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Long Progression-free-survival Pancreatic Carcinosarcoma Under Gemcitabine-nabpaclitaxel First Line Chemotherapy

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Introduction

Carcinosarcoma of the pancreas is a rare entity with short case series reported in the literature. Diagnosis is established by immunohistochemical examination including both carcinomatous and sarcomatous components. Prognosis is usually limited to 6-9 months life expectancy. Standard chemotherapy regimen is not well defined.

We present a case of pancreatic carcinosarcoma with long-time progression-free-survival under first line chemotherapy treatment with gemcitabine-nabpaclitaxel combination. Tumor histopathological and clinical characteristics are reviewed.

Keywords: Carcinosarcoma; Pancreas; Gemcitabine-Nabpaclitaxel; Cytokeratin; Vimentin

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Clinical case.

A 76-year-old woman with medical history of hypertension and dyslipidaemia consulted in August 2018 due to 3 months mesogastric abdominal pain. She did not refer any other symptom. She was admitted to Gastroenterology department to be studied.

Her performance (Eastern Cooperative Group, ECOG) and nutritional status were not altered. Her physical examination did not reveal any alteration. Her body mass index was 27,3. Complete blood test did not show any alteration, including normal cancer antigen 19.9 (Ca-19.9).

Abdominal CT scan revealed a heterogeneous mass at the pancreatic head-body union (Figures

1 and 2). Its size was 39x50x48 mm and caused common bile duct dilation and pancreatic body and tale atrophy. It did not contact with arterial vessels, but there was important infiltration of the porto-mesenteric confluence veins, which defined a not resectable tumor.

The patient underwent endoscopic ultrasound and fine-needle aspiration was performed. Histology was diagnostic for carcinosarcoma: fusocellular proliferation of atypical cells with intimate admixture of carcinomatous and sarcomatous components: positive immunochemistry for AE1 and AE3 cytokeratin, vimentin and actin, and Mib-1 proliferative index greater than 50% (Figures 3, 4, 5, 6 and 7).

Staging workup by body CT scan was negative for metastasis. Following the American Joint Committee on Cancer (AJCC) staging system, she was finally diagnosed of an unresectable stage IIA (cT3N0M0) pancreatic carcinosarcoma due to venous vascular affection.

The patient was assessed by Medical Oncology. It was not found homogeneity on chemotherapy options on a wide literature search focused on this rare entity. It was decided to treat following ductal adenocarcinomas usual chemotherapy regimens.

The patient started on September 2018 first line chemotherapy for advanced and unresectable pancreatic carcinosarcoma with gemcitabine 1000 mg/m^2 and nabpaclitaxel 125 mg/m^2 combination. It was administrated every two weeks with a 20% dose reduction due to her advanced age. She experienced good tolerance to first cycles, being most relevant toxicities grade I fatigue, nausea and emesis.

First follow-up CT scan after three months of treatment (December 2018) showed partial response (Figures 8 and 9). The current tumoral mass size was 31x27x38 mm, still presenting vascular compromise. The patient did not refer any other symptom than intermittent mild abdominal pain. Her performance and nutritional status were good and Ca-19.9 was not altered. Treatment with gemcitabine-nabpaclitaxel was continued.

Second follow-up CT scan after six months of treatment (March 2019) showed partial response. The current tumoral mass size was 29x24x30 mm, still presenting vascular compromise. Patient's abdominal pain had resolved. Ca-19.9 was not altered. Treatment with gemcitabine-nabpaclitaxel was continued.

Third follow-up CT scan after nine months of treatment (June 2019) was unfavourable. Tumoral mass size had increased and was 40x39x49 mm, and vascular compromise had worsened presenting inferior mesenteric vein partial thrombosis. CT scan also revealed incidental pulmonary thromboembolism. Her abdominal pain had returned, but she did not refer any respiratory symptom. Ca-19.9 was not elevated. Progression free survival under first line chemotherapy treatment was ten months (September 2018-June 2019).

Patient's performance and nutritional status were little altered but still good (ECOG 1), so it was decided to start second line chemotherapy treatment in July 2019. Oxaliplatin and capecitabine combination were provided every three weeks. Tolerance was not good, and the patient presented gastrointestinal grade II toxicity with diarrhoea, nausea and emesis, requiring some treatment interruptions and dose reduction.

First follow-up CT scan after three months of second line treatment (September 2019) was unfavourable. Tumoral mass size had increased, and Ca-19.9 was elevated to 66,6 U/ml. Performance status was still ECOG 1, so it was decided to start third line chemotherapy. 5-fluoracil and liposomal irinotecan combination was provided every two weeks.

After the second cycle, in October 2019, the patient presented important toxicity with grade III-IV gastrointestinal and haematological affection, requiring long hospital admission. It was decided to stop chemotherapy treatment and providing best supportive care by palliative care service.

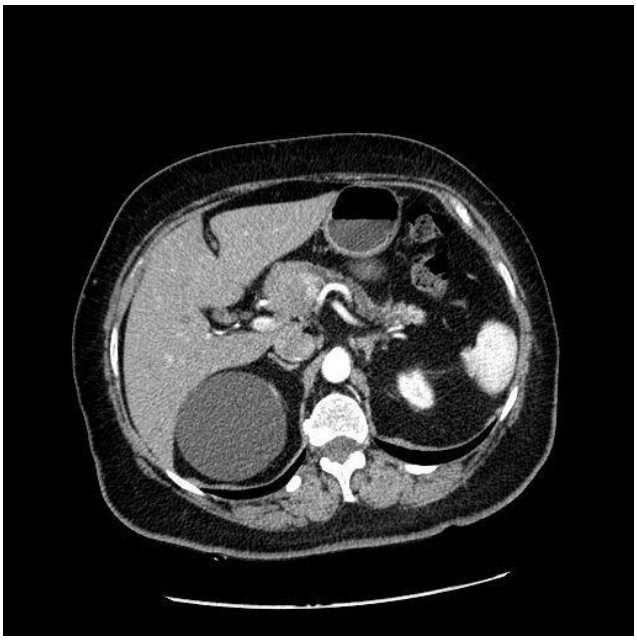

Figure 1. Diagnosis transverse plan abdominal CT scan image. It reveals a heterogeneous mass at the pancreatic head-body union. Its size is 39x50x48 mm. It causes common bile duct dilation and pancreatic body and tale atrophy. There is important infiltration of the porto-mesenteric confluence veins.

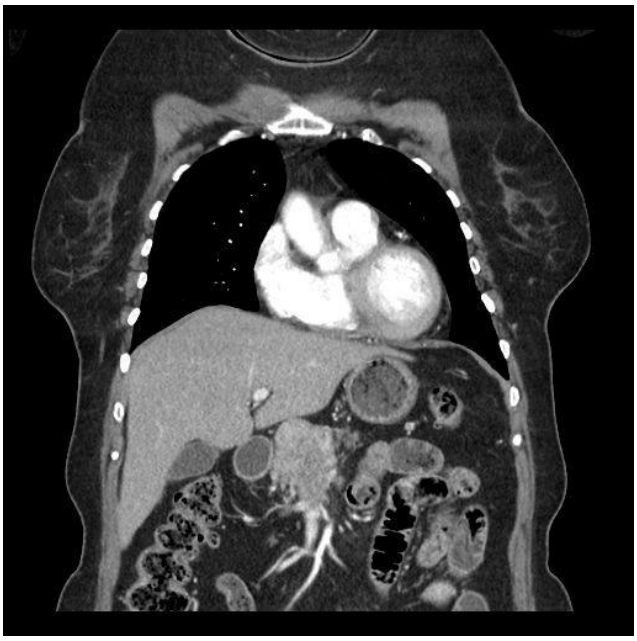

Figure 2. Diagnosis coronal plan abdominal CT scan image. It reveals a heterogeneous mass at the pancreatic head-body union.

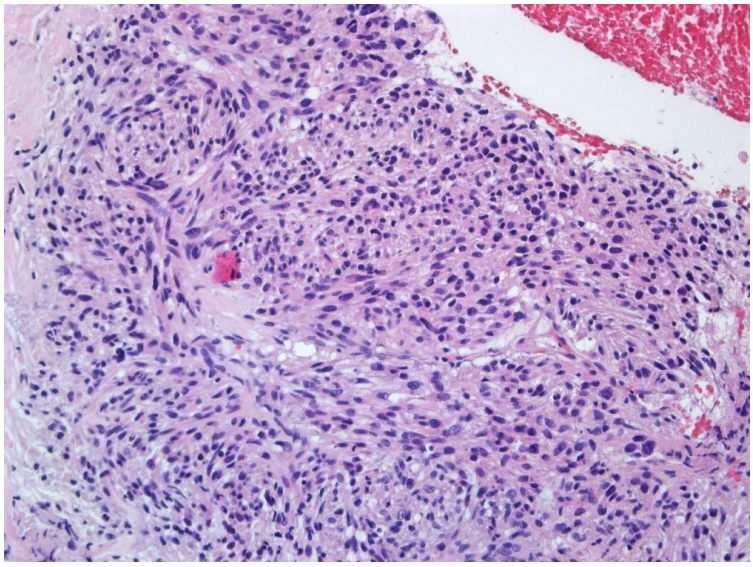

Figure 3. Hematoxylin-eosin fusocellular proliferation of atypical cells.

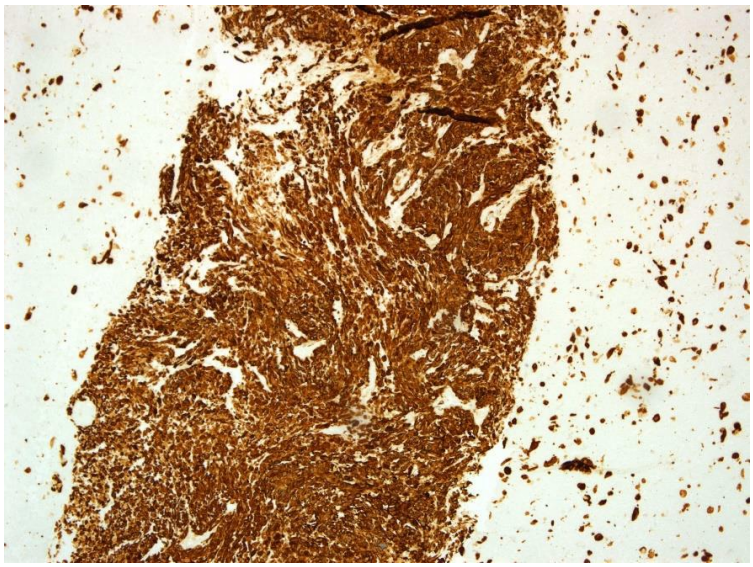

Figure 4. Positive immunochemistry for actin.

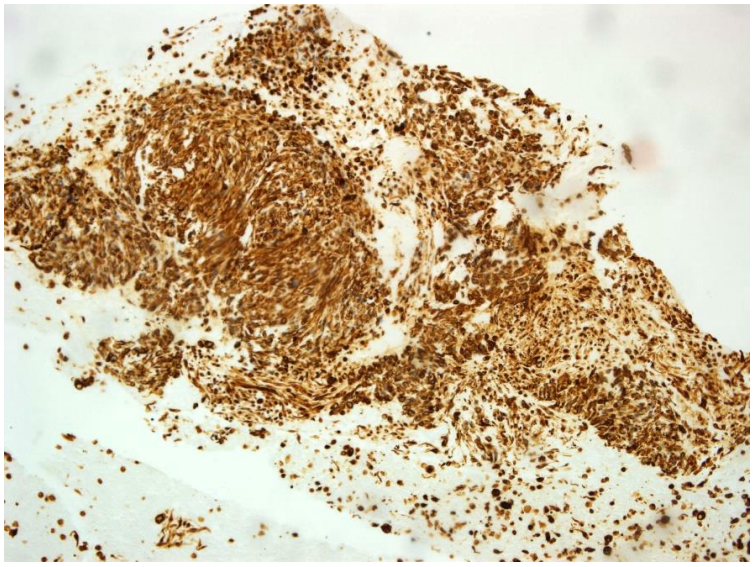

Figure 5. Positive immunochemistry for vimentin.

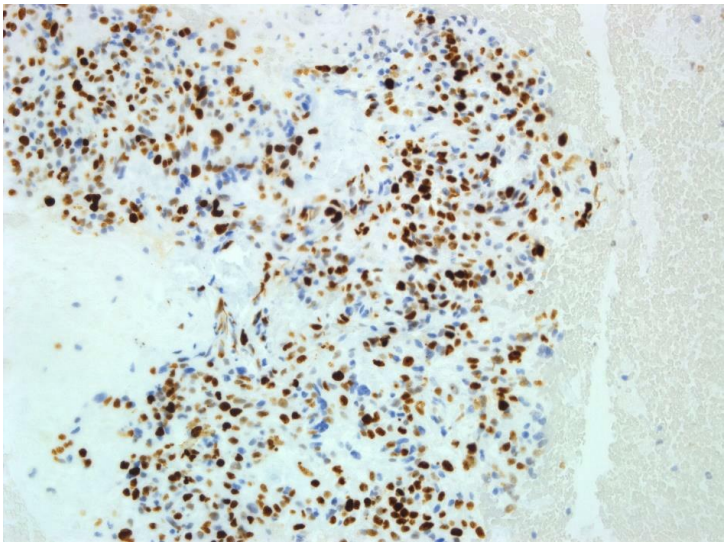

Figure 6. Mib-1 proliferative index greater than 50%.

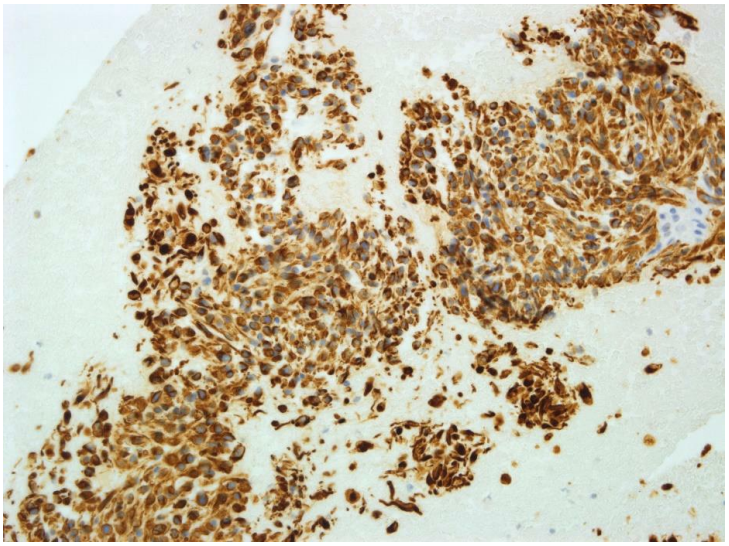

Figure 7. Positive immunochemistry for AE1 and AE3 cytokeratin.

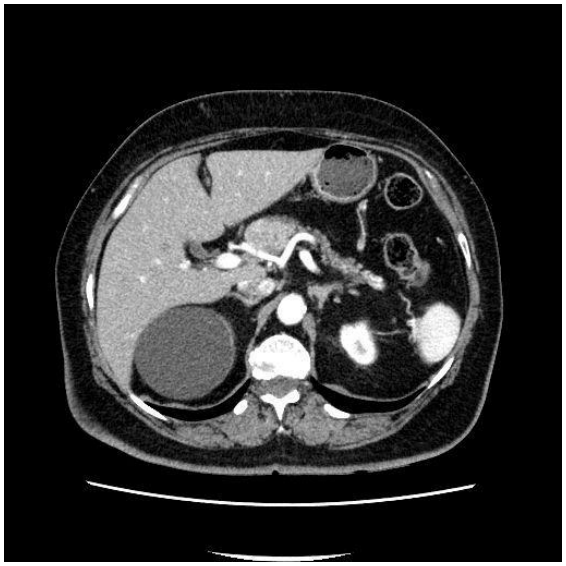

Figure 8. First follow-up transverse plan abdominal CT scan image. It reveals partial response with decreased tumoral mass size, still presenting vascular compromise.

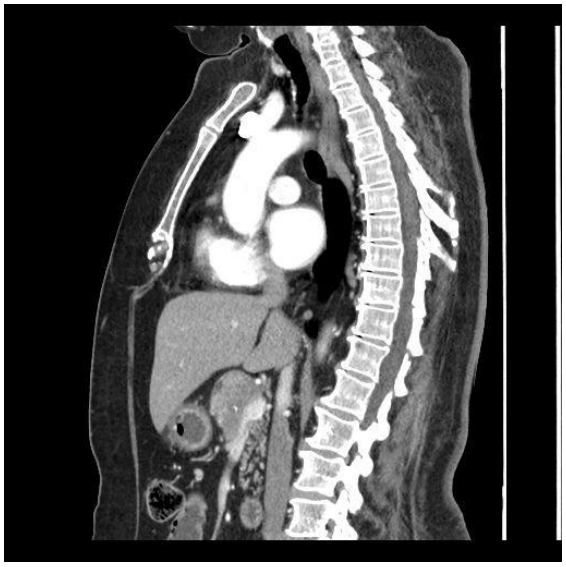

Figure 9. First follow-up sagittal plan abdominal CT scan image. It reveals partial response with decreased tumoral mass size, still presenting vascular compromise.

Discussion

Carcinosarcoma of the pancreas is a rare entity comprising a small subset of all pancreatic neoplasms. They are biphasic neoplasms consisting of malignant epithelial and mesenchymal components. Very few clinical data and treatment options have been reported in the literature. Prognosis is usually limited to several months after diagnosis [1, 2, 3, 4, 5, 6].

According to World Health Organization (WHO) classification it is classified together with sarcomatoid carcinoma and anaplastic giant cell carcinomas in undifferentiated (anaplastic) carcinoma of pancreas [7].

The concept of carcinosarcoma is a malignant neoplasm composed of an intimate admixture of carcinomatous and sarcomatous elements. Cases fulfilling these histopathological characteristics are rare, but their incidence is higher in other locations, predominantly located in the uterus [8, 9, 10, 11].

Immunohistochemical diagnosis is established by reactivity of the carcinomatous and sarcomatous elements to cytokeratin and vimentin, respectively. Carcinosarcomas must be differentiated from sarcomatoid carcinomas, which immunohistochemically show only cytokeratin reactivity and are therefore considered to be true carcinomas. They also have to be separated from epithelioid sarcomas which are defined as sarcomas as they lack cytokeratin reactivity but they do not contain two components [12].

The carcinomatous components are varied. Pancreatic ductal adenocarcinoma is the most commonly reported, followed by mucinous cystadenocarcinoma. There are also different sarcomatous elements, including spindle cell sarcoma, leiomyosarcoma, malignant fibrous histiocytoma and osteosarcoma.

The histogenesis of carcinosarcoma remains to be elucidated. Some hypotheses have been proposed [13, 14, 15, 16, 17, 18]:

- Collision theory. Tumors of different origin, carcinomatous and sarcomatous elements, arise independently but in close proximity.

- Conversion and combination theories. Mesenchymal (sarcomatous) component evolves from its epithelial (carcinomatous) counterparts from a monoclonal origin. This is probably the most accepted theory because most cases have identical DNA sequences in multiple genes, supporting that they derive from a single stem cell.

According to the literature, pancreatic carcinosarcoma is more common in elderly and women. The incidence at the head of pancreas is twice that of pancreatic body and tail. Most common

symptoms are abdominal pain, obstructive jaundice, anorexia, nausea and vomiting. Some of the most common signs are anemia, deep vein thrombosis, glucose abnormality and CA-19.9 elevation [19].

Radiology reveals that, compared to ductal adenocarcinoma, which represents its main differential diagnosis, pancreatic carcinosarcoma has more vascularity. On the other hand, it seldom presents perineural and vascular invasion, parenchyma atrophy, duct dilatation, and adjacent organs invasion. It easily metastasizes to the liver and peritoneum [20, 21].

The prognosis of carcinosarcoma of the pancreas is limited. Patients median survival time after diagnosis is 6-9 months. The primary cause of mortality is severe postoperative complications or peritoneum and liver metastasis.

Treatment options are similar to pancreatic carcinoma. Radical resection is the best option. Systemic chemotherapy is indicated for patients with distant metastasis or contraindication to surgery. It is known that chemotherapy, can alter the balance of tumor elements and may ultimately lead to progression of a single cell lineage. On the literature, most patients have been treated with gemcitabine monotherapy. Some others regimen in different case reports are: gemcitabine combined with raltitrexed, gemcitabine combined with doxorubicin, cisplatin, etc. [22, 23, 24].

Conclusion.

We present an unique case of unresectable pancreatic carcinosarcoma with 10 months progression free survival under gemcitabine-nabpaclitaxel first line chemotherapy. This is, as far as we are concerned, the longest progression free survival reported in this rare entity.

Case reports about uncommon neoplasms must be communicated in order to provide the first step of clinical evidence to those clinicians who approach them.

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