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

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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.

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-
ultrasound (EUS) revealed a mass invading duode-
num. Computed tomography (CT) scan of the ab-
domen showed a 5 cm mass in the pancreatic head
susicious for malignancy. EUS-guided needle bi-
opsy demonstrated partly necrotic tissue with
atypical hyperchromatic pleomorphic cells and gi-
ant multinuclear cells which expressed positive re-
aaction for vimentin and focally for cytokeratin.

The patient underwent duodenopancreatec-
tomy with partial gastrectomy and cholecystecto-
my. The specimen of tumor was 6 cm in largest
diameter, brown, well-circumscribed, infiltrating
small intestine (Figure 1. A, B). Microscopic exam-
ination revealed the tumor composed of solid
ests of atypical, poorly differentiated, pleomor-
phic, 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 diagno-
sis of undifferentiated pancreatic carcinoma with
osteoclastic giant cells was established.

Six month later, ultrasound and CT scan dis-
covered a 5 cm cystic mass in the tail of pancreas.
Cytological findings showed poorly differentiated
carcinoma. Patient was treated with chemothera-
py with gemcitabatin.

Four years later, MSCT scan discovered solid
expansive mass 2,1 cm in upper left lung. Patient
underwent surgery and pathological findings re-
vealed 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 Reg-
istry 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 hypothy-
reosis who was presented to an outside hospital
with an epigastric pain clinically suspicious for
pancreatic neoplasm.

The patient underwent pancreactomy with
splenectomy in our hospital. The tumor was local-
ized in pancreatic head, measuring 5 cm in diam-
eter, necrotic and well-circumscribed. Microscopi-
cally, the tumor was composed of solid nests of
atypical, poorly differentiated, pleomorphic, spin-
dle cells with high mitotic activity and multinucle-
ated osteoclast-like giant cells (Figure 2. A, B). An
extensive perineural invasion was present in the
tumor while resection margins and nodal metas-
tases were negative. Immunohistochemistry
showed positive reaction to CK7, panCK and vi-
mentin, while p53, chromogranin A, synaptophy-
sin and e-cadherin were negative (Figure 2. C, D,
E). Histological and immunohistochemical analy-
sis confirmed undifferentiated pancreatic carcino-
ma with osteoclastic giant cells.

After the surgery we lost from follow-up.

By inspecting Croatian National Cancer Reg-
istry 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 car-
cinoma (UPC) belongs into group of uncommon
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 is 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.

REFERENCES

Sažetak

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

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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 kliničkog 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 stanicce