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Cancer Prone Disease Section

Mini Review

Multiple endocrine neoplasia type 1 (MEN1)

Alain Calender

Service de génétique moléculaire et médicale, hôpital Edouard-Herriot, bâtiment B7, 5, place d'Arsonval, 69437 Lyon 03, France (AC)

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Identity

Alias: Wermer's syndrome

Note: Multiple Endocrine Neoplasia type 1 or Wermer's syndrome (MEN1) is a complex disease predisposing to a variety of endocrine tumors multifocal and/or bilateral localization and uncommonly to non-endocrine tumors mainly of the skin and central nervous system.

Inheritance: An autosomal dominant disorder with high penetrance (increasing with age: 90% by age 50 years) but variable expressivity (with phenotype/genotype correlations); frequency is unkown but estimated between 1/50000 and 1/30000.

Clinics

Phenotype and clinics

Onset of the disease occurs commonly between 15 and 40 years and most patients (90-100%) present primary hyperparathyroidism related to multiglandular hyperplasia and/or adenomas; other endocrine lesions and relative percentages are neuroendocrine tumors of the pancreas (either functionnal such as gastrinomas, insulinoma, and more rarely glucagonoma, VIPoma or non functionnal) (50-70%), pituitary adenoma (20-40%), adrenocortical hyperplasia, adenomas or cancers (20-70%) and thymic/bronchial neuroendocrine tumors (5-10%); cutaneous lesions, such as angiofibromas, collagenomas, lentiginosis, melanocytic lesions and lipoma might occur in 5-10% of MEN1 patients; less common lesions are infratentorial papillary ependymoma, rhabdomyosarcoma and leiomyosarcoma, and renal and thyroid cancers.

Neoplastic risk

Pancreatic neuroendocrine tumors such as gastrinoma have malignant evolution in 30 to 50% of the cases. Insulinoma might be frequently benign. Most agressive tumors are glucagonoma and VIPoma (VIP: vasoactive intestinal peptide) in pancreas and some tumors occuring in the adrenal cortex.
Pituitary adenomas in MEN1 are classical benign lesions but complications might be related to local nervous compression by the tumor.
Parathyroid adenomas in MEN1 remain benign lesions.
Cutaneous and CNS (Central Nervous System) lesions in MEN1 might be malignant in a few cases. Strikingly, melanomas, ependymomas and rare astrocytomas observed in the MEN1 context have better prognosis than the same lesions occuring sporadically.

Treatment

Parathyroids: the recommended procedure is 3 and half parathyroidectomy and cautious exploration of the thymic tissues in which ectopic adenomas and/or carcinoids (neuroendocrine tumors) have been described.
Pancreas: in most cases (insulinoma, glucagonomas, > 2cm non functionnal tumors, surgery is a best procedure and might be duodenopancreactomy in the heavy cases; nevertheless, in gastrinomas and non functionnal small tumors identified by US endoscopy, the best procedure is the medical (antiacid) treatment and a careful follow-up of patients.
Pituitary adenomas: the treatment is the same than for sporadic lesions.
Adrenal glands tumors: surgery is the best recommended procedure when lesions are clearly identified by imagery.

Thymic/bronchial carcinoids: they must be cured by surgery because they are malignant and alter prognosis in MEN1 patients.

Prognosis

according to the severity of the disease in a given patient, and to the quality of a regular follow up; mean age at death is relatively similar to that of the general population; nevertheless, death may occur early in life (10 to 50 year) due to the complications of hormonal secretions by tumors (hemorrhagic ulcers, malignant hypercalcaemia, carcinoid syndromes) or evolution of the maligant process (pancreatic neuroendocrine tumors and thoracic carcinoids): 50 years; a presymptomatic diagnosis improves survival data and might prevent earlier the main causes of death in this disease.

Genes involved and proteins

MEN1

Location

11q13

DNA/RNA

Description: 10 exons.
Transcription: Different splicing.

Protein

Description: 610 amino-acids, 67 Kda; contains two nuclear localization signals.
Expression: Wide.
Function: Growth-suppressor gene.

Mutations

Germinal: Causes multiple endocrine neoplasia type 1.

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