# Multiple Endocrine Neoplasia Syndromes
## A Comprehensive Imaging Review

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**KEYWORDS**

• Multiple endocrine neoplasia • MEN1 • MEN2 • MEN4 • Neuroendocrine tumor

**KEY POINTS**

- Multiple endocrine neoplasia is composed of a series of genetically inherited disorders involving concomitant tumors within two or more endocrine organs.
- Patients with MEN1 develop tumors of the parathyroid gland, pancreas, and pituitary gland and adrenal cortical tumors and neuroendocrine tumors of the thymus, bronchi, and stomach.
- MEN2 is comprised of three subtypes (MEN2A, MEN2B, and familial medullary thyroid carcinoma), the hallmark of which is medullary thyroid cancer, adrenal pheochromocytoma, and parathyroid tumor.
- MEN4 represents a newly described group of patients who develop parathyroid and pituitary tumors.

## INTRODUCTION

Multiple endocrine neoplasia (MEN) encompasses a series of familial, genetically inherited conditions in which tumors simultaneously occur in two or more endocrine organs. MEN syndromes are autosomal-dominant disorders categorized into three main patterns: (1) MEN1 (Wermer syndrome), (2) MEN2 (including MEN2A or Sipple syndrome, MEN2B or Wagenmann-Froboese syndrome, and familial medullary thyroid cancer [FMTC]), and (3) MEN4. Although MEN1 and MEN2 are most common and usually manifest as distinct syndromes, other presentations do occur, including hyperparathyroidism–jaw tumor syndrome and "overlap syndromes," in which tumors typically associated with one syndrome develop in combination. This article outlines the imaging characteristics of the endocrine tumors that occur in patients with MEN syndromes.

## MEN1 SYNDROME

Patients with MEN1 (or Wermer) syndrome develop germline-inactivating mutations of the MEN1 tumor suppressor gene, resulting in tumors of the parathyroid gland (95%), pancreas (40%), and pituitary gland (30%).[1] Other tumors occurring with MEN1 include angiofibromas (88%), collagenomas (72%), adrenal cortical tumors (35%), and facial ependymomas (<5%).[1] Clinical symptoms of MEN1 syndrome almost uniformly present by the fifth decade and are seen in children at 5 years of age.[2–4]

Disclosures: None.

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**Table 1**
**Imaging features of parathyroid adenomas**

| | |
|---|---|
| Echogenicity on ultrasound | • Typically uniformly hypoechoic relative to the thyroid gland on gray-scale imaging (perhaps caused by compact cellularity)<br>• Commonly detected on gray-scale alone when >1 cm in size |
| Shape | • Usually oval or bean-shaped<br>• Larger adenomas can be multilobulated |
| Vascularity on ultrasound | • Classic extrathyroidal feeding vessel supplying the upper or lower pole of the parathyroid glad (usually a branch of the inferior thyroidal artery)<br>• Characteristic rim of vascularity (resulting from branching of the feeding vessel around the periphery of the gland before diving deeper) (Fig. 1)<br>• Color Doppler imaging of the overlying thyroid gland may show focal asymmetric hypervascularity, which may help direct identification of an underlying parathyroid adenoma |
| $^{99m}$Tc-sestamibi uptake | • Initial planar images shortly after radiotracer administration: uptake in thyroid gland and normal parathyroid tissue<br>• Early dynamic images: asymmetric focal activity within the abnormal parathyroid gland (adenoma or hyperplasia) superimposed on normal thyroid uptake<br>• Delayed images: retained radiotracer activity within hyperfunctioning parathyroid tissue (typically at 2-hour delay) (Fig. 2) |

*Data from* Johnson NA, Tublin ME, Ogilvie JB. Parathyroid imaging: technique and role in the preoperative evaluation of primary hyperparathyroidism. AJR Am J Roentgenol 2007;188(6):1706–15.

## *MEN1 Tumors*

### *Parathyroid tumors*

Parathyroid adenomas are the most common tumors associated with MEN1. They typically present as the initial manifestation of the syndrome, usually occurring in the third decade of life.[1] Patients with primary hyperparathyroidism can be asymptomatic with biochemical abnormalities or demonstrate the classic symptoms of abdominal pain/constipation/peptic ulceration, nephrolithiasis/polyuria/polydipsia, confusion/dementia/depression, and fatigue/aching/fractures (commonly referred to as moans, stones, groans, and bones).

Cross-sectional investigation for a parathyroid adenoma usually begins with high-resolution ultrasound, which has a sensitivity of up to 82% when performed by experienced sonographers.[5] Computed tomography (CT) does not add additional information other than localizing ectopic parathyroid glands within the superior mediastinum. Parathyroid glands are typically T1 hypointense and T2 hyperintense on MR imaging. Although MR imaging is slightly more sensitive than CT in the detection of parathyroid adenomas, it is also not frequently used for this purpose. Planar and single-photon emission CT sestamibi imaging has a high sensitivity for detection of parathyroid adenomas, particularly when used in conjunction with ultrasound. Adenomas demonstrate asymmetric focal radiotracer uptake with retention on delayed imaging (Table 1).

### *Pancreatic neuroendocrine tumors*

Pancreatic neuroendocrine tumors (NETs) are the second most common neoplasm associated with MEN1, occurring in up to 80% of patients.[4] NETs are functioning or nonfunctioning, and present with biochemical abnormalities or screening imaging of patients with known MEN syndromes.[3] More than half of pancreatic NETs are gastrinomas; one-third are insulinomas; and less than 5% are glucagonomas, vasoactive intestinal

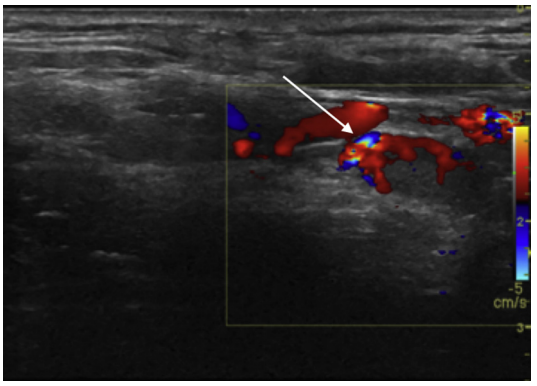


**Fig. 1.** Color Doppler sagittal ultrasound image demonstrating an ovoid soft tissue nodule, which is slightly hypoechoic to the adjacent thyroid gland (not shown). The peripheral flow emanating from a feeding vessel at the superior pole of this nodule (*arrow*) is the typical sonographic appearance of a parathyroid gland.