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NET Management Strategies: What's New & Relevant?

ENETS/NANETS YOUNG INVESTIGATOR SESSION

KI-67 HETEROGENEITY IN GASTRO-ENTERO-PANCREATIC NEUROENDOCRINE TUMOURS

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Background:

The neuroendocrine tumor (NET) proliferation-based grading system (ENETs) has proved reliable for prognostic stratification, however concerns exist on Ki-67 heterogeneity. Our aim was to evaluate intratumor Ki-67 index heterogeneity in primary and metastatic sites.

Grade	Mitoses/10HPF	Ki67 %
G1	<2	≤ 2
G2	2-20	3-20
G3	>20	>20

Aim:

Retrospectively study a series of GEP NETs and:

- **Compare mitotic index evaluation and Ki-67 evaluation**
- **Evaluate Ki-67 in different samples of the same lesion - heterogeneity**
- **Evaluate Ki-67 between multiple primitive NETs on first diagnosis.**
- **Evaluate Ki-67 in recurrent disease, local or distant.**

Methods:

- 170 GEP-NETs from the Histopathology archives at the University of Genova, San Martino Hospital, dating from 1993-2011
- 50 with clinical follow-up (mean follow up was 59 months, range 2-168 months).

25 cases satisfied the following criteria:

1) NETs with multiple tissue samples of the same primary lesion;
2) Multiple primitive NETs;
3) NETs with synchronous metastases, distant or local;
4) NETs with subsequent metachronous metastases, at least 6 months after initial presentation (mean to recurrence 96 months, range 24-144 months).

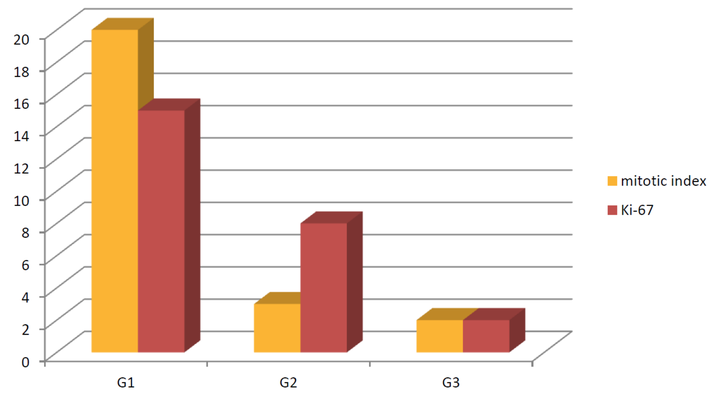
- For each location a minimum/maximum of **3 paraffin tissue blocks** were selected.
- In case of multiple primitive NETs, at least one sample of each separate lesion was chosen.

Mitoses were counted in 50 HPF and Ki-67 staining was manually counted (MC) in hot spots as mean of 2000 neoplastic cells

Results:

Concordance between mitoses and Ki-67 evaluation

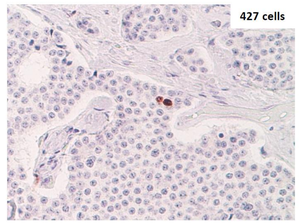
G2 were significantly underdiagnosed when using mitotic count alone with respect to Ki-67 evaluation **(5/8 cases (63%) had < 2 mitoses but Ki-67 between 3-20%).**



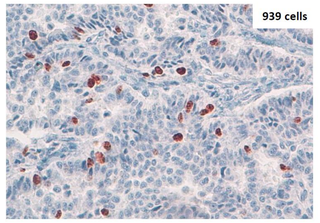
Heterogeneity of the primary tumour

Exactly the same Ki67 index	**13 (62%)**
Different Ki67 index but same grade	**6 (29%)**
Different Ki67 index and different grade	**2 (10%)***
Total	**21**

*both these cases changed from 1% (G1) to 5 and 7% (G2) respectively in different paraffin blocks

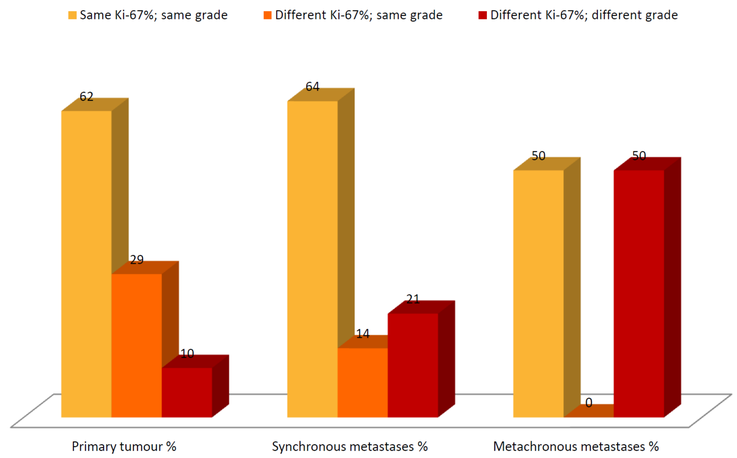


Ki67-index: 0,7% (on 2000 cells)



Ki67-index: 4,9% (on 2000 cells)

Heterogeneity between the primary tumour and metastases



Conclusions: Differences in grade between primary and metastatic sites are important and evaluation of Ki67 at all sites may be significant for patient management.