B6

Are Primary And Metastatic Tumors The Same?

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Introduction: Commonly only one tumor site is biopsied for determination of the histological features of neuroendocrine tumors (NETS). We hypothesized that there are significant differences in primary neuroendocrine tumors and their nodal or organ metastasis based on an assessment of their rate of cellular proliferation (Ki-67), degree of tumor differentiation (quantative chromogranin A (CGA) and synaptophysin stains) and angiogenic indices (CD 31 and Factor VIII stains). We also propose that sampling one tumor site could lead to erroneous assumptions about the tumor's clinical behavior.

Methods: Thirteen (13) patients with metastatic well differentiated NETS underwent cytoreductive surgery which removed primary tumor, nodal metastasis and organ metastasis. Each site sample was stained for Ki-67, Chromogranin A (CGA), synaptophysin, CD 31 and Factor VIII. Test results for Ki-67 were categorized into three groups based on its proliferative rate (%). CGA and synaptophysin stains were recorded as percent of cells demonstrating 3+ staining. CD 31 and Factor VIII stains recorded as the average number of vessels per high field (10 fields). We compared results of each test in the three tumor locations for each patient. All specimens were collected during the same surgical procedure; the same technician did all of the stains at one time, and the same pathologist read all slides in one sitting.

Results: We found that CGA, Synaptophysin, CD31 and Factor VIII varied considerably within each patient's tissue samples, while Ki-67 was not significantly different between tumor sites. The maximum variability in test results was found in the tumor differentiation markers CGA and Synaptophysin.

Conclusions: We demonstrated considerable differences in primary tumor, lymph node and organ metastasis in tumor

proliferation, differentiation and angiogenic markers from the same patient. Based on this data we feel that sampling only one NET tumor site could lead to erroneous assumptions about the tumor's clinical behavior.

Table 1: Mean represents the average of three locations sampled. Range is the maximum score difference between two different tumor locations in one patient.

Tumor Stain	Mean	Range
Ki-67%	1	5
Chromogranin	36	90
Synaptophysin	37	95
CD 31	14	59
Factor VIII	7	24