PROGNOSIS AND PREDICTIVE FACTORS

Microadenomas are considered benign. 55%-75% of all other NETs are associated with evidence of malignant behavior (extrapancreatic spread, metastasis or recurrence) with some patients dying as long as 10 years after surgery and >25% initially presenting with distant metastasis.

Prognostic factors including tumor size (>2cm), invasiveness, necrosis, regional lymph nodes and tumor grade all increase the likelihood of metastasis with the proliferation rate and degree of differentiation being the being the most important histologic factors. Additionally abnormal peptide secretion is an adverse prognostic factor when associated with a clinical syndrome.

Treatment for NET G-3 is yet not standardized and are at present being treated as other G-1 and G-2 NETs. In non-metastatic neuroendocrine tumors, the European and American guidelines recommended a surgical resection with regional lymph node dissection for localized NETs, irrespective of the tumor grading. [5] Somatostatin analogs and Peptide receptor radionucleotide therapy (PPRT) on the basis of Somatostatin scan results can additionally be given in NETs for symptom stabilization or in recurrent tumors [5]. On the other hand, platinum-based therapy are used primarily for treatment of NECs and are less effective in metastatic NET G-3 than in NEC [1,6].

Other important changes in this classification was that the terminology of mixed neoplasm was changed to Mixed neuroendocrine- non-neuroendocrine neoplasms (MiNEN) in stead of Mixed adenoneuroendocrine neoplasms (MANEC). Also the category of hyperplastic and preneoplastic lesions included in the 2010 WHO classification has been abolished.[4]

To conclude NET G-3 is a new entity described in WHO 2017 classification of NENs of GI tract and represents up to 6% of NET. Prognosis and response rate seem to be close to well-differentiated NET G-1/2 with a worse overall survival. It seems that the cell differentiation should be first taken in consideration and along with mitotic count and Ki-67 index must be known before therapeutic intervention. In addition, there is an urgent need to identify reliable biological markers such as P53 and others that would guide the physicians in stratification and predict treatment response in these patients especially in cases with ambiguous morphology.