

Borderline-resectable Undifferentiated Carcinoma with Osteoclast-like Giant Cells of the Pancreas: upfront Surgery or Neoadjuvant Chemotherapy?

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ABSTRACT

Undifferentiated carcinoma with osteoclast-like giant cells (UDC-OGC) of the pancreas is an extremely rare entity, thus an obvious discrepancy regarding their treatment approach exists in the current literature. A 52-year female patient with a two-weeks history of jaundice was diagnosed as borderline-resectable pancreatic mass located in the uncinate process of a size of 5×4 cm. Pancreaticoduodenectomy (PD) with partial portal vein resection was successfully performed following neoadjuvant chemotherapy (NACT). The pathology was interpreted as UDC-OGC without lymph node involvement. Considering their aggressive behavior, NACT followed by surgery seems to be a good option in case of borderline-resectable UDC-OGC.

Key Words: Neoadjuvant chemotherapy, Pancreatic neoplasms, Undifferentiated carcinoma, giant cells, Pancreaticoduodenectomy.

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INTRODUCTION

Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGC) represents less than 1% of pancreatic malignancies.^{1,2} UC-OGC is composed of 2 cellular components: the multinucleated osteoclast-like giant cells and ovoid-to-spindle-shaped mononuclear cells originating in ductal adenocarcinomas.^{3,4} This combination causes the tumor to be more aggressive than plain adenocarcinoma. However, the prognosis is controversial due to its low incidence with less than 100 reported cases to date.¹ Therefore, contributing every new insight about UC-OGC is essential for further elucidating its clinical aspects, prognosis, and treatment options. We present the first case of borderline-resectable UC-OGC located in the uncinate process of the pancreas treated by neoadjuvant chemotherapy (NACT) followed by pancreaticoduodenectomy (PD).

CASE REPORT

A 52-year female patient with a two-week history of jaundice and whole-body itching was admitted to our clinic. She also experienced 5 kg weight loss over the past three months. Her medical and family history was unremarkable.

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Figure 1: Computed tomography findings of the tumor. (A) Imaging of the tumor before neoadjuvant treatment, invasion of portal vein marked with arrow. (B) Imaging of the tumor after neoadjuvant treatment, down-sizing marked with arrow.

On physical examination, her sclerae and skin were icteric, and she had itching scars on her abdomen. She had no fever and palpable mass or lymph nodes. Her laboratory parameters and imaging studies were studied to make differential diagnosis of jaundice.

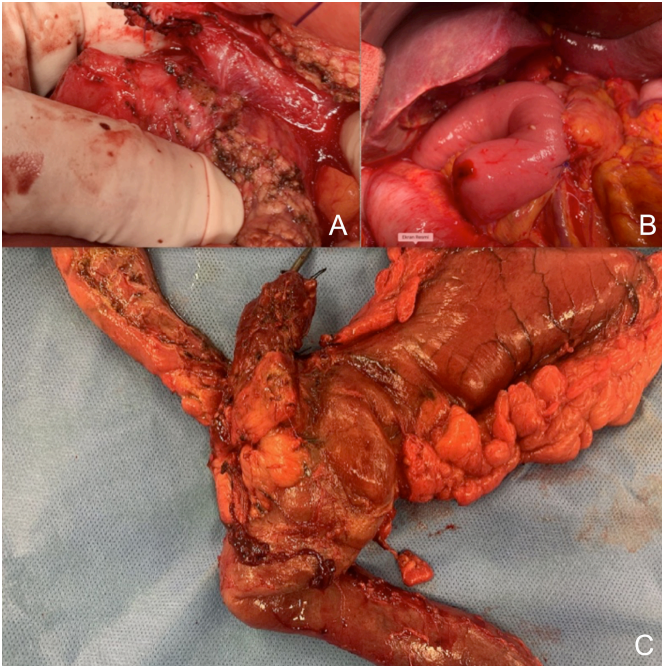


Figure 2: Intraoperative view of the mass. (A) The mass abutting with portal vein. (B) Completed reconstruction of the pancreatic duct with jejunal loop. (C) Pancreatoduodenectomy specimen (the mass marked with arrow).

The initial laboratory parameters revealed: Aspartate aminotransferase (AST): 143 U/L, Alanine aminotransferase (ALT): 293 U/L, Alkaline phosphatase (ALP): 502 u/L, Gama-glutamyl-transferase (GGT): 769 U/L, total bilirubin: 9.03 mg/dL, and direct bilirubin: 5.31 mg/dL. Tumor markers including carcinoembryonic antigen (CEA): 4.4 ng/ml, carbohydrate antigen 19.9 (CA 19.9): 0.8 U/ml, and carbohydrate antigen 125 (CA-125): 19.1 U/ml were in the normal range. All hepatitis markers were normal. Abdominal ultrasonography showed a hydroptic gallbladder with a dilated common bile duct at a diameter of 13 cm and a mixed cystic and solid 5×4 cm mass located in the head of the pancreas. Triphasic abdominal computed tomography (CT) demonstrated a 5×4 cm irregular solid mass with a cystic component located in the uncinate process of the pancreas compatible with mucinous cystic neoplasm. In addition, the mass had invaded the portal vein (PV) for 180°, and the superior mesenteric vein (SMV) was partially invaded less than 90°. Superior mesenteric artery (SMA) and common hepatic artery (CHA) were not invaded. Positron emission tomography (PET-CT) confirmed the pancreatic mass (suv-max: 3.8); however, no distant metastases were detected. Although endoscopic ultrasonography (EUS)/fine-needle aspiration biopsy (FNA) is preferable to CT-guided FNA, the biopsy was taken by CT-guided FNA due to the unavailability of EUS at that time. The biopsy was interpreted as pancreatic adenocarcinoma. These results were assessed by the multidisciplinary team at the oncology council. The mass was accepted as borderline-resectable pancreatic tumor. According to National Comprehensive Cancer Network (NCCN) guidelines, NACT (modified FOLFIRINOX (5-FU, oxaliplatin, leucovorin and irinotecan for 3 months) was planned by

medical oncology. In order to avoid cholangitis during the treatment period, a 7-Fr pigtail biliary stent was placed via endoscopic retrograde cholangiopancreatography (ERCP).

The patient's course was uneventful during NACT period. Two weeks after accomplishing the NACT, the patient was re-evaluated. CT demonstrated that the mass was significantly downstaged. The mass remained localized at the uncinate process of the pancreas; however, it was slightly invading PV less than 90°. There were no signs of invasion of SMV, SMA, CHA, or distant metastases (Figure 1). A written informed consent concerning the risks of the operation, as well as publication rights, was taken from the patient. On exploration, the tumor had partially invaded along the right lateral wall of the PV for about 2-cm. PD with partial PV resection was successfully performed. PV was repaired with a continuous 4/0 polypropylene suture. The surgery was completed in 7-hours without any intra-operative complications (Figure 2). The postoperative course was uneventful. The patient was discharged from the hospital on postoperative day 8. The patient was disease-free without any symptoms 20 months following surgery.

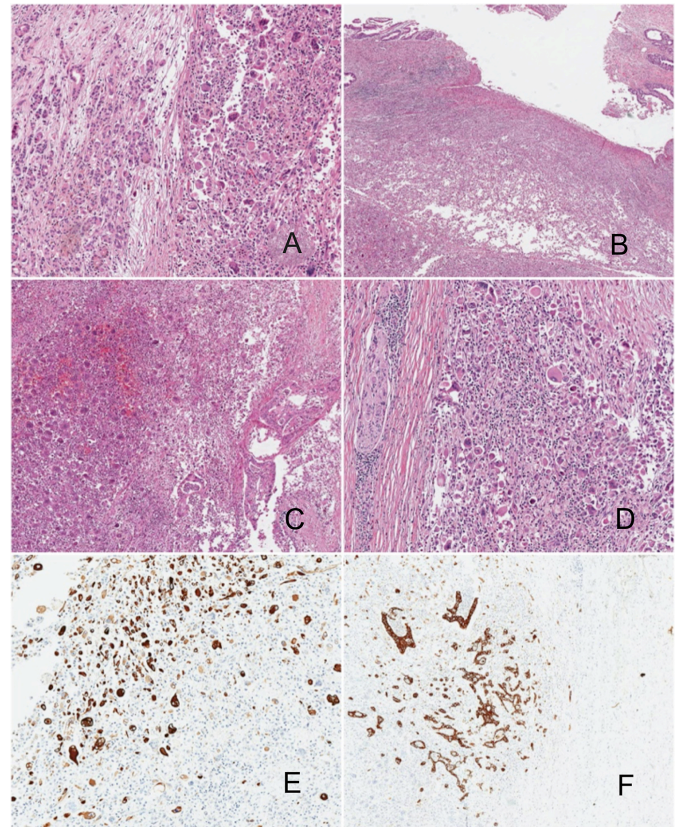


Figure 3: Histopathologic examination of the specimen. (A) Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGC) and native pancreatic tissue (HE, ×10). (B) CBD involvement. (HE, ×2) (C) UC-OGC associated with conventional adenocarcinoma (HE, ×4) (D) Perineural invasion of the tumor (HE, ×10) (E) Immunoreactivity with CK-AE1 and AE3 of UDC-OGD. (panCK, ×10) (F) UDC-OGD associated with conventional adenocarcinoma. (panCK, ×4).
Abb: CBD = Common bile duct.

The final pathology report was interpreted as UDC-OGC (80% component) associated with pancreatic ductal adenocarci-

noma (PDA) (20% component) (Figure 3). The tumour was arising from uncinate process with a dimension of 2.5×2 cm without lymph node involvement (0/13). The surgical margins were free (1 cm).

DISCUSSION

UC-OGC is an extremely rare histopathologic type that comprises <1% of all pancreatic carcinomas. Considering the few reports regarding UC-OGC in the current literature, a significant clinical discrepancy exists regarding treatment approaches and the prognosis of the tumor. Therefore, it is important to contribute such rare cases to literature to expand knowledge of the clinical aspects and prognosis of UC-OGC.

UC-OGC is usually detected in the elderly with a wide age range from 50 to 72 years, with an equal male to female ratio⁵. The demographic features of this patient were compatible with the previously reported patients.

Despite advances in imaging studies, the accurate diagnosis of pancreatic lesions remains a diagnostic dilemma. However, UC-OGC has a distinct appearance on CT and EUS which may help to differentiate it from conventional pancreatic carcinomas. Unlike the uniformly hypoechogenic appearance of PDAs, UC-OGC possesses a typical appearance as heterogeneous with both well-demarcated hyper and hypoechoic areas, closely located within the same lesion.^{6,7} On CT, it appears as a heterogeneous cystic mass with hemorrhage and necrosis which is possibly related to the rapid growth of tumour cells and increased inflammatory reaction. However, this appearance resembles cystic neoplasms or pseudocysts of the pancreas which may lead to misdiagnosis as we experienced. Our initial diagnosis was mucinous cystic neoplasm of the pancreas even though the biopsy had not confirmed us. Furthermore, preoperative biopsy failed to diagnose UC-OGC, as well.

In fact, UC-OGC is a pathologic diagnosis. The clinical manifestations are mainly associated with the localisation of the mass as in ordinary pancreatic carcinomas. Clinical symptoms vary from asymptomatic to obstructive jaundice.^{3,8} Unlike this case, the body and the tail of the pancreas are the most common reported localisations of UC-OGC.^{1,3} Unfortunately, the insidious onset of clinical symptoms is typical at these locations even in routine cases, thus the patient is usually diagnosed at a locally advanced or terminal stage. On the other hand, UC-OGC located at the head or uncinate process of the pancreas can be detected when the tumor size is smaller as compared to other locations because of relatively early clinical presentations such as, unexplained weight loss, anemia, and painless jaundice, as in this case. Therefore, surgical removal of the lesion with an early diagnosis may contribute to a relatively favorable prognosis when the mass is located in the head or uncinate process of the pancreas, regardless of histopathology.

PD with a 1 cm free surgical margin is the optimal treatment for pancreatic carcinomas located in the head of the pancreas. However, optimal timing for surgery of borderline pancreatic tumor is still a subject of investigation. Unfortunately, upfront

surgery usually results in failure of R0 resection or major vascular resections that can lead to high postoperative morbidity and mortality, high recurrence rates, and decreased survival time. In recent years, NACT has been found to be associated with promising results in up to 60% of patients in terms of downstaging, thereby enabling R0 resection of the tumor without major vascular or adjacent organ resections.⁹ Furthermore, it also enables the selection of patients with favorable tumor biology who will benefit from radical resections. Although we failed to reveal exact histopathology before surgery, we incidentally revealed a moderate response of UC-OGC to NACT. Considering the discrepancy in the treatment approach of UC-OGC in the current literature, this outcome is valuable.

Because of the rarity and uncertain nature of the UC-OGC, the prognosis and the survival of patients are controversial. Some authors consider UC-OGC as more aggressive than PDAs, whereas the others do not.^{1,3,8,10} Palliative resection does not improve disease status or survival. However, favorable long disease-free survival is expected if proper surgery is performed with optimal timing.

In conclusion, we reported a pancreatic cancer patient with UDC-OGC who was treated with NACT before resection. We are aware that it is difficult to draw a definitive conclusion from a single case, but we suggest that NACT followed by surgery seems to be a good option in case of borderline-resectable UDC-OGC. Further research is needed to support our conclusion.

PATIENT'S CONSENT:

A written informed consent was obtained for publishing the data.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

AS: writing the manuscript and literature research.

EA: Acquisition of data.

All authors approved the final version of the manuscript to be published.

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