoid-to-fusiform mononuclear tumor cells (hematoxylin and eosin, ×200).

was defined as having an obscure boundary and irregular form. The internal manifestations of these tumors were divided into 5 categories: solid (liquid-free), solid based (solid mass with little liquid), mixed (mixed cystic-solid mass that were difficult to classify as cystic or solid based), cystic based (cystic mass with few separation and/or nodular protrusion), and cystic (pure cystic without spacers or nodular protrusion) (Tables 1 and 2).

Pancreatic UC-OGC is more common in middle-aged and elderly patients, 94% of whom are over 50 years of age, and the average age is 63 years. Most patients are females (male:female = 7:10). The clinical symptoms are atypical, and mostly manifest as upper abdominal pain and/or weight loss. Loss of appetite, abnormal taste, nausea, steatorrhea, and some other gastrointestinal symptoms have also been reported in some cases.[24] Jaundice and anemia have been reported occasionally. In our case, the patient presented only with weight loss, without any other discomforts. Seven of 14 patients had elevated CA199 levels (range 41.26–392 U/mL) and 2/8 presented with elevated CEA (range 29.6–196 ng/mL). UC-OGC is invasive and usually has a poor prognosis. Previous reports showed an average postoperative survival of 10 to 20 months,[5,10] compared to 24 months in our review. However, the survival time span is very large, ranging from 3 to 84 months, which may be related to the histologic heterogeneity of the tumor and the extent of the lesion at the time of discovery.[17] There were 2 female patients who survived >6 years after surgery, one patient had UC-OGC alone and another had UC-OGC combined with PGCC. They both underwent radical surgery and gemcitabine chemotherapy.[13,20] Two patients with postoperative survivals <5 months had extensive lesions that could not be radically resected.[11,12] Therefore, early radical resection is essential. Chemotherapy and radiation therapy may be effective in some advanced cases[13,14,16,20,23]; however, experience and objective evidence are lacking throughout the literature.

The neoplasms are mostly located in the body and tail of the pancreas (13/17 cases). Previous studies confirmed the incidence in the pancreas body and tail to be about 70%.[18,25] The tumor is usually found in a large volume, with an average diameter of 8 cm. The tumor mostly manifests as a cystic-based or mixed cystic-solid mass (14/17 cases), and only 1 small tumor with a maximum diameter of 1.0 cm appeared to be solid in our

**Table 1**

**Literature review of pancreatic UC-OGC, showing clinical features and pathologic types.**

| First Author | Year | Age, y/gender | Symptoms | Serum tumor markers | Treatment | Survival, mo | Pathology |
|---|---|---|---|---|---|---|---|
| Nai GA[8] | 2005 | 69/M | UAP, WL, jaundice | / | Surg. | 12 | UC-OGC + MCN |
| Pan ZG[10] | 2007 | 70/F | WL, abnormal taste, anemia, anorexia | / | Surg. | >4 | UC-OGC + MCN |
| Singhal A[6] | 2010 | 62/M | UAP, nausea | CA199(−) CEA(−) | Surg. | >6 | UC-OGC |
| Hur YH[11] | 2011 | 77/F | UAP, anorexia | CA199(−) | Surg. | 3 | UC-OGC |
| Wada T[12] | 2011 | 59/M | Anorexia | CA199(+) CEA(+) | Surg. | 4 | UC-OGC + MCN |
| Kobayashi S[13] | 2014 | 37/F | UAP | CA199(+) | Surg.+ Chem. | 84 | UC-OGC |
| Temesgen WM[14] | 2014 | 57/F | UAP | CA199(+) | Surg.+ Chem.+ RT | >6 | UC-OGC |
| Jo S[15] | 2014 | 67/F | UAP, WL | CA199(+) | Surg. | 9 | UC-OGC |
| Chiarelli M[16] | 2015 | 68/F | abdominal discomfort | CEA(+) CA199(+) | Surg.+ Chem. | 10 | UC-OGC + PGC + MCN |
| Yang KY[17] | 2015 | 58/M | UAP, WL | CA199(−) CEA(−) | Surg. | / | UC-OGC |
| Sah SK[18] | 2015 | 54/F | UAP, WL | CA199(+) | Surg. | / | UC-OGC |
| Georgios K[19] | 2016 | 75/F | UAP, WL, steatorrhea | CA199(+) CEA(−) | Surg. | 10 | UC-OGC |
| Saito H[20] | 2016 | 61/F | UAP | CA199(−) CEA(−) | Surg.+ Chem. | 72 | UC-OGC + PGC |
| Sakhi R[21] | 2017 | 69/M | – | CA199(−) | Surg. | / | UC-OGC |
| Fu LP[22] | 2017 | 66/F | UAP | / | Surg. | 10 | UC-OGC |
| Zhang L[23] | 2018 | 57/M | UAP, WL | CA199(−) CEA(−) | Surg.+ Chem. | / | UC-OGC |
| This case | 2018 | 65/M | WL | CA199(−) CEA(−) | Surg. | >10 | UC-OGC |

(−) = negative, (+) = positive, / = not mentioned in the literature, CA199 = carbohydrate antigen 199, CEA = carcinoembryonic antigen, Chem = chemotherapy, F = female, M = male, MCN = mucinous cystic neoplasm, PGC = polymorphic giant cell, RT = radiation therapy, Surg. = surgery, UAP = upper abdominal pain, UC-OGC = carcinoma with osteoclast-like giant cells of pancreas, WL = weight loss.

**Table 2**

**Literature review of pancreatic UC-OGC, showing CT findings.**

| First author | Location | Max. diameter, cm | Margin | Form | Internal | Pancreatic duct | Distant metastasis |
|---|---|---|---|---|---|---|---|
| Nai GA[8] | H | 4.7 | Clear | Regular | Solid based | Dilated | Liver |
| Pan ZG[10] | B&T | 10.4 | Clear | Regular | Cystic-based | / | (–) |
| Singhal A[6] | T | 13.0 | Clear | Irregular | mixed | / | (–) |
| Hur YH[11] | T | 12.0 | Clear | Regular | Cystic-based | / | (–) |
| Wada T[12] | T | 14.0 | Clear | Regular | Cystic-based | Normal | liver |
| Kobayashi S[13] | H | 4.0 | Obscure | Regular | Cystic-based | / | (–) |
| Temesgen WM[14] | T | 18.0 | Clear | Irregular | solid-based | / | (–) |
| Jo S[15] | N&B | 10.0 | Clear | Regular | Cystic-based | / | Bone |
| Chiarelli M[16] | N&B | 6.0 | Obscure | Irregular | Mixed | Dilated | Liver, lung |
| Yang KY[17] | B | 5.0 | Obscure | Irregular | Cystic-based | Dilated | (–) |
| Sah SK[18] | B&T | 10.5 | Clear | Regular | Cystic-based, small calcification | / | (–) |
| Georgios K[19] | H | 4.0 | Clear | Regular | Cystic-based | Dilated | (–) |
| Saito H[20] | T | 11.5 | Clear | Regular | Mixed | / | (–) |
| Sakhi R[21] | B | 2.5 | Clear | Regular | Cystic-based, partially calcified | / | (–) |
| Fu LP[22] | B | 1.0 | Obscure | Irregular | Solid | Dilated | (–) |
| Zhang L[23] | T | 12.0 | Clear | Irregular | mixed | / | Lungs |
| This case | H | 6.0 | Clear | Regular | mixed | Dilated | (–) |

(–) = the event did not happen, / = not mentioned in the literature, B = body, CT = computed tomography, H = head, N = neck, T = tail, UC-OGC = carcinoma with osteoclast-like giant cells of pancreas.

review.[22] Hemorrhagic necrosis is common, and small calcifications are occasionally visible. The margin is usually clear (13/17 cases), and most tumors have a regular form that is round or oval like (10/17 cases). CECT usually shows a slight peripheral enhancement, internal solid parts in the arterial phase, and continuous enhancement at portal venous and delayed phases. We found the mass to be poorly developed in 3-dimensional revascularization, suggesting low blood supply. Tumors in the head and neck of the pancreas tend to cause dilatation of the pancreatic duct, which is characteristic of malignant tumors. UC-OGCs are nodular and promote marginal growth. Despite the large volume, tissue infiltration and lymph node metastases are not common in CT images.[5] Distant metastases may occur in advanced stages and are most common in the liver, lung, and bone.[8,12,15,16,23] Magnetic resonance (MR) T1-weighted imaging shows low signal intensity with or without patchy high signals. T2-weighted imaging shows a high-intensity central cystic portion with low-intensity septa and peripheral solid tissue.[11,16,17,23]$^{18}$F-fluorodeoxyglucose positron-emission tomography-CT revealed high uptake within the tumor.[22]

The UC-OGC of the pancreas needs to be differentiated from pancreatic MCT, SPN, and intraductal papillary mucinous neoplasm (IPMN). MCT is more common in older females and often occurs in the tail of the pancreas, with large cystic cavities, thick septa, and nodular protuberances in the mass. Image identification is difficult, and the pathology shows ovarian-type stroma.[16,23] SPN is more common in young women and usually manifests as a solid-based, soft texture mass without pancreatic duct expansion. SPN is a borderline tumor with good prognosis, and local infiltration or distant metastases are extremely rare.[26] IPMN is more common in older men and often occurs in the head of the pancreas and may cause jaundice. The mass is connected to the pancreatic duct.[16]

In conclusion, UC-OGC of the pancreas is a rare pancreatic undifferentiated carcinoma with a complex tissue origin. It is more common in elderly female patient, and about 50% of patients have elevated CA199. The disease progresses rapidly; however, there are still reports of postoperative survival for more than 6 years. Surgery combined with chemotherapy is effective. It is more common in the body and tail of the pancreas and is usually found as large cystic-solid mass with a clear boundary. Tumors in the head or neck of the pancreas tend to cause dilatation of the pancreatic duct. CECT reveals slight enhancement of the solid parts. CT is a sensitive imaging method for detecting the neoplasm, and histologic examination can confirm the diagnosis.

## Author contributions

**Conceptualization:** Yun-lei Guo.
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**Methodology:** Yun-lei Guo.
**Project administration:** Li-tao Ruan.
**Resources:** Qiu-ping Wang, Jie Lian.
**Supervision:** Li-tao Ruan.
**Writing – original draft:** Yun-lei Guo.
**Writing – review & editing:** Li-tao Ruan.

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