Multiple Endocrine Neoplasia Type 1

Multiple endocrine neoplasia type 1 (MEN1) is a hereditary syndrome caused by pathogenic variants in the *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[1,2]

Symptoms

- MEN1 can include development of multiple endocrine and nonendocrine tumors[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

MEN1

Inheritance

Autosomal dominant

Tests to Consider

Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing and Deletion/Duplication 2005360

Method: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

Preferred initial test to confirm diagnosis of MEN1

Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing 2005359

Method: Polymerase Chain Reaction/Sequencing

Acceptable initial test to confirm diagnosis of MEN1

Familial Mutation, Targeted Sequencing 2001961

Method: Polymerase Chain Reaction/Sequencing

Useful when a pathogenic familial variant identifiable by sequencing is known

See Related Tests for tumor testing and screening including anterior pituitary and carcinoid tumor testing, gastrinoma testing, medullary thyroid carcinoma testing, pancreatic neuroendocrine tumor testing, parathyroid tumor testing, and pheochromocytoma testing.

Penetrance

Variable[4,5,6]

- ~50% by 20 years
- >95% by 40 years

De novo variants: ~10%

Variants

Inactivating variants of *MEN1* tumor suppressor gene

Test Interpretation

Clinical Sensitivity

Combined testing: ~94%

- Sequencing: 90%[3]
- Deletion/duplication: 4%[3]

Results

- Positive:
  - One pathogenic variant detected in *MEN1*
  - Confirms diagnosis and etiology of MEN1
- Negative:
  - No detectable pathogenic variant detected in *MEN1*
  - Reduces, but does not exclude, a diagnosis of 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 *MEN1*
- Diagnostic errors can occur due to rare sequence variations

References

1. Brandi ML. Rare Disease Database: multiple endocrine neoplasia type 1. National Organization for Rare Disorders. [Published: 2018; Accessed: Sep 2019]
2. Ki Wong F, Burgess J, Nordenskjöld M, et al. Multiple endocrine neoplasia type 1. Semin Cancer Biol. 2000;10(4):299-312. PubMed
3. Giusti F, Marini F, Brandi ML. Multiple endocrine neoplasia type 1. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews, University of Washington; 1993-2020. [Last Update: Dec 2017; Accessed: Feb 2020]
4. Online Mendelian Inheritance in Man. Multiple endocrine neoplasia type 1. [Edited: Feb 2017; Accessed: Mar 2020]
5. Bassett JH, Forbes SA, Pannett AA, et al. Characterization of mutations in patients with multiple endocrine neoplasia type 1. Am J Hum Genet. 1998;62(2):232-244. PubMed

6. Carroll RW. Multiple endocrine neoplasia type 1 (MEN1). Asia Pac J Clin Oncol. 2013;9(4):297-309. PubMed

Additional Resources

Thakker RV, Newey PJ, Walls GV, et al. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). J Clin Endocrinol Metab. 2012;97(9):2990-3011. PubMed

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, Serum 3002867

Method: Immunofluorescence

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

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
Content Review September 2019 | Last Update August 2020