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SHORT COMMUNICATION

Complete remission of a metastatic neuroendocrine tumor of the pancreas with capecitabine (Xeloda®) monotherapy

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Pancreatic neuroendocrine tumors (NETs) consist of a wide group of neoplasms with different biologic and clinical characteristics. Surgery is believed to be the only curative approach but diagnosis is often delayed due to slow growth and difficult interpretation of symptoms due to tumor-related hormone production. In addition to surgery, biological therapies with somatostatin analogues and interferon, radioligand therapies and chemotherapies with newer toxic agents have been studied in metastatic disease. In this report, we describe a patient who achieved a complete radiologic and biochemical remission of a metastatic pancreatic neuroendocrine tumor during sole treatment with capecitabine.

A 51-year-old male patient suffered from chronic abdominal pain. A CT scan revealed a tumor mass in the pancreas of 4 × 3 cm and multiple hepatic lesions of up to 2.9 cm (Fig. 1). An In-111 (octreotide-) tumorscan showed positive regions at the same anatomic sites. The cytologic analysis of a fine needle aspiration of the pancreatic mass and of a liver lesion confirmed the diagnosis of a neuroendocrine tumor of the pancreas with liver metastasis. Neoplastic cells stained positive for chromogranin A. Cytologically, grading of the tumor was difficult. The tumor cells showed all the typical characteristics of neuroendocrine neoplasms with low grade nuclear polymorphism. In accordance with these findings, serum levels of chromogranin A were elevated (4 × upper limit of normal) and the serum liver parameters were moderately elevated. The tumor marker CA19.9, typically elevated with adenocarcinoma of the pancreas, was in the normal range.

To offer an oral chemotherapy regimen, the patient was treated with capecitabine monotherapy from April 2006 to May 2007. The patient initially received three cycles of capecitabine at a dosage of 1,250 mg/m^2 daily (2 weeks on, 1 week off) followed by 10 cycles at a dosage of 1,500 mg/m^2 daily. The treatment was well tolerated. The patient, suffering from dry skin of the hands before initiating therapy suffered from a slight aggravation of these symptoms but no hand–foot-syndrome developed. During this treatment, serum levels of chromogranin A (Fig. 2) as well as the elevated liver parameters decreased gradually to normal during therapy. A complete remission of the pancreatic mass and of all hepatic lesions was achieved in the CT scan in May 2007. To our knowledge this is the first report of a significant objective response of a neuroendocrine pancreatic tumor to oral capecitabine monotherapy.

In a recently published study patients with neuroendocrine tumors of different origins were treated with oxaliplatin and capecitabine [1]. The treatment was particularly effective in patients with well-differentiated neuroendocrine tumors after disease progression under therapy with somatostatin analogues: 30% of the patients achieved a partial response and 48% showed stable disease. It has been reported that combination therapies with 5-fluorouracil (combinations of 5-fluorouracil with streptozocin, adriamycin, cisplatin or lomustine) achieved response rates between 20 and 40% (partial responses or stable disease). For a systematic overview of published clinical studies and current

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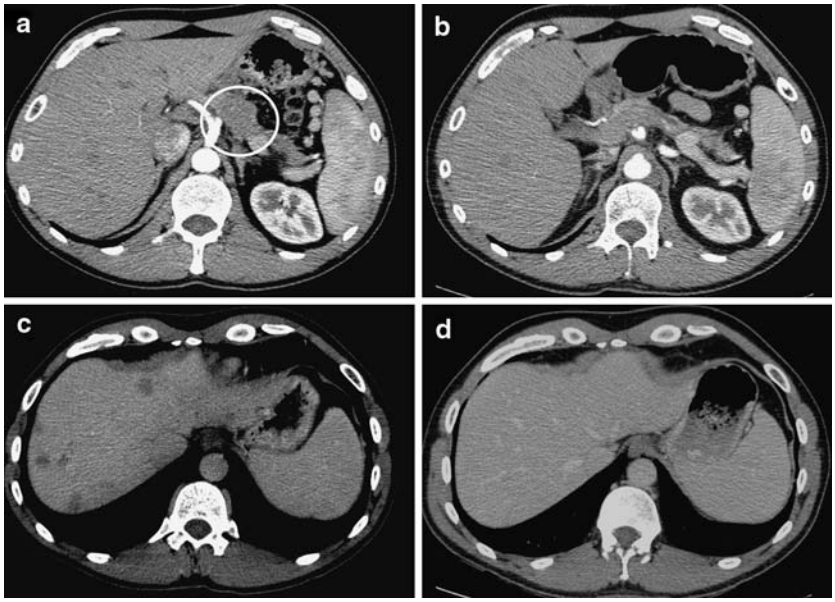

Fig. 1 Pancreatic mass **a** and liver metastasis **b** at the time of diagnosis and CT scans after 12 months of chemotherapy with capecitabine **c**, **d** respectively

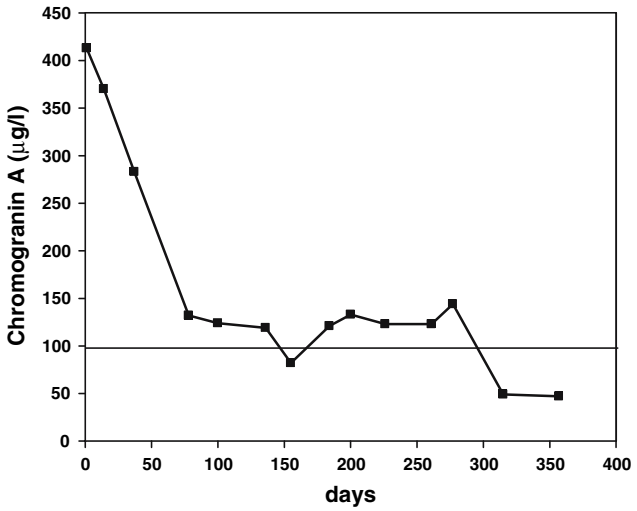

Fig. 2 Level of chromogranin A in serum at the time of diagnosis (day 0) and during the course of chemotherapy. *Line* depicts upper limit of normal range (98 µg/l)

medical treatment of pancreatic neuroendocrine tumors we refer to the recent review of Yalcin [2].

Currently, there are two open clinical trials including 5-fluorouracil (Clinical trials. gov number NCT00227617, UCSF Comprehensive Cancer Center) or capecitabine (NCT00398320, Standford Comprehensive Cancer Center) for the treatment of advanced neuroendocrine tumors. Both studies combine these drugs with oxaliplatin and bevacizumab. The rationale of these combinations is the known activity of oxaliplatin in combination with capecitabine in the treatment of neuroendocrine tumors on one side [1] and the known activity of bevacizumab on the other side [3]. Current clinical trials for gastroenteropancreatic neuroendocrine tumors have recently been reviewed by Strosberg [4].

Based on our observation, we support further evaluation of the role of capecitabine- and combination-therapies with capecitabine for the treatment of subgroups of neuroendocrine tumors. In particular, slow growing low-grade tumors may be sensitive to the continuous therapy with capecitabine.

References

1. Bajetta E, Catena L, Procopio G, De Dosso S, Bichisao E, Ferrari L, Martinetti A, Platania M, Verzoni E, Formisano B, Bajetta R (2007) Are capecitabine and oxaliplatin (XELOX) suitable treatments for progressing low-grade and high-grade neuroendocrine tumours? Cancer Chemother Pharmacol 59:637–642
2. Yalcin S, Oyan B, Bayraktar Y (2007) Current medical treatment of pancreatic neuroendocrine tumors. Hepatogastroenterology 54:278–284 (Review)
3. Yao J, Hoff P, Phan T, Hess K (2005) Improved progression free survival (PFS) and rapid sustained decreased perfusion among patients with advanced carcinoid treated with bevacizumab. J Clin Oncol Supp 23(16S):4007 (Abstract)
4. Strosberg JR, Kvols LK (2007) A review of the current clinical trials for gastroenteropancreatic neuroendocrine tumours. Expert Opin Investig Drugs 16:219–224 (Review)