LETTER

Is There a Role for Liver Transplantation in Metastatic Pancreatic Neuroendocrine Tumors (PNET)?

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Dear Sir,

recently, we published an important report on the role of radiotherapy in pancreatic neuroendocrine tumors (PNET) consisting of our experience and the data presented at the 2012 ASCO Gastrointestinal Cancers Symposium by the University of Maryland School of Medicine, Baltimore, MD, USA and Johns Hopkins University School of Medicine, Baltimore, MD, USA [1, 2]. We received multiple calls, emails as well as questions by the patients about the role of liver transplant in this population of patients with PNET. This question probably received a lot of attention in the media with the unfortunate passing of Steve Jobs in 2011. In 2009, Mr. Jobs was the recipient of a liver transplant, an unusual treatment for this disease.

Pancreatic neuroendocrine tumors are estimated to account for approximately 10% of pancreatic cancers by prevalence. While these are generally considered to be more indolent than the more common pancreatic adenocarcinoma, the presence of liver metastases portends a poorer prognosis, with 5-year survival rates in untreated patients thought to be approximately 30%, with chemotherapy providing adding only 12-24 months to life [3]. If possible, surgery is considered to be first line for liver metastases in patients with PNET [4]. The focused removal of any hepatic metastases improves quality of life and sometimes even large portions of the liver can be removed given the liver's unique ability to regenerate. In 2003, the Mayo Clinic, Rochester, MN, USA reported a median response rate of 45 months in patients with metastatic lesions who underwent surgical resections of these lesions [5].

Received April 11th, 2012 - Accepted April 18th, 2012

Key words Chemoradiotherapy; General Surgery Neoplasm Metastasis; Neuroendocrine Tumors; Pancreas; Transplantation

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In reviewing the literature, we were unable to find any prospective controlled trial evidence of liver transplantation being used to extend survival in patients with PNET, presumably given both the rarity of this condition and the logistical difficulties with transplantation. However, there are a fair number of retrospective trials and case series related to this. In one of the larger retrospective analyses of 103 patients with neuroendocrine carcinoma, Lehnert reported the 2-year and 5-year survival to be 60% and 47%, respectively, but recurrence-free 5-year survival was less than 24% [6]. Certain prognostic indicators including age greater than 50 years and association with a Whipple procedure were associated with poorer prognoses in this evaluation. Similarly, a retrospective analysis of 19 patients suggested that a low Ki67 expression (less than 5%) and regular E-cadherin staining was associated with improved outcomes after transplantation, especially if seen in combination [6, 7]. Coppa *et al.* have tried to further classify which patients are most appropriate for liver transplantation in this setting, and their classification included the following criteria: age less than 50, confirmed carcinoid by histology, less than 50% liver replacement by metastases, absence of extrahepatic disease, and stable disease in the pre-transplantation period [8].

While not a firmly established indication for liver transplantation, metastatic PNET is interesting in that there is some possibility of improvement with transplant, especially in patients who are not amenable to other means of hepatic metastasis removal and otherwise have good prognostic indicators. However, further large numbered prospective studies are warranted to show a more substantial benefit to this treatment.

Conflict of interest The authors have no potential Fax:

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