Multiple Endocrine Neoplasia Type 1

Multiple endocrine neoplasia type 1 (MEN1) is a hereditary syndrome caused by pathogenic variants in the \textit{MEN1} gene and is associated with a combination of endocrine and nonendocrine tumors. In MEN1, tumors are most often found in the parathyroid gland, islet cells of the pancreas, and pituitary gland. Tumors can also form in other endocrine glands and the digestive tract. The majority of MEN1 tumors are benign but tumors of the gastroenteropancreatic tract and thymic carcinoids may be malignant. Endocrine tumors cause an increased hormone production based on tumor type, resulting in a wide range of symptoms.

Disease Overview

Incidence

1/30,000\textsuperscript{1,2}

Symptoms

- MEN1 can include development of multiple endocrine and nonendocrine tumors\textsuperscript{3}
- Common endocrine tumors:
  - Parathyroid
  - Gastroenteropancreatic tract (gastrinoma, insulinoma, glucagonoma, pancreatic islet cell tumor)
  - Pituitary (prolactinoma)
  - Gastrinoma
  - Carcinoid (thymic, bronchial, gastric)
  - Adrenal
  - Medullary carcinoma of the thyroid
- Nonendocrine tumors:
  - Facial angiofibromas
  - Collagenomas
  - Lipomas
  - Meningiomas
  - Ependymomas
  - Leiomyomas

Genetics

Gene

\textit{MEN1}
Inheritance

Autosomal dominant

Penetrance

Variable\textsuperscript{4,5,6}

- \sim 50\% by 20 years
- >95\% by 40 years
De novo variants: \sim 10\%

Variants

Inactivating variants of \textit{MEN1} tumor suppressor gene

Test Interpretation

Clinical Sensitivity

Combined testing: \sim 94\%

- Sequencing: 90\%\textsuperscript{3}
- Deletion/duplication: 4\%\textsuperscript{3}

Results

- Positive:
  - One pathogenic variant detected in \textit{MEN1}
  - Confirms diagnosis and etiology of \textit{MEN1}
- Negative:
  - No detectable pathogenic variant detected in \textit{MEN1}
  - Reduces, but does not exclude, a diagnosis of \textit{MEN1}
- Uncertain: variants of unknown clinical significance may be detected

Limitations

- Not evaluated:
  - Regulatory region or deep intronic variants
  - Breakpoints of large deletions/duplications
  - Variants in genes other than \textit{MEN1}
- Diagnostic errors can occur due to rare sequence variations

References

1. Brandi ML. \textit{Rare Disease Database: Multiple Endocrine Neoplasia Type 1}. National Organization for Rare Disorders Jul 1905; [Year Published: Jul 1905; Accessed: Sep 2019]


Related Information

Multiple Endocrine Neoplasias - MEN

Related Tests

Somatostatin Quantitative, Plasma 2010001
Method: Quantitative Extraction/Immunoassay

Metanephrines Fractionated by HPLC-MS/MS, Urine 2007996
Method: Quantitative High Performance Liquid Chromatography-Tandem Mass Spectrometry

Insulin-Like Growth Factor 1 (IGF-1) with Calculated Z-Score 2007698
Method: Quantitative Chemiluminescent Immunoassay

Thyroid Stimulating Hormone with reflex to Free Thyroxine 2006108
Method: Quantitative Electrochemiluminescent Immunoassay

Pancreatic Polypeptide 0099436
Method: Quantitative Radioimmunoassay

Vasoactive Intestinal Peptide 0099435
Method: Quantitative Radioimmunoassay

Glucagon 0099165
Method: Quantitative Radioimmunoassay

Chromogranin A 0080469
Method: Quantitative Enzyme Immunoassay

5-Hydroxyindoleacetic Acid (HIAA), Urine 0080420
Method: Quantitative High Performance Liquid Chromatography - Tandem Mass Spectrometry

Serotonin, Whole Blood 0080395
Method: Quantitative High Performance Liquid Chromatography

Proinsulin, Intact/Insulin Ratio 0070256
**Method:** Quantitative Chemiluminescent Immunoassay/Quantitative Chemiluminescent Immunoassay

**Parathyroid Hormone, Intact with Calcium 0070172**

**Method:** Quantitative Electrochemiluminescent Immunoassay

**Prolactin 0070115**

**Method:** Quantitative Chemiluminescent Immunoassay

**C-Peptide, Serum or Plasma 0070103**

**Method:** Quantitative Chemiluminescent Immunoassay

**Gastrin 0070075**

**Method:** Quantitative Chemiluminescent Immunoassay

**Adrenocorticotropic Hormone 0070010**

**Method:** Quantitative Electrochemiluminescent Immunoassay (ECLIA)

**Calcitonin 0070006**

**Method:** Quantitative Chemiluminescent Immunoassay

**Metanephrines, Plasma (Free) 0050184**

**Method:** Quantitative Liquid Chromatography-Tandem Mass Spectrometry