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Chemotherapy of pancreatic solid pseudopapillary carcinoma – A case report and a literature review

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ABSTRACT

Introduction: Solid pseudopapillary tumors of the pancreas are rare neoplasms of low malignant potential that affect mostly young women. With a free-margin surgical resection, the prognosis is usually excellent; however, in some cases, curative surgery cannot be performed due to the extent of the tumor mass and metastatic spread. Optimal therapeutic option in such cases remains elusive.
Case presentation: We analyze a case of a 36-year-old female patient treated with chemotherapy due to advanced stage of solid pseudopapillary tumors. Among a number of administered chemotherapeutic regimens – Folfox-4 (folinic acid + fluorouracil + oxaliplatin) gave particularly good results and was well tolerated, with few adverse effects. Partial response was achieved and significant improvement in the patient's life quality was reported.
Discussion: Solid pseudopapillary tumors of the pancreas present slow growth pattern and an excellent prognosis in most cases. Different approaches are needed for patients with multiple, unresectable metastases and oxaliplatin based chemotherapy should be considered as effective and safe therapeutic option.
Conclusion: The absence of proper guidelines for unresectable SPTs and second-line chemotherapy for gemcitabine-refractory patients with metastatic pancreatic pseudopapillary tumors emphasizes the importance of seizing new therapeutic options.

1. Introduction

Solid pseudopapillary tumors (SPTs) of the pancreas are rare neoplasms with a low malignant potential. First described by Franz in 1959, they comprise 1–2% of all pancreatic tumors [1,2]. Most of these tumors have been reported in the last 10 years, which probably reflects the increasing awareness and the widespread usage of imaging techniques [3].

SPTs develop predominantly in young women in third decade of life. Patients most often present with unspecific abdominal pain and a palpable mass in the epigastrial region. Even with the presence of metastases, the prognosis remains good, with a 5-year overall survival of 95% [4]. However, 10–15% of cases can be described as malignant and are therefore referred to as “solid pseudopapillary carcinomas” [5,6]. According to the WHO classification system, aggressive behavior is characterized by: angioinvasion, perineural invasion, deep invasion of the surrounding pancreatic parenchyma, or distant metastases [7]. At a microscopic level, extensive necrosis, nuclear atypia, high mitotic rate, immunohistochemistry findings of expression of Ki-67, and sarcomatoid areas may be associated with malignancy [8].

The current expert consensus is that surgical resection is the best treatment method [9], even when the excision is aggressive or necessitates a liver transplant [10]. Typical radiological picture of solid pseudopapillary tumor of solid mass with a lobulating contour and heterogeneous progressive enhancement and hypoenhancement on the arterial and venous phases – is used as an indication for surgery. The technique of choice is tumor resection with sparing of pancreatic tissue [2,11,12]. The treatment for patients with unresectable metastases remains experimental and based on few data. We present a case of a patient with SPT of the pancreas, diagnosed with metastatic disease, disqualified from surgical treatment and treated with four lines of palliative chemotherapy, with best response to oxaliplatin regimen.

2. Case report

A 36-year-old woman admitted to Regional General Hospital because of a history of a non-characteristic pain and a feeling of fullness in the upper abdomen. A CT showed a solid, cystic mass $5 \times 6 \times 5$ cm in pancreas tail, infiltrating the spleen. A similar,

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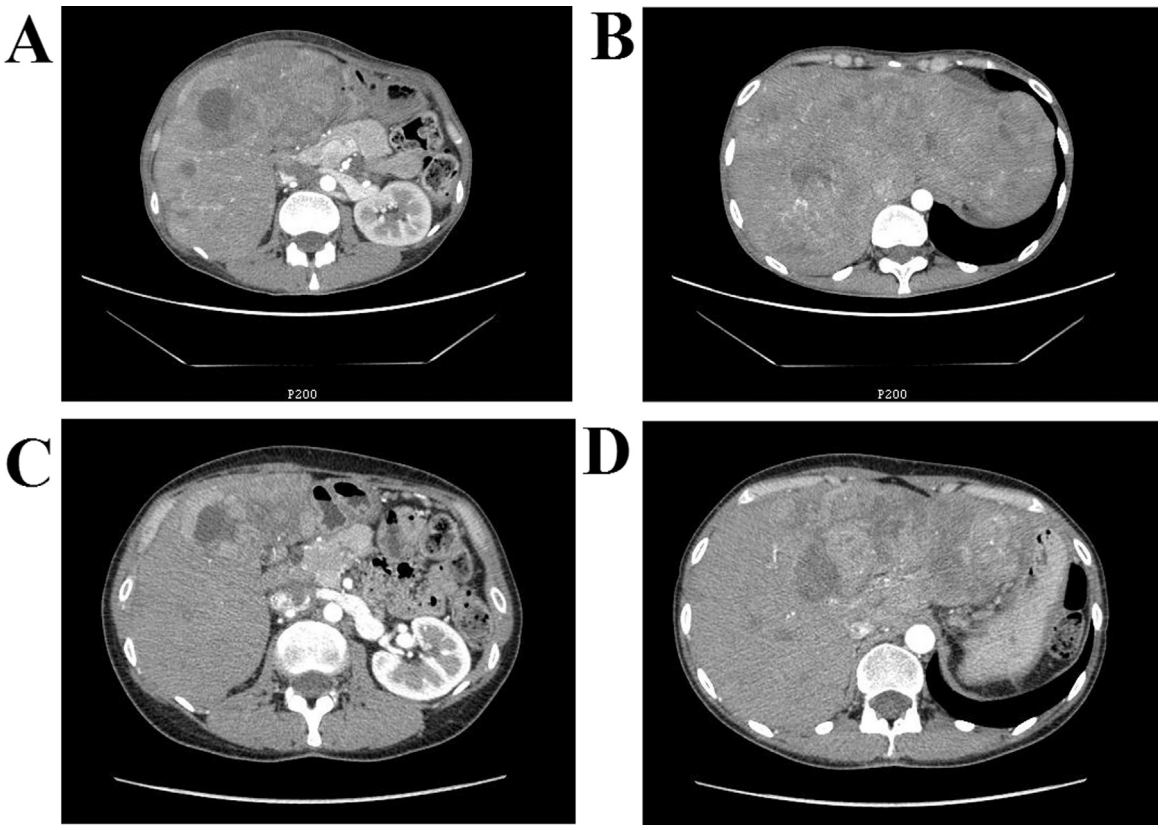

Fig. 1. Changes of the liver and tumor size during the treatment: (A) multiple tumor metastases, the biggest 116 mm in diameter , (B) initial liver size, (C) significantly reduced number of visible metastases, the largest focus 100 mm in diameter, (D) decreased liver size.

slightly smaller mass was present in the third liver segment. In October 2011 the patient underwent subtotal pancreatectomy, splenectomy, and a resection of a metastasis located in the left hepatic lobe. The postoperative course was uneventful and she was discharged from the hospital in a good condition (ECOG 1).

2.1. Histopathology

The histopathology report described an oval, 4 cm diameter tumor in the pancreas tail, a 5.5 cm mass of disintegrated tumor tissue in the spleen, and altered metastatic regional lymph nodes. Tumor invasion was reported in the peripancreatic fat tissue, with angio- and perineural infiltration. Multiple necrotic lesions were present in the tumor tissue, along with very high mitotic activity. Resection margins were free of cancer. A liver lobe showed a small, well-encapsulated metastasis with multiple microscopic satellite tumors and clearly visible cancer angioinvasion of the liver tissue. The patient was diagnosed with solid pseudopapillary carcinoma of pT3N1M1 stage.

2.2. Further treatment

A control CT performed 3 months after surgery showed multiple merging metastases in the liver (Fig. 1). The patient was referred to our hospital – Military Institute of Medicine – for further treatment.

In April 2012, the patient was considered as a candidate for radioembolization; however, due to a massive and unfavorably located tumor mass, the procedure was not feasible and was finally not performed. The patient was also referred to a transplantation unit for consult, but was disqualified for a liver transplant based on the histopathological description and the extent of the disease. Between June 2012 and October 2012, patient was treated with gemcitabine 1 g/m2 d 1, 8, 15, q 4 weeks at 80% of dosage expected for BSA. Gemcitabine was chosen as it was approved showing increased median progression free survival (PFS) duration and increased one year survival rates in pancreatic cancer patients when compared to 5-FU alone. In our patient dose was reduce due to intermediate performance status of patient and significant weight lost in months before the treatment. Gemcitabine treatment was withdrawn after the fifth cycle due to poor tolerance progression of the disease (PD). Significant enlargement of liver metastases was revealed and 25×25 mm recurrence mass over the pancreas head, multiple enlarged lymph nodes and significantly increased, amount of fluid in the abdomen (ascites) were shown. In November 2012 Folfox-4 (oxaliplatin/5-FU/levofolic) chemoregimen treatment was initiated. On day one oxaliplatin 85 mg/m^2 IV infusion was given and followed by leucovorin 200 mg/m^2 IV infusion given over 120 min, followed by 5-FU 400 mg/m^2 IV bolus given over 2–4 min, followed by 5-FU 600 mg/m^2 IV infusion as a 22-h continuous infusion. On day two Leucovorin 200 mg/m^2 IV infusion over 120 min, followed by 5-FU 400 mg/m^2 IV bolus given over 2–4 min, followed by 5-FU 600 mg/m^2 IV infusion as a 22-h continuous infusion was given. As previously 20% dosage reduction was applied. The patient tolerated the new regimen surprisingly well and, until February 2013, six courses were administered. Based on next CT, a partial regression (PR) was reported: the liver and all metastatic changes were significantly smaller ($>30\%$) and the peritoneal space was fluid free (ascites resolved). A decision was made to continue the chemotherapy until contraindicated by hematological toxicities, other clinical contraindications or PD. The patient was treated with Folfox-4 until March 2014 and received 30 courses in total. During this time, patient experienced relief in disease symptoms and was able to continue active life style with the family. The last three doses were accompanied by symptoms that we interpreted