CASE REPORT

Lib Oncol. 2022;50(1):39–43
doi: 10.20471/LO.2022.50.01.07

UNDIFFERENTIATED CARCINOMA OF THE PANCREAS WITH OSTEOCLAST-LIKE GIANT CELLS: REPORT OF TWO CASES

KRISTINA VNUK[1], IVANA PAVIĆ[2], DANIJEL BRLETIĆ[3], MARIO ZOVAK[3] and BOŽO KRUŠLIN[2,4]

[1]Department of Pathology and Cytology, Zabok General Hospital, Zabok, Croatia;
[2]*Ljudevit Jurak* Department of Pathology and Cytology,
Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[3]Department of Surgery, Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[4]Department of Pathology, School of Medicine, University Zagreb, Zagreb, Croatia

Summary

We present two cases of very uncommon, undifferentiated pancreatic carcinoma (UPC) with osteoclastic cells. First case is a 52-year-old female with no previous health issues presented with unintentional, significant weight loss, not specified epigastric pain and microcytic anemia. After clinical examination the pancreatic neoplasm was found. Histopathological analysis suggested UPC. Four years later, MSCT scan discovered solid mass in lung and after histopathological analysis metastasis of UPC. Second case is a 72-year-old male with past medical history of diabetes type 2 and hypothyreosis who presented with an epigastric pain. Clinical diagnosis was pancreatic neoplasm. After histopathological examination undifferentiated pancreatic carcinoma with osteoclastic giant cells was diagnosed.

KEYWORDS: *pancreatic neoplasms, adenocarcinoma, osteoclasts, giant cells*

INTRODUCTION

Undifferentiated pancreatic carcinoma (UPC) with osteoclastic giant cells is an exceedingly rare exocrine tumor, that accounts for less than 1% of all pancreatic malignancies. Histologically, it resembles a giant cell tumor of the bone containing osteoclastic-like multi-nucleated cells and mononuclear cells(1). In 2019, the World Health Organization classified these tumors as variants of pancreatic ductal adenocarcinoma under the heading *undifferentiated carcinoma with osteoclastic giant cells* and they have been identified as fundamentally epithelial-derived tumors with mesenchymal differentiation(2). The mean age of patients with an undifferentiated carcinoma with osteoclastic-like giant cells is 62 years, but there is a wide age range (32 – 93 years). It occurs mostly in the pancreas but rarely also in the bile ducts and other organs. It contains three cell types: non-neoplastic osteoclast-like multinucleated giant cells, a mononuclear histiocytic component, and the neoplastic mononuclear cell component. The clinical behaviour of this tumor type appears to be unpredictable, but many behave unexpectedly well and in fact a substantial proportion of patients are alive after many years(3). We present two cases of undifferentiated pancreatic carcinoma with osteoclastic giant cells.

***Coresponding author**: Kristina Vnuk, Department of Pathology and Cytology, Zabok General Hospital, Bračak 8, 49210, Bračak, Zabok, Croatia. e-mail: kristina.vnuk11@gmail.com*

CASE REPORTS

First case is a 52-year-old female presented with unintentional weight loss of 7 kg, periodically not specified epigastric pain and microcytic anemia. Tumor markers were negative. Endoscopic ul-

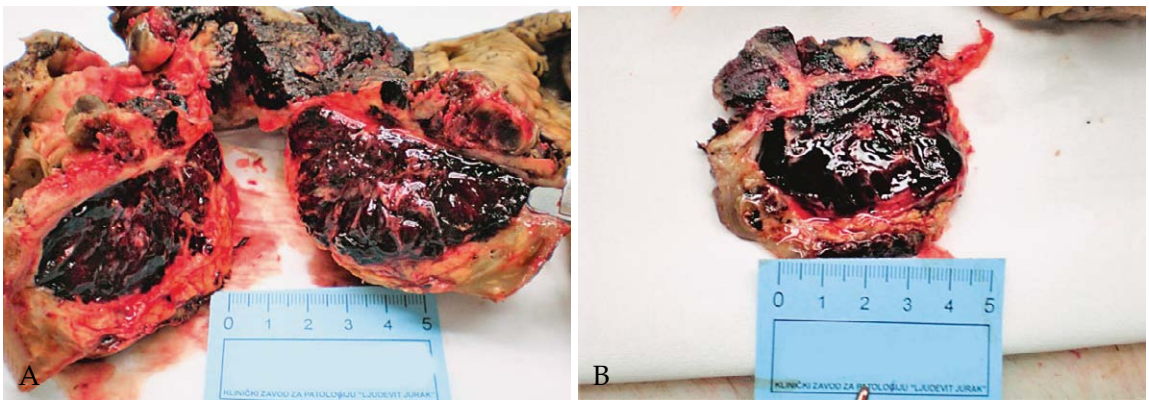

Figure 1. Gross appearance of undifferentiated pancreatic carcinoma with osteoclastic cells (A, B).

trasound (EUS) revealed a mass invading duodenum. Computed tomography (CT) scan of the abdomen showed a 5 cm mass in the pancreatic head suspicious for malignancy. EUS-guided needle biopsy demonstrated partly necrotic tissue with atypical hyperchromatic pleomorphic cells and giant multinuclear cells which expressed positive reaction for vimentin and focally for cytokeratin.

The patient underwent duodenopancreatectomy with partial gastrectomy and cholecystectomy. The specimen of tumor was 6 cm in largest diameter, brown, well-circumscribed, infiltrating small intestine (Figure 1. A, B). Microscopic examination revealed the tumor composed of solid nests of atypical, poorly differentiated, pleomorphic, spindle cells with high mitotic activity and multinucleated osteoclast-like giant cells with a large areas of hemorrhage. The tumor invaded small intestine and one lymph node. The diagnosis of undifferentiated pancreatic carcinoma with osteoclastic giant cells was established.

Six month later, ultrasound and CT scan discovered a 5 cm cystic mass in the tail of pancreas. Cytological findings showed poorly differentiated carcinoma. Patient was treated with chemotherapy with gemcitabin.

Four years later, MSCT scan discovered solid expansive mass 2,1 cm in upper left lung. Patient underwent surgery and pathological findings revealed metastasis of undifferentiated pancreatic carcinoma with osteoclastic giant cells.

Patient had an oncology appointment after which we lost from follow-up.

By inspecting Croatian National Cancer Registry of Croatian Institute of Public Health we learned that patient had died a year later.

Second case is a 72-year-old male with a past medical history of diabetes type 2 and hypothyreosis who was presented to an outside hospital with an epigastric pain clinically suspicious for pancreatic neoplasm.

The patient underwent pancreatectomy with splenectomy in our hospital. The tumor was localized in pancreatic head, measuring 5 cm in diameter, necrotic and well-circumscribed. Microscopically, the tumor was composed of solid nests of atypical, poorly differentiated, pleomorphic, spindle cells with high mitotic activity and multinucleated osteoclast-like giant cells (Figure 2. A, B). An extensive perineural invasion was present in the tumor while resection margins and nodal metastases were negative. Immunohistochemistry showed positive reaction to CK7, panCK and vimentin, while p53, chromogranin A, synaptophysin and e-cadherin were negative (Figure 2. C, D, E). Histological and immunohistochemical analysis confirmed undifferentiated pancreatic carcinoma with osteoclastic giant cells.

After the surgery we lost from follow-up.

By inspecting Croatian National Cancer Registry of Croatian Institute of Public Health we learned that patient had died four months after the surgery.

DISCUSSION

Pancreatic neoplasms are relatively common gastrointestinal malignancies, in which pancreatic ductal adenocarcinoma (PDAC) is second most common tumor. Undifferentiated pancreatic carcinoma (UPC) belongs into group of uncommon

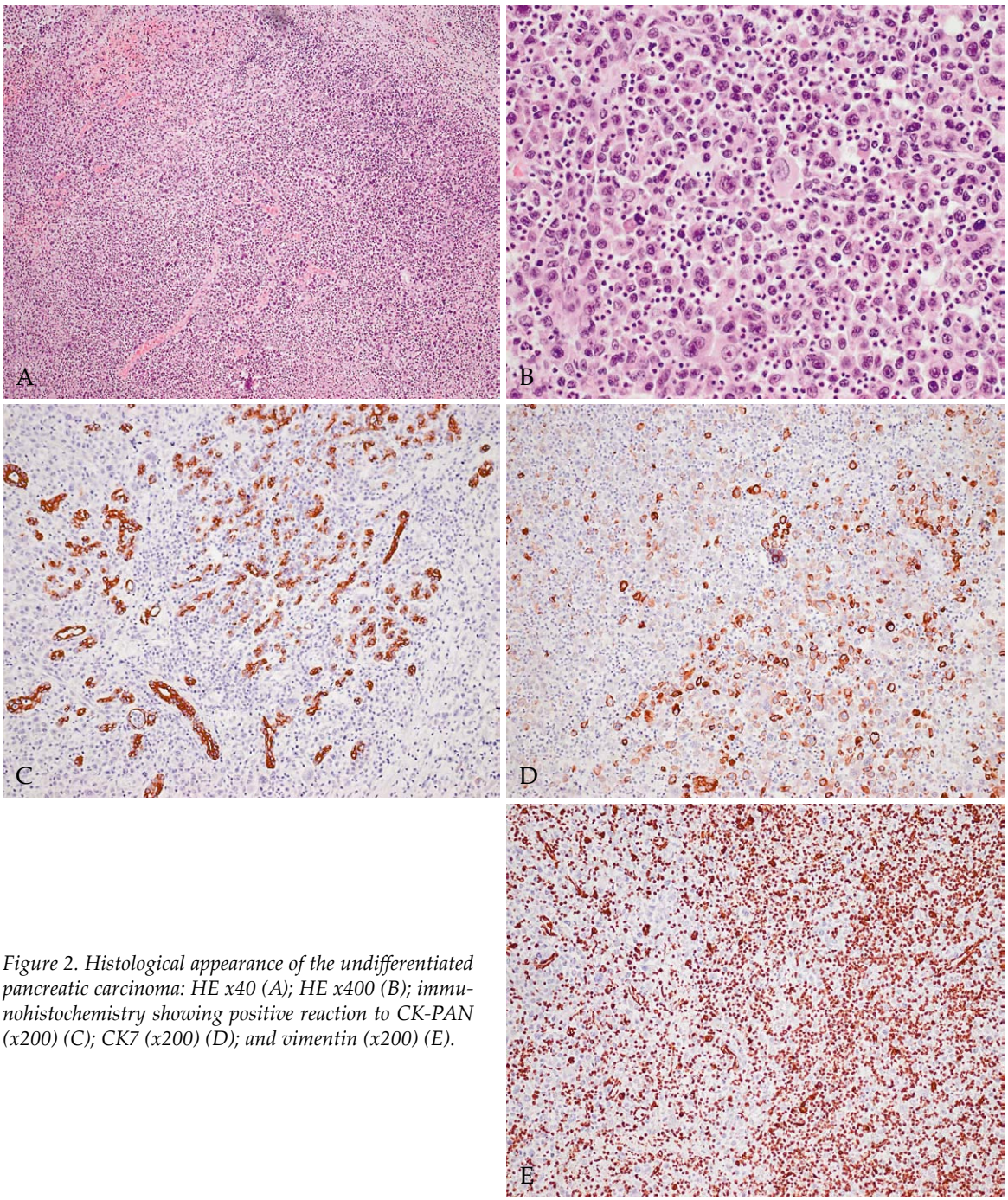

Figure 2. Histological appearance of the undifferentiated pancreatic carcinoma: HE x40 (A); HE x400 (B); immunohistochemistry showing positive reaction to CK-PAN (x200) (C); CK7 (x200) (D); and vimentin (x200) (E).

pancreatic cancer sub-types. In 1968, a first case of undifferentiated carcinoma with osteoclast-like giant cells was described(1). UPCs resemble benign-appearing giant cell tumors of bone, and contain osteoclast-like multinucleated cells and two types of mononuclear cells(4). The multinucleated cells expressing histiocytic markers and lacking epithelial differentiation are often found in areas adjacent to haemorrhage or necrosis. The mononuclear histiocytic component may be inconspicuous by routine histology but is abundantly demonstrated by immunohistochemistry for

histiocytic markers. The neoplastic mononuclear cells vary from spindle-shaped to epitheloid, sometimes being very large and pleomorphic usually are non-cohesive and may be found within the cytoplasm of the osteoclast-like giant cells(3). The histogenesis is controversial suggesting both epithelial and mesenchymal origin. The positive immunohistochemical staining for CEA and keratin favor epithelial derivation, whereas CD68 and vimentin positivity and cytokeratin negativity favor mesenchymal origin(4). There are few case reports suggesting the origin of those tumors; from acinar cells, mesenchymal cells, undifferentiated precursors or stem cells. However, the World Health Organization in classification 2010 established that UPC originates from ductal epithelial cells being one of the pancreatic ductal adenocarcinoma variants. A histopathological analysis, showing coexistence of adenocarcinoma and undifferentiated carcinoma component positive for vimentin, suggests the tumor originate from pancreatic ductal cells with mesenchymal differentiation(1).

UPC with osteoclast-like giant cells clinical presentation is nonspecific, ranging from abdominal pain, a palpable mass, weight loss, etc., to CA 19-9 tumor markers being increased in up to half of the cases. This tumor is usually large, moderately to highly hypervascular, exophytic in which large areas of intratumoral necrosis and hemorrhage are found(5). It has predilection toward males with an average age of 60 years and it is more likely to occur within the body and the tail of the pancreas(6,7).

This tumor has a less aggressive course with slow metastasis and lymph node spread having with prognosis in comparison to pancreatic ductal adenocarcinoma. Distant metastasis usually occur in an advanced stage and most commonly in liver, lung and bone. The interval to death or disease progression ranges from 4 months to 10 years from initial diagnosis(1,4).

Surgical en-bloc resection is considered the first line of treatment, while the role of adjuvant therapy in unclear. Considering the radio-sensitivity of giant cell tumors of the bone, there is a theoretical benefit of abdominal radiotherapy for this tumor as well. Given the epithelial origin of the mononuclear neoplastic cells, it may be reasonable to consider agents such as gemcitabine in cases of disseminated disease or incomplete resection(4).

CONCLUSION

Undifferentiated pancreatic carcinoma with osteoclastic giant cells is a very rare tumor type with unique pathological characteristics. En-bloc resection is the first line of treatment. The role of adjuvant and neo-adjuvant chemotherapy or radiotherapy has not been clearly established. Long term follow-up of patients with these rare tumors is essential in order to compile more information to help guide treatment.

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Sažetak

NEDIFERENCIRANI KARCINOM GUŠTERAČE S ORIJAŠKIM STANICAMA TIPA OSTEOKLASTA: PRIKAZ DVA SLUČAJA

K. Vnuk, I. Pavić, D. Brletić, M. Zovak, B. Krušlin

Predstavljamo dva slučaja nediferenciranog karcinoma gušterače s orijaškim stanicama tipa osteoklasta. Prvi slučaj je 52-godišnjakinja bez prethodnih zdravstvenih problema s nenamjernim, značajnim gubitkom težine, nespecifičnom boli u epigastriju i mikrocitnom anemijom. Nakon kliničog pregleda pronađena je novotvorina gušterače. Patohistološka analiza je ustanovila nediferencirani karcinom gušterače s orijaškim stanicama tipa osteoklasta. Četiri godine kasnije, MSCT-om je otkrivena slidna lezija u plućima i nakon patohistološke analize ustaovljena je metastaza. Drugi slučaj je 72-godišnji muškarac s dijabetesom tip 2 i hipotireozom u anamnezi koji se žalio na bol u epigastriju. Klinička dijagnoza je bila neoplazma gušterače, a nakon patohistološke analize utvrđen je nediferencirani karcinom gušterače s orijaškim stanicama tipa osteoklasta.

KLJUČNE RIJEČI: *novotvorina gušterače, adenokarcinom, osteoklasti, orijaške stanice*