


Multiple Endocrine Neoplasia Type 1 (MEN-1)

S. Kassem, B. Glaser, D. Barak, DJ. Gross

Hadassah Medical Center



MEN-1

- Prevalence: 2-4/100000.
 - Autosomal dominant.
 - 50% mortality by age 50.
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MEN-1: Definition

CONSENSUS

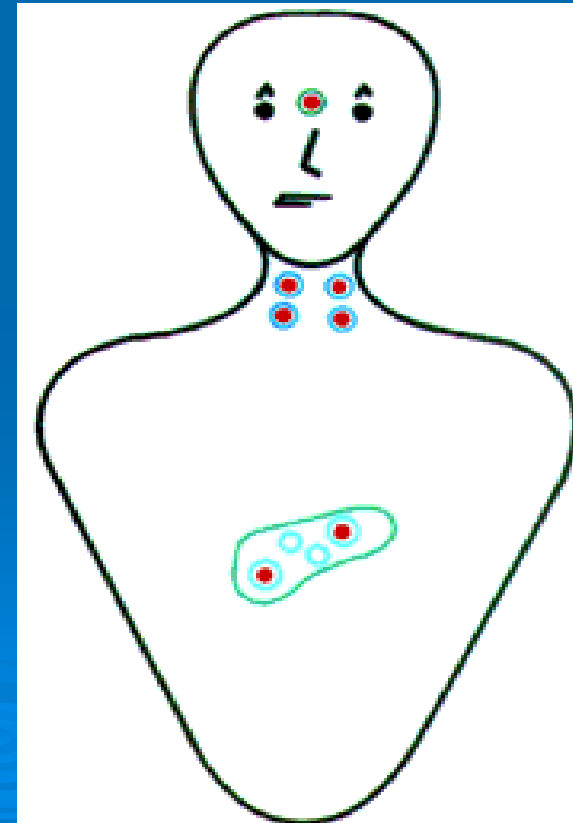
Guidelines for Diagnosis and Therapy of MEN Type 1 and Type 2

J Clin Endocrinol Metab, December 2001, 86(12):5658–5671 5659

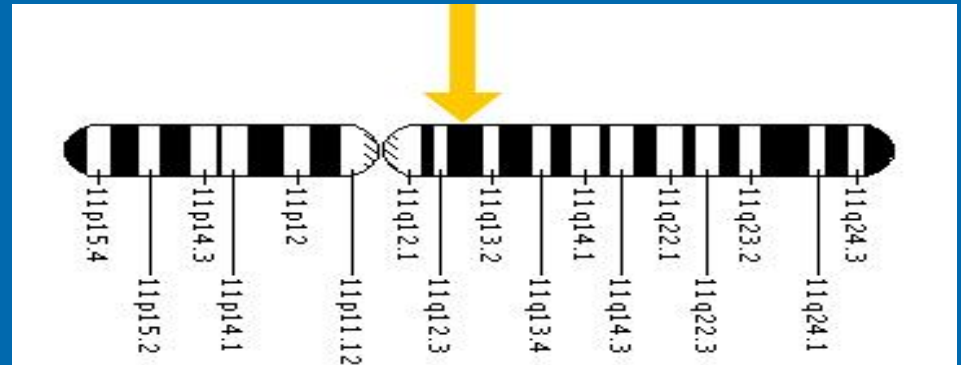
PPP

MEN-1: 2/3 main MEN1 tumor types (parathyroid, entero-pancreatic endocrine adenomas, and pituitary adenomas).

Familial MEN-1: An index MEN1 case with at least one relative who has one of the three main MEN1 tumors.



MEN-1: Genetics



- Ch11q13.
- Menin 610AA.
- tumor suppressor gene.
- JunD, NF-kB, Smad3, DNA methylation.
- Cell proliferation/ apoptosis.

MEN-1: Genetics

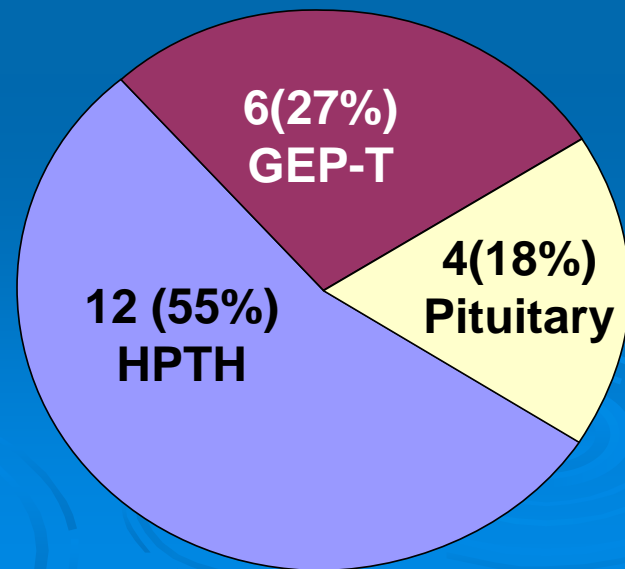
- >400 Mutations (80-90%)
- Knudson's two hit hypothesis.
- Indications for genetic testing:
 - Confirm clinical diagnosis.
 - Screening family members.
- Biochemical evaluation:
 - Ca, PTH
 - Prolactin, IGF-1
 - Gastrin, CgA

Multiple Endocrine Neoplasia Type 1 (MEN-1), The Hadassah-Hebrew University Medical Center Experience

- Clinical data 2003-2009.
- Genetic analysis: Lyon, France; NIH, USA.
- Analysis: exons 2-10 of the menin gene.

Multiple Endocrine Neoplasia Type 1 (MEN-1), The Hadassah-Hebrew University Medical Center Experience

- 25 subjects, 20 families. Information available: 22.
- Average age at presentation 36 (17-75).
- Initial presentation:



Multiple Endocrine Neoplasia Type 1 (MEN-1), The Hadassah-Hebrew University Medical Center Experience

- MEN-1 manifestations:
 - 19 (86%) HPTH
 - 15 (68%) GEP tumors (7 non-secreting , 6 gastrinomas, 2 insulinomas)
 - 12 (55%) pituitary tumors (9 prolactin, 2 ACTH and 1 null).
 - 2 (9%) metastatic carcinoid tumors (intestinal)
 - 1 (4.5%) thymic carcinoid.

- Genetic testing:
 - 18 subjects.
 - 12 (67%) positive.
 - 1 (5.5%) genetic variant of unknown significance.

Multiple Endocrine Neoplasia Type 1 (MEN-1), The Hadassah-Hebrew University Medical Center Experience

➤ Treatments

- HPTH:
 - 8: parathyroid surgery
- GEP-T:
 - 11: abdominal surgery
 - 7: somatostatin analogs
 - 2 : PRRT
- Pituitary:
 - 6: cabergoline
 - 3: TSS

Multiple Endocrine Neoplasia Type 1 (MEN-1), The Hadassah-Hebrew University Medical Center Experience

➤ Survival:

- 22/25 are alive (age 45.4 ± 10 years).
- All 3 died of metastatic GEP tumors at the ages 41, 45 and 56.

Conclusions

- MEN-1 is a complex genetic disorder.
- Hyperparathyroidism is the most common and earliest manifestation.
- GEP tumors cause most of mortality associated with MEN-1.
- Menin mutations or variants were found in 72% of patients with clinically defined MEN-1.

Thank You

