C19

Mitotic index and somatostatin receptor status are independent predictors of survival after resection of neuroendocrine tumors metastatic to the liver

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Background: Mitotic activity of neuroendocrine tumors (NET) has been shown to predict survival after resection. However, other markers of outcome are lacking.

Methods: Patients undergoing resection of hepatic metastases of NET between Jan1988 and Jan 2009 were reviewed. Inclusion criteria required the surgeon to feel he/she could treat all gross disease with a combination of resection and ablation. The primary and metastatic tumors were histologically and immunohistochemichally examined. Survival was estimated with the Kaplan-Meier method and compared using log rank. Multivariate analysis was conducted with Cox regression.

Results: 70 patients underwent hepatic resection of NET. There have been 29 deaths including 3 (4%) within 30 days. The median survival was 96.5 months with 5yr and 10 yr survivals of 72% and 43%. Mitoses per 10 high power field (HPF) and percentage of cells staining positive for Ki67 were significantly higher in the liver metastases than in the primary tumors on paired T-test. On univariate analysis of the primary tumors, a pancreatic primary, size>3cm, >2 mitoses/10HPF, Ki67 staining >1% of cells, weak staining for somatostatin receptor, and strong staining for CEA were significantly associated with shorter survival. On univariate analysis of the liver metastases, >2 mitoses/10HPF, Ki67 staining >1% of cells, and weak staining for somatostatin receptor were all significantly associated with shorter survival. Multivariate analysis of the primary tumors found no independent predictor of survival. Multivariate analysis of the metastatic tumors showed:

Variable	Hazard Ratio	95% Confidence	p
>2 mitoses /10HPF liver mets	6.2	1.6-25	0.009
Weak somatostatin receptor stain liver mets	7.3	1.1-38	0.041

Conclusions: Resection of hepatic metastases of NET can achieve excellent results. Mitotic activity was significantly higher in the liver metastases than in the primary tumors. Mitoses per 10 HPF and staining for somatostatin receptors in the liver metastases are significant and independent predictors of survival.