Symposium IV

# Surgical Approach for Hepatic Metastases of NET (Neuroendocrine Tumor)/SPT (Solid Pseudopapillary Tumor of Pancreas)

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## Surgical Management of Neuroendocrine Hepatic Metastases

NETs constitute a group of tumors that originate from the diffuse neuroendocrine cells throughout the body. NETs occur most frequently in the G-I tract (66%), with the second most common location in the bronchopulmonary system (31%) and most are sporadic. The liver is the most common site of metastatic disease for neuroendocrine tumors andultimately dictates outcomes in most patients. Liver involvement develops in 46% to 93% of patients with NET over the course of their disease. Typically, NETs have an indolent natural history, even in the setting ofmetastatic disease. Historically,patients with untreated neuroendocrine liver metastases (NELM) have been reported to havealmost 30% 5-year survival rates with median survival 3 years. The majority of patients with NELM have a multiplicity of lesions. Patients with minimal localized NELM are relatively few as only 5–15% of patients with NELM have tumor localized to one lobe, or adiscrete, limited number of (fewer than five) metastases in two lobes that would be fullyresectable. In various published studies, patients with curativeresectionhad 5-yearsurvival rates of 61–85%, which is believed to increase survival overthose who have not undergone surgical resection. However, there areno prospective randomized controlled trials in which patients with NELM have been randomized to appropriately matched controlgroups without liver surgery. Nevertheless, results from the various studies suggest that surgical resection shouldbe an accepted treatment modality in selected patients,as it increases survival rates and controlsendocrine-related symptoms. Afterhepatectomy of NELM, intrahepatic recurrences are detectablein more than 60% of the patients at 5years and 75% at 10 years,suggesting that tiny tumor depositsare probably already present in the remaining liver at the time of thehepatectomy. Recently, using thin-slice pathologicalexamination of resected liver specimens, Elias et al. reported that fewer than 50% of the NELM were detectedby preoperative imaging modalities compared with a finaldetailed pathologic count.Whencomplete resection of gross liver metastases is not feasible or in the presence of unresectable extrahepatic disease, treatment of thesetumors is directed towards controlling the symptomatic and growth effects of liver metastases. Cytoreductive surgery as a tumor debulking strategy should be consideredin patients with extreme hormonal symptoms refractory to other treatments. However, at least 90% of the tumor burdenshould beresected, and the operative risk should not be high. Various reports showed that significant relief of symptoms could be achieved in 90-100% of patients who survived palliative resection for hormonal symptoms and might be associatedwith a survival benefit. Current recommendations by various authors forpatients with NELM support resection if preoperative evaluation showsthat 100% of the primary/regional disease and at least 90% of the metastatic disease can be removed. This seems to be true for both symptomatic andasymptomatic tumors. Radiofrequency ablation (RFA) can provide local control and short-term symptomaticrelief from NELM when resection is not possible. Combinations of resectionand ablation also can be used to achieve complete tumor response when all liver diseasecannot be resected. Liver transplantation (LT) had initially been proposed in thetreatment of NET as a salvage to ‘cure’ a few desperatepatients presenting mostly huge or diffuse tumors with orwithout invalidating hormonal syndromes refractory toany medical treatment.

Early results of LT was extremely variable with 5-year post-transplant patient survival (PS) rates ranging from 36% to 90% and disease free survival (DFS) rates ranging from 9% to 77%, which mean an important selection bias in the reported series. Milan group improved the results ofLT for NET by prospectively applying strict inclusion criteria. These criteria are (1) Well-differentiatedlow-gradeneuroendocrine tumorswith or without syndrome. A Ki67 proliferation indexof <10% is a characteristic of well-differentiated tumor,which authors have adopted as a cut-off value to considerpatients for possible LT (2) Primary tumor drained by the portal system (pancreas andintermediate gut: from distal stomach to sigmoid colon) removed with a curative resection through surgical proceduresdifferent and separate from transplantation (3) hepatic tumor involvement of <50% of theliver volume (4) Goodresponseor stable disease for at least 6 months duringthe pre-transplantation period (5) Age <55 year. Following the initial encouraging results,remarkable 5-year PS and DFS survival rates of 90% and 77% were obtained. LT is a valid optionfor very well selected NET patients with unresectablehepatic metastases. It is alsoclear that more clinical trials and detailed analysis of larger transplant experiencesare necessary to further improve our knowledge and tooptimize the use of a scarce organ resource.

## Surgical Treatment of Liver Metastases from a Solid Pseudopapillary Tumor of the Pancreas

Solid pseudopapillary tumor (SPT) of the pancreas is arare neoplasm. It frequently affects young women. Most primary tumors are confined tothe pancreas at the time of diagnosis and are consideredneoplasms of low malignant potential. Most cases of SPT of the pancreas are cured by complete resection with more than 90% survival. The incidence ofliver metastases varies from 2% to 28% in differentseries, with a median of 14%. Till 2007 year, 47 patients with liver metastasis have beenreported in the English and Japanese medical literature. When the metastatic lesion is resected, theprognosis is as good as that of SPT without metastasis. However, treatment for patients with unresectableliver metastases remains indeterminable. Recently, there were two successful LDLT case reports in English literature. Both are young girls (14 and 20 years) with unresectable liver metastases of SPT of the pancreas. They were disease free at 2 years after LT. OLT is a potentially curative strategy. Importanceof good selection of patients cannot be overemphasized

### References

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