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The prognostic impact of primary tumor resection in pancreatic neuroendocrine tumors with synchronous multifocal liver metastases

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ABSTRACT

Background: Whether primary tumor resection benefits patients with synchronous multifocal liver metastases from pancreatic neuroendocrine tumors remains controversial. We investigated whether primary tumor resection significantly affects survival in this study.
Methods: A retrospective study of patients with synchronous multifocal liver metastases from pancreatic neuroendocrine tumors between 1998 and 2016 was performed. Patient demographics, operation details, adjuvant treatment, and pathological and survival information were collected, and relevant clinicopathological parameters were assessed in univariate and multivariate survival analyses.
Results: Sixty-three patients were included in this study, including 35 who underwent primary tumor resection. The median survival time and 5-year survival rate of this cohort were 50 months and 44.5%, respectively. Median survival time in the resected group was significantly longer at 72 months than that of 32 months in the nonresected group ($p = 0.010$). Multivariate analysis showed that primary tumor surgery was a significant independent prognostic factor (HR 0.312, 95% CI: 0.128–0.762, $p = 0.011$).
Conclusions: Primary tumor resection significantly benefits patients with synchronous multifocal liver metastases from pancreatic neuroendocrine tumors.

Introduction

Pancreatic neuroendocrine tumors (pNETs) are rare, with a reported incidence of 0.22–0.32 per 100,000 person-years [1,2]. Although pNETs are usually considered indolent, some tumors with malignant behavior can display distant metastases. Approximately more than 50% of pNETs are reported to show liver metastases (LM) [3], with bilobar metastases identified in 80% of cases [4].

Complete resection of primary and metastatic tumors is the only potential method of curing pNETs with LM. In fact, achieving curative surgery in cases of bilobar LM is not easy. For multifocal LM from pNETs that cannot be cured, primary tumor resection has been recommended to alleviate symptoms related to the tumor burden or functional tumors [3], but its prognostic effect is controversial. The median overall survival (OS) of primary tumor resection patients has been shown to be higher than that among patients who did not undergo primary tumor resection, but the difference was not significant [5–7]. Improved survival after primary tumor resection was identified among patients with unresectable LM [8], and patients with resectable pNETs in the pancreatic body and tail could especially benefit from primary resection [9].

Therefore, the objective of the current study was to explore the prognostic role of primary tumor resection for pNETs with synchronous multifocal unresectable LM at a single center and to provide more useful evidence for clinicians.

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Materials and methods

From 1998 to 2016, the clinical records of 129 patients diagnosed with pNET and LM at Peking Union Medical College Hospital (PUMCH) were identified. The inclusion criteria were 1) pNET with synchronous LM detected either before or during surgery or within 6 months after the first available imaging results [10,11]; 2) bilobar or diffuse LM without the possibility of curative treatment; and 3) pathologically diagnosed pNET. The exclusion criteria were 1) the presence of other malignant tumors; 2) metachronous LM; 3) impending radical surgery; 4) mixed adenoneuroendocrine carcinoma of the pancreas; 5) unilobar LM; 6) perioperative death; 7) extra-abdominal metastasis; and 8) LM resection without primary tumor resection. After applying the inclusion and exclusion criteria, 63 patients were included in our study (shown in Fig. 1). The collected information included age at diagnosis, gender, clinical symptoms, surgical information, site of the primary neoplasm, adjuvant treatment, pathological diagnosis, WHO grade and status at the last follow-up. This study was approved by the Institutional Ethics Committee of PUMCH, Chinese Academy of Medical Sciences.

The patients were categorized into two groups: group 1, primary tumor resection, and group 2, no resection of the primary tumor. The surgical strategy was standardized and was conducted by experienced surgeons in our center. All patients were assessed regarding the feasibility of primary tumor resection. After surgery, all patients were recommended to receive systemic therapy including octreotide administration, targeted therapy, and/or systemic chemotherapy. For the patients who did not undergo primary tumor resection, treatment consisted of observation, octreotide administration, targeted therapy, and/or systemic chemotherapy. Liver-directed therapy included liver surgery, chemoembolization and liver ablation. Hepatic resection was reported to be associated with prolonged OS in patients with neuroendocrine LM [12]. In group 1, several patients underwent liver resection and the prognostic effect of liver resection might influence the survival of patients in group 1. Therefore, we further subdivided group 1 into two subgroups to explore the prognostic effect of primary tumor resection in this cohort: group 1a – liver resection, and group 1b – no resection of LM. To exclude the prognostic effect of liver resection on group 2 when we compare the survival between group 1a, group 1b and group 2, one patient who underwent liver resection during an exploratory laparotomy in group 2 was excluded. The patients were followed up until death or the end of May 2017 via outpatient clinic visits or telephone calls.

Computed tomography (CT), ultrasound (US), magnetic resonance imaging (MRI), endoscopic ultrasonography (EU), positron emission tomography/computed tomography (PET/CT) and angiography were used to locate the primary tumor. CT and US were the two main methods used (50.0% and 37.5%, respectively). In 2 patients, angiography was the final method used to confirm the tumors when CT, MRI and US could not detect the neoplasms.

Statistical analysis

Continuous variables are expressed as the mean and standard deviation (SD) or the median [interquartile range (IQR)], and

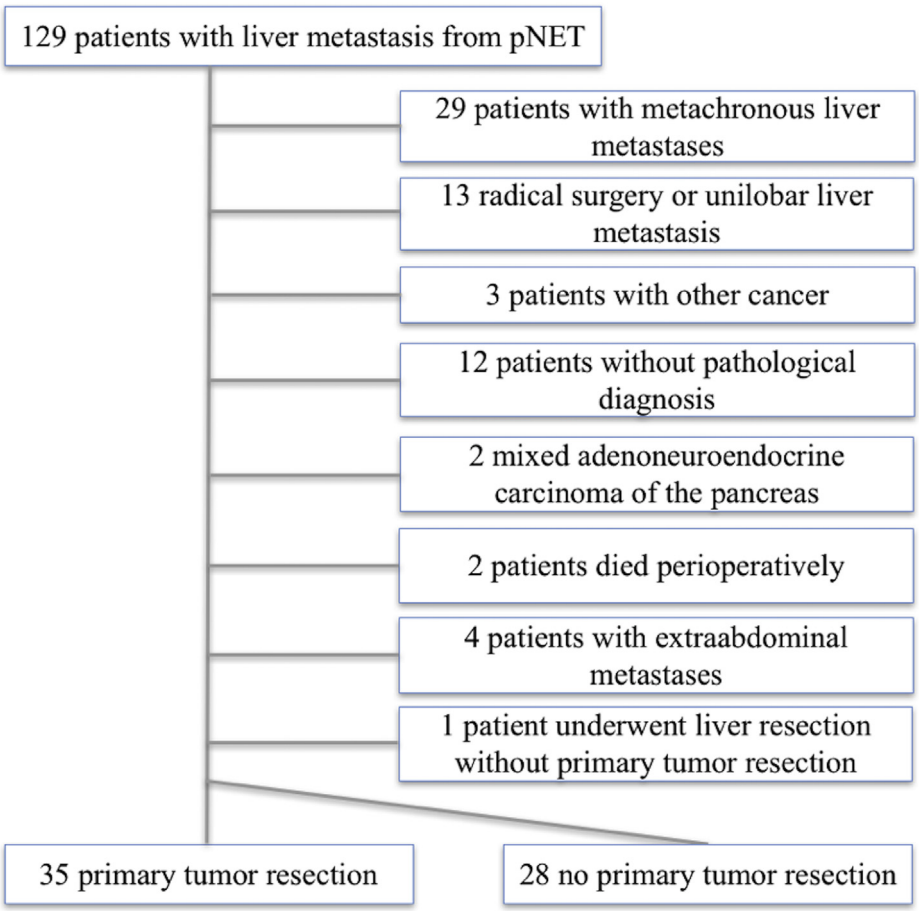

Fig. 1. Patient flow diagram.

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