Neoplasms of the Parathyroid Glands

CLASSIFICATION OF NEOPLASMS OF THE PARATHYROID GLANDS (Box 33-1)

PARATHYROID ADENOMA (Figs. 33-1 through 33-22, Table 33-1)

Definition: Benign neoplasm of the parathyroid parenchymal cells, including chief cells and/or oncocytic cells.

Clinical

- More common in females (F:M = 3 to 4:1); occur over a broad age range but are most frequently discovered in the fourth and fifth decades.
- Represents the major cause of primary hyperparathyroidism.
- Clinical findings are essentially the same as those associated with primary hyperparathyroidism due to hyperplasia (see Chapter 32).
- As in primary hyperparathyroidism due to hyperplasia, the symptomatology in patients with parathyroid adenomas is changing as a result of routine biochemical screening and early detection:
  - Hypercalcemia may be incidentally discovered in asymptomatic patients, and many patients complain only of fatigue, weakness, or depression.
  - Nephrolithiasis is documented in 69% of men and 36% of women with adenomas overall, but the incidence has been decreasing in recent years to between 5% and 20%.
  - Severe bone disease, once a common complication, is now rare; however, osteopenia is often present, and joint disease similar to that found in patients with parathyroid hyperplasia occurs.
  - Serum calcium levels are generally higher than in patients with primary chief cell hyperplasia but not usually as high as in parathyroid carcinoma.
  - Hypophosphatemia, hyperphosphaturia, and elevated serum parathormone levels are found.

- Rarely parathyroid adenomas present as a palpable mass.
- Radiology:
  - Several imaging methods have been used for localization of hyperfunctioning parathyroid tissue, including retrograde phlebotomy for determination of serum parathormone levels, CT scanning, ultrasonography, magnetic resonance imaging (MRI), thallium subtraction scanning, and technetium-99m sestamibi imaging.
  - Technetium-99m sestamibi imaging appears to be the most useful, with localization of more than 90% of adenomas, and has been most widely used in patients with anatomic distortion due to previous surgery and in patients who are high surgical risks; however, more routine utilization has gained support.
  - Multidimensional CT (referred to as 4D-CT) emerging technique used in detection when a lesion is not identified by more conventional techniques (e.g., ultrasonography, sestamibi imaging).
- May be associated with hyperparathyroidism-jaw tumor syndrome (HPT-JT):
  - Autosomal-dominant disorder with germline mutation in HRPT-2 gene on chromosome 1q25-31.
  - Characterized by:
    - Parathyroid adenoma or carcinoma
    - Fibro-osseous lesions of the jaw (e.g., ossifying fibroma of mandible or maxilla): 30% of cases
    - Renal cyst, hamartoma, carcinoma: 20% of cases
  - Approximately 80% of patients develop hyperparathyroidism:
    - Usually presents late in adolescence
    - Hypercalcemia tends to be severe.
    - Higher incidence of parathyroid carcinoma in MEN-1 and MEN-2A
  - Renal lesions may include:
    - Renal cysts, polycystic renal disease, renal hamartoma
    - Papillary renal cell carcinoma, renal cortical adenomas, Wilms tumor
- 90% of adenomas are found in parathyroid glands in their usual locations:
  - Lower glands are more commonly involved.
CHAPTER 33 Neoplasms of the Parathyroid Glands

- Reports of adenomas occurring in supernumerary glands include tumors arising in the vagus nerve, pericardium, or other soft tissue sites in the neck.

**Pathology**

**Cytology**

- Occasionally enlarged parathyroid glands, either hyperplastic or, more commonly, adenomatous, have been serendipitously subjected to fine-needle aspiration as a clinically suspected “solitary thyroid nodule”; reports of ultrasonically guided fine-needle aspiration for localization and confirmation of parathyroid proliferative disease have appeared.

- An awareness of the typical cytologic appearance of adenomas parathyroid tissue can be helpful during intraoperative examination of biopsies during a neck exploration for hyperparathyroidism, as examination of touch preparations provides a rapid means of confirming the presence of parathyroid tissue.

- Aspirates of parathyroid tissue typically contain numerous naked nuclei, as well as small sheets of cells, sometimes forming acinar or follicular structures; small aggregates of dense colloid-like material may be seen but are not numerous.

- The cells are generally small, with predominantly round nuclei; anisonucleosis in scattered cells and occasional large, atypical, naked nuclei are common.

- The cytoplasm is granular and may exhibit scattered large metachromatic granules with a May-Grünwald-Giemsa stain; Papanicolaou-stained cells have clear to finely granular cytoplasm.

- The nuclei are generally hyperchromatic with coarse chromatin typical of neuroendocrine cells.

- The distinction from follicular epithelium of the thyroid may be difficult, although the cells are usually smaller than those of the thyroid:

**Gross**

- Adenomas are almost always solitary (see below for Double Adenoma).

- Adenomas have rounded borders, are firm, brown to tan, and are contained within a delicate capsule; they may be ovoid or lobulated.

- A remnant of uninvolved parathyroid tissue at the periphery of the tumor may be visible.

- Cystic change may be present, and when marked may mask the neoplastic nature of the proliferation; marked cystic degeneration is frequently associated with scarring and calcification.

- There is significant variation in weight, with most adenomas weighing between 0.3 and 1.0 g.

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**Fig. 33.1. Classic parathyroid adenoma identified on ultrasonography.**

A, Sagittal ultrasonographic image shows a hypoechoic, well-defined mass just below the inferior pole of the right thyroid gland. B, Transverse ultrasonographic image with color flow Doppler shows the increased peripheral arch of vascularity of the mass frequently seen with adenomas. (From Som PM, Curtin HD: Head and neck imaging, ed 5, Philadelphia, 2011, Elsevier, Fig. 41-95, p 2663.)
Fig. 33-2. Parathyroid adenoma.

Parathyroid adenoma detected by $^{201}$Tl/$^{99m}$Tc-pertechnetate subtraction imaging (A to C) and by $^{99m}$Tc-sestamibi subtraction imaging with $^{123}$I (D). A, $^{99m}$Tc-pertechnetate concentrated within the thyroid gland. B, $^{201}$Tl concentrated within thyroid and parathyroid glands. C, Computer techniques allow technetium concentrated in the thyroid gland to be subtracted from thallium that accumulates within thyroid and parathyroid tissue. After thyroid subtraction, a parathyroid adenoma is noted as a focus of increased thallium uptake (arrows). D, $^{99m}$Tc-sestamibi subtraction imaging with $^{123}$I shows an adenoma below the inferior pole of the left lobe of the thyroid gland. (From Som PM, Curtin HD: Head and neck imaging, ed 5, Philadelphia, 2011, Elsevier, Fig. 41-103, p 2669.)

**Histology**

- Well circumscribed and uncommonly surrounded by a thin fibrous capsule;
- Complete encapsulation not commonly seen;
- Hypercellular proliferation lacking intraparenchymal fat cells with diffuse growth; vague nodularity may be present and rarely may be multinodular.
- A rim of non-neoplastic parathyroid tissue found in association with only about half of the adenomas;
  - Very helpful finding, if present, in making the distinction between adenoma and hyperplasia;
  - “Rim” generally contains abundant stromal fat cells, in contrast to the very cellular adenoma.
Fig. 33-3. 4D-CT in the detection of a small adenoma.

A, Unenhanced CT scan at the level of the lower poles of the thyroid gland shows no discrete adenoma.

B, Immediate first-pass image following contrast administration shows a tiny, avidly enhancing adenoma in the right paraesophageal region (anterior to *).

C, Second pass at 60 seconds shows some washout of enhancement, which is clearly less than on the immediate postcontrast scan.

D, Last pass delayed image at 90 seconds shows little enhancement of the adenoma, which is still readily identifiable. On another patient:

E, Coronal reconstructed CT image from immediate first-pass enhanced CT scan shows a large adenoma below the inferior pole of the left thyroid lobe (arrow).
Parathyroid Glands

Fig. 33-4. Parathyroid adenoma.
Parathyroid adenoma appearing as a large encapsulated lesion bulging into the operative field. Adenomas are typically easily dissected free of adjacent structures; difficulty in removing a parathyroid tumor should raise suspicion for a parathyroid carcinoma.

Fig. 33-5. Parathyroid adenoma.
Cut section of a parathyroid adenoma shows a homogeneous, light tan appearance; a delicate inconspicuous capsule is present. A remnant of uninvolved parathyroid tissue is not grossly visible.

F, Coronal maximum intensity projection image in anterior projection shows the adenoma (arrow). G, Coronal maximum intensity projection image in the posterior projection shows the adenoma (*) posterior to the common carotid artery.

(Cases courtesy of Dr. Lawrence Ginsberg. From Som PM, Curtin HD: Head and neck imaging, ed 5, Philadelphia, 2011, Elsevier, Fig. 41-101, p 2667.)
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Fig. 33-6. Parathyroid adenoma.
Parathyroid adenoma appearing as a nodular focus with cystic change and associated calcification.

- Nuclei of residual normal or atrophic parathyroid gland typically smaller than the nuclei of the adenoma.
- Growth patterns include solid (diffuse) sheets, cords, nests, acini, follicles, and microcysts.
- Follicle formation may contain eosinophilic “colloid-like” material.
- Distinct trabecular pattern is uncommon.
- Predominantly composed of chief cells.
- Nuclei round and regular with central to slightly basophilic location within the cell and have inconspicuous nucleoli; usually lack significant pleomorphism:
  - Cells with hyperchromatic enlarged nuclei as well as multinucleated cells are common and can be found scattered throughout the tumor or may be clustered in small foci; these scattered atypical nuclei are not an indicator of malignancy in the absence of other evidence of a malignancy (see section on parathyroid carcinoma).
- Cytoplasm varies, including slightly eosinophilic, amphophilic, clear, or oxyphilic.
- Chief cells of an adenoma frequently larger than the non-neoplastic chief cells in the uninvolved rim of parathyroid tissue, if one is present.
- Oncocytic cells may be seen in variable numbers, focally admixed with chief cells or as nodular aggregates.
- Mitotic figures are identifiable in many adenomas, but usually number fewer than 1 per 10 high-power fields; mitotic rates as high as 4 mitoses per 10 high-power fields have been described in occasional cases.
- Delicate vascular network composed of thin fibrovascular stroma, sinusoid-like blood vessels or capillaries traverse the neoplasm.

Fig. 33-7. Parathyroid adenoma, fine-needle aspiration.

A, Cellular smear with cohesive groups of small epithelial cells and fragments of pink colloid-like material may suggest a follicular neoplasm of thyroid origin; the colloid-like material, however, is somewhat sparse (Diff-Quick stain). B, The cells are fragile, yielding smears with numerous naked nuclei, some of which are large and hyperchromatic; scattered large atypical nuclei are common in parathyroid adenomas (Diff-Quick). C, Papanicolaou-stained smear shows scattered compact clusters of small epithelial cells with distinct cell borders and a rim of clear cytoplasm; the nuclei are small and hyperchromatic.
Parathyroid adenoma.

**A.** Parathyroid adenoma characterized by hypercellular proliferation devoid of intraparenchymal fat, which in the lower portion of the illustration has a well-defined capsule separating the cellular proliferation from a thin rim of compressed normal parathyroid gland parenchyma. **B.** At higher magnification, the cells and nuclei of the adenoma (bottom) are larger than those of the residual non-neoplastic parathyroid gland parenchyma (top).

- Intraparenchymal fat cells absent but may focally be seen as single cells or groups in the peripheral aspect of the neoplasm.
- Neoplastic cells usually have less intracellular fat than do the cells in the uninvolved (or suppressed) parathyroid tissue, either in other glands or in a rim of non-neoplastic parathyroid tissue in an adenomatous gland.
- Cells with markedly enlarged and hyperchromatic pleomorphic or bizarre-appearing nuclei may be present and when present:
  - Appear admixed with bland-appearing nuclei.
  - Tend to be focally and not diffusely identified.
  - Occur in the absence of increased mitotic activity and/or other features that may be associated with parathyroid carcinoma.

**Fig. 33-8. Parathyroid adenoma.**

- Reactive and degenerative changes may be present, including cyst formation, edema, fibrosis, hemorrhage (fresh or in the form of hemosiderin deposition), or infarction:
  - May occur spontaneously or may occur following a traumatic event such as prior surgery to the neck or fine-needle aspiration biopsy.
  - Presence of reactive and degenerative changes, especially fibrosis, may cause adherence to adjacent structures, suggesting invasive growth and a possible diagnosis of parathyroid carcinoma.
  - Infarcted tumor may retain antigenicity for parathyroid hormone.
- Rarely, an associated mature lymphocytic cell infiltrate may be present.
- Uninvolved parathyroid parenchymal cells in patients with adenomas are typically smaller and often have more stromal fat cells than the glands in patients.
**Fig. 33-10. Parathyroid adenoma.**
Parathyroid adenomas may be composed of an admixture of (A) chief cells, (B) oncocytic cells, and/or (C) clear cells. In any given tumor two or all of the cell types may be present, creating a mosaic pattern.

**Fig. 33-11. IHC staining in parathyroid adenoma.**
Lesional cells of parathyroid adenomas are immunoreactive for (A) parathyroid hormone and (B) parafibromin (diffuse nuclear staining).

**Fig. 33-12. Parathyroid adenoma.**
Parathyroid adenoma showing cord-like or trabecular growth composed of cells with clear-appearing cytoplasm.
Fig. 33-13. Parathyroid adenoma.

A, Parathyroid adenoma showing a follicular pattern of growth (so-called follicular variant) that may cause confusion with thyroid follicular neoplasms; immunoreactivity for (B) parathyroid hormone and (C) parafibromin (nuclear), coupled to the absence of thyroglobulin and TTF1 (not shown) allow for differentiating parathyroid adenoma from a thyroid follicular lesion.

Fig. 33-14.

A, Parathyroid adenoma composed of uniform and bland-appearing nuclei in lower portion of image as well as numerous large cells with hyperchromatic nuclei; intralesional fibrosis is also present. B, Bizarre-appearing pleomorphic and hyperchromatic nuclei admixed with bland-appearing nuclei. Such findings in the absence of increased mitotic activity and/or other features associated with parathyroid carcinoma can be seen in parathyroid adenomas.

without hyperparathyroidism; they also have more cytoplasmic fat, often found as large droplets, than normally functioning parathyroid glands.

- Histochemical stains:
  - Colloid-like material in follicular structures are PAS positive.
  - Considerable variation in the literature regarding the utility of fat stains in the diagnosis of parathyroid proliferative diseases.
  - Generally, hyperfunctioning cells have a significantly decreased amount of intracellular fat (using Sudan black or oil red O) compared with
Parathyroid adenoma with associated reactive and degenerative changes, including fibrosis and hemorrhage may result in adherence to surrounding structures, clinically suggesting a possible diagnosis of parathyroid carcinoma. Such changes may occur spontaneously or may occur following a traumatic event such as prior surgery to the neck or fine-needle aspiration biopsy.

- Normal or suppressed parenchymal cells; there is, however, variability in this finding.
- Fat stains, when used with adequate clinical information, intraoperative findings, and histologic examination, are useful if their limitations are kept in mind.
- Immunohistochemistry:
  - Positive for parathyroid hormone and parafibromin (nuclear staining):
  - Majority of parathyroid adenomas express parafibromin
  - Loss of parafibromin expression may be seen in patients with hyperparathyroidism-jaw tumor syndrome indicative of gene inactivation through mutation of the HRPT-2 gene.
  - Cytokeratin, chromogranin A positive
  - Calcitonin and synaptophysin typically negative but in small percentage of cases may be focally positive
  - PAX8 (nuclear) reactivity present in approximately 40% of adenomas and hyperplasia
  - Galectin 3 rarely positive (< 5%).
  - Ki67 (MIb1) proliferative index is low:
  - An index greater than 5% should raise suspicion for carcinoma, but the diagnosis of carcinoma requires confirmatory diagnostic findings.
  - Proliferative indices in differentiating adenoma from carcinoma are of limited utility given overlapping findings in these lesions.

- Cyclin D1 staining in 39% of cases
- Negative for thyroglobulin and TTF-1
- Electron microscopy:
- Adenomas associated with very high serum calcium levels may have a large number of microvilli, which are thought to reflect a higher level of endocrine activity
- Adenomas often have more abundant rough endoplasmic reticulum and more prominent Golgi apparatus than non-neoplastic cells.
- Annulate lamellae may be seen.
- Cytogenetic and molecular findings:
- Approximately 5% show pericentric inversion of chromosome 11, causing translocation of cyclin

**Fig. 33-15. Parathyroid adenoma.**

**Fig. 33-16. Parathyroid adenoma.**

**A,** Parathyroid adenoma with infarction but retention of ghost outlines of the neoplasm. Note the residual noninfarcted and non-neoplastic parathyroid parenchyma, including mature fat. **B,** Parathyroid hormone immunoreactivity is present in the infarcted tumor and in the residual non-neoplastic parathyroid parenchyma.
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**Fig. 33-17. Intrathyroidal parathyroid adenoma.**

A. Intrathyroidal parathyroid adenoma (lower) predominantly composed of chief cells as well as oncocytic cells (arrow) and clear cells (arrowhead) surrounded by thyroid follicular epithelial cells and an adenomatoid nodule (upper right). B. Histologically, the intrathyroidal parathyroid adenoma shows typical morphologic findings predominantly composed of chief cells and sharply separated from the colloid-filled thyroid follicles (left side).

**Fig. 33-18. Oncocytic parathyroid adenoma.**

A. The tumor is encapsulated and (B) exclusively composed of cells with granular eosinophilic-appearing cytoplasm.

- Distinction between hyperplasia and adenoma may be extremely difficult and requires the pathologic examination of more than a single gland.
- Diagnostic criteria for double adenomas include:
  - 2 enlarged, hypercellular parathyroid glands
  - Intraoperative confirmation that remaining parathyroid glands are normal and/or biopsy proven histologically normal parathyroid glands
  - Absence of family history of MEN or familial hyperparathyroidism
  - Permanent cure of hypercalcemia following excision of enlarged glands:
    - Arguably the most definitive criterion
    - Requires years of follow-up to include monitoring of serum calcium and parathyroid hormone levels

**Double Parathyroid Adenomas**

- Most “multiple adenomas” represent cases of asymmetric or nodular hyperplasia:
  - 20% have somatic mutation in MEN-1 gene at 11q13 in 40% of cases
  - Absence of RET mutation
  - 5% have somatic mutation in CDKN1B gene (p27Kip1)

D1 (CCND-1/PRAD-1) gene with parathyroid hormone gene, resulting in overexpression of cyclin D1.

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Fig. 33-19. Parathyroid lipoadenoma.
Lipoadenomas form cords, islands, and follicles admixed with stromal fat cells with mature adipocytes, the latter making up from 20% to 90% of the neoplasm. Lipoadenomas are encapsulated and may be associated with a rim of “normal” gland (not shown) and can be difficult to distinguish from normal parathyroid gland in small biopsies.

Fig. 33-20. Parathyroid adenoma associated with osteitis fibrosa cystica.
Left panel, The adenoma is typical with a distinct capsule and a rim of normal parathyroid parenchyma including mature fat (lower); right panel, the tumor is composed of chief cells. The patient had a pathologic fracture of the humerus as well as generalized osteopenia with multiple lytic skeletal lesions. At the time of presentation he had hypercalcemia. The initial clinical impression was metastatic carcinoma with secondary hypercalcemia.

Histologic Variants of Parathyroid Adenoma
- Oncocytic (oxyphilic) adenoma (see Fig. 33-18): Exclusively composed of oncocytic cells with prominent eosinophilic granular cytoplasm.
- Demographic features are similar to those of the more common adenomas composed of chief cells.
- Thought to be nonfunctional; usually associated with lesser degree of hypercalcemia; however, several reports document an association with primary hyperparathyroidism.
- Composed of large cells with abundant eosinophilic granular cytoplasm and hyperchromatic nuclei:
  - Scattered large atypical nuclei or multinucleated cells may be seen.
  - Cytoplasm is stuffed with mitochondria on electron microscopy.
- An important differential consideration is the frequent presence of nodular oncocytic cell change seen in normal glands with increasing age.
- Intrathyroidal localization may suggest a diagnosis of an oncocytic thyroid follicular (so-called Hurthle cell) neoplasm.
- Parathyroid oncocytic adenomas have more distinct cell membranes.

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Brown tumor of hyperparathyroidism characterized by proliferation of numerous multinucleated giant cells and mononuclear cells, as well as foci of hemorrhage; the giant cells tend to be clustered rather than diffusely distributed. The nuclei of the multinucleated giant cells are rather bland and are similar to those of the surrounding mononuclear cells. A mitotic figure (arrow) is present. The brown tumor of hyperparathyroidism is histologically similar to giant cell (reparative) granuloma, thereby requiring clinical and laboratory correlation to differentiate these lesions.

- Presence of thyroglobulin and TTF1 support lesion of thyroid origin.
- Lipoadenoma (see Fig. 33-19)
- Also referred to as parathyroid hamartoma
- Rare benign neoplasm characterized by proliferation of chief and oxyphilic cells forming cords, islands, and follicles admixed with mature adipocytes.
- Mature adipocytes make up from 20% to 90% of the neoplasm.
- Circumscription and/or encapsulation as well as u0675 large size (1 to 15 cm) support adenomatous nature:
  - May be associated with a compressed rim of u0680 “normal” gland
  - May be difficult to recognize as “abnormal” u0685 parathyroid tissue in small biopsies, when they are easily mistaken for normal parathyroid tissue because of the abundance of stromal fat
  - Stromal fat often contains areas of fibrosis or u0690 myxoid alteration.
  - Most are associated with hyperparathyroidism. u0695
- Other rare variants of parathyroid adenoma include: u0700
  - Papillary variant characterized by prominent u0705 papillary architecture:
    - May not be a “true” variant but papillary u0710 architecture, especially in association with fibrosis and hemorrhage (recent and remote), likely is a reactive/regenerative phenomenon
  - Follicular variant characterized by prominent u0715 follicular (acinar) architecture
  - Water-clear variant characterized by presence of u0720 polygonal cells with clear cytoplasm and distinct cell membranes.
- Atypical parathyroid adenoma: u0725
  - Definition: parathyroid tumor showing features u0730 worrisome for parathyroid carcinoma but lacking absolute diagnostic features for parathyroid carcinoma
  - Synonyms include atypical parathyroid neoplasm, u0735 parathyroid neoplasm of uncertain biologic significance, or parathyroid neoplasm inconclusive for malignancy
- Atypical histologic features suggesting carcinoma u0740 but falling short for this diagnosis may include:
  - Capsular irregularities or invasion without u0745 infiltration into adjacent soft tissues
  - Increased mitotic activity (>5 per 10 high- u0750 power fields)
  - Intralysosomal fibrosis characterized by broad u0755 fibrous bands coursing through the lesion
  - Coagulative necrosis u0760
  - Diffuse cellular atypia u0765
  - Diffuse sheet-like growth of monotonous u0770 cells with increased nuclear-to-cytoplasmic ratio
  - Macronucleoli in many cells u0775
- Atypical parathyroid adenomas lack conclusive u0780 features diagnostic for carcinoma including:
  - Invasion of surrounding soft tissues u0785
  - Invasion of surrounding structures including u0790 thyroid gland, larynx, trachea, pharynx, esophagus, carotid artery, recurrent laryngeal nerves
  - Angioinvasion u0795
  - Perineural invasion u0800
  - Metastasis u0805

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### TABLE 33-1 Comparative Features of Parathyroid Proliferative Diseases

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hyperplasia</th>
<th>Adenoma</th>
<th>Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender; age</td>
<td>Slight female predilection; most common in 5th-6th decades</td>
<td>More common in women; most common in 4th decade</td>
<td>Equal gender predilection; wide age range</td>
</tr>
<tr>
<td>Clinical</td>
<td>Asymptomatic or complaints of lethargy, weakness, polyuria, polydipsia, arthralgia, constipation, and depression</td>
<td>Similar to hyperplasia</td>
<td>Similar to hyperparathyroidism of benign cause but more severe due to the higher serum calcium levels; higher proportion of renal disease (nephrolithiasis) and bone disease; peptic ulcer disease; palpable neck mass more common than in adenoma</td>
</tr>
<tr>
<td>Serum calcium</td>
<td>11.7 mg/dl (average)</td>
<td>12.5-13.5 mg/dl</td>
<td>Often &gt;14 mg/dl</td>
</tr>
<tr>
<td>Intraoperative findings</td>
<td>2 or more glands enlarged, easily dissected; enlargement may be very asymmetric</td>
<td>1 gland enlarged; easily dissected; more frequent in lower glands or ectopic sites</td>
<td>1 gland enlarged; often adherent to surrounding tissues</td>
</tr>
<tr>
<td>Weight</td>
<td>Total gland weight usually &lt;1 g, but may be up to 5 g</td>
<td>0.3-1.0 g commonly, but may weigh several grams in patients with bone disease</td>
<td>&gt;1.5 g (often much larger)</td>
</tr>
<tr>
<td>Capsule</td>
<td>Circumscribed by capsule of parathyroid gland, may be incomplete. No compressed rim of atrophic or normal parathyroid tissue</td>
<td>Thin tumor capsule, often surrounded by rim of uninvolved parathyroid, which may appear atrophic</td>
<td>Thickened capsule; rim of normal parathyroid rarely seen</td>
</tr>
<tr>
<td>Gross appearance</td>
<td>Gray-brown, soft. Cut surface may be homogeneous or nodular. Lacks fibrous bands</td>
<td>Red-brown, firm. Usually homogeneous, lacks fibrous bands</td>
<td>Gray-white, firm, often lobulated or irregular. Fibrous bands often produce coarse nodularity</td>
</tr>
<tr>
<td>Histologic pattern</td>
<td>Diffuse or nodular, sometimes pseudofollicular or acinar</td>
<td>Diffuse or nodular, frequently pseudofollicular or acinar</td>
<td>Diffuse, nodular, pseudofollicular, or acinar; often trabecular pattern with distinctive nuclear palisading predominates</td>
</tr>
<tr>
<td>Cytologic features</td>
<td>Chief cells predominate; transitional and oncocytic cells often present</td>
<td>Chief cells predominate, but mixture of chief, transitional, and oncocytic cells may be seen; rarely, purely oncocytic</td>
<td>Cells usually resemble chief cells, but variable cytoplasmic oncocytic change may be seen; cell borders often indistinct</td>
</tr>
<tr>
<td>Intracytoplasmic lipid</td>
<td>Decreased</td>
<td>Decreased in tumor; abundant in atrophic rim of parathyroid</td>
<td>Usually absent</td>
</tr>
<tr>
<td>Stromal fat cells</td>
<td>Scanty to absent</td>
<td>Usually absent in tumor; present rim of atrophic parathyroid</td>
<td>Absent</td>
</tr>
<tr>
<td>Nuclear morphology</td>
<td>Normal to slightly increased N-to-C ratio; usually without nuclear pleomorphism</td>
<td>Nuclei enlarged, with variability in size; scattered groups of large pleomorphic, hyperchromatic nuclei, or multinucleated cells</td>
<td>Increased N-to-C ratio; enlarged atypical nuclei; often with monotonous (bland appearing) nuclei</td>
</tr>
<tr>
<td>Nucleoli</td>
<td>Inconspicuous to small</td>
<td>Inconspicuous to small</td>
<td>Frequently prominent and enlarged</td>
</tr>
<tr>
<td>Mitoses</td>
<td>Common (60% of cases; most with &lt;1 mitotic figure/10 HPF)</td>
<td>Common (70% of cases; most with &lt;1 mitotic figure/10 HPF)</td>
<td>Common (80% of cases), may include atypical mitoses; may be numerous</td>
</tr>
</tbody>
</table>

*Continued*
### TABLE 33-1 Comparative Features of Parathyroid Proliferative Diseases—cont’d

<table>
<thead>
<tr>
<th>Hyperplasia</th>
<th>Adenoma</th>
<th>Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsular and vascular invasion</td>
<td>Absent</td>
<td>Absent; entrapment of tumor cells may occur in capsule if degenerative changes present</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remainder of gland</td>
<td>Entire gland is abnormal</td>
<td>Normal or atrophic</td>
</tr>
<tr>
<td>Degenerative changes</td>
<td>May be seen in very large glands includes hemorrhage, areas of fibrosis, and cystic change</td>
<td>Common, especially in larger adenomas; includes hemorrhage, fibrosis, and cystic change, sometimes calcification</td>
</tr>
<tr>
<td>Treatment</td>
<td>Subtotal parathyroidectomy with surgical removal of three glands, leaving a remnant of the 4th or total parathyroidectomy* with autotransplantation of parathyroid tissue in forearm</td>
<td>Surgical removal of the enlarged gland</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Excellent</td>
<td>Excellent</td>
</tr>
<tr>
<td>Recurrence and metastasis</td>
<td>Recurrence in approximately 16% of cases due to inadequate neck exploration and may not be evident for years</td>
<td>Absent</td>
</tr>
<tr>
<td>Familial and/or MEN association</td>
<td>Yes, in approximately 20% of cases</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>

- **Differential Diagnosis**
  - Primary chief cell hyperplasia (see Table 33-1)
  - Parathyroid carcinoma (see Table 33-1)
  - Follicular neoplasm of thyroid gland

- **Treatment and Prognosis**
  - Most widely accepted therapy is excision of the adenomatous gland with biopsy of at least one additional gland that is “normal” in size

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*Particularly in cases of familial hyperparathyroidism.*

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CHAPTER 33 Neoplasms of the Parathyroid Glands

Some favor a full bilateral neck exploration with subtotal parathyroidectomy and have reported a lower incidence of recurrent hypercalcaemia that required reoperation:

- There is an increased incidence of postoperative hypoparathyroidism with this procedure.
- Recurrence rates vary significantly and may reflect problems in classification, particularly in cases of hyperplasia with nodules, which may erroneously be designated as adenomas.

Although generalized osteopenia is now more common, osteitis fibrosa cystica, also known as brown tumor of hyperparathyroidism is occasionally seen (see Figs. 33-20 to 33-22):

- May occur in hyperparathyroidism of any cause but is related to degree and duration of serum calcium elevation
- Lesions are characterized by resorption of bone, which is replaced by fibrous tissue, probably as a reparative response to microfractures
- Hemorrhage within the fibrous tissue leads to the accumulation of hemosiderin and a proliferation of multinucleated giant cells in addition to the osteoclasts
- With time degenerative changes lead to the formation of cystic spaces
- Osteitis fibrosa cystica cannot be distinguished histologically from the giant cell (reparative) granuloma of the jaw, clinical information is needed.

Recurrent hyperparathyroidism following surgery for an adenoma may also result from incomplete excision, rupture of the tumor capsule with spillage into the operative field, or from hyperfunction of autografted parathyroid tissue following subtotal parathyroidectomy.

PARATHYROID CARCINOMA

(Figs. 33-23 through 33-38, see Table 33-1)

Definition: Malignant neoplasm of parathyroid parenchymal cells.

Clinical

- Rare neoplasm; responsible for approximately 2% of cases of hyperparathyroidism
- No gender predilection; most common in fifth and sixth decades
- Affect patients approximately a decade younger than those with adenomas
- Rare cases reported in children
- Clinical findings associated with parathyroid carcinoma are listed in Box 33-2.

Most patients have severe hypercalcaemia and hypophosphatemia:
- Mean serum calcium 14.0 mg/dl, in contrast to mean serum calcium of 12.0 mg/dl in benign hyperparathyroidism
- Occasional normocalcemic patients may occur.
- Symptoms are due to excessive parathyroid hormone secretion and are similar to those in patients with hyperparathyroidism of benign cause but tend to be more severe due to the higher serum calcium levels:
  - Presenting symptoms include polyuria, polydipsia, fatigue and weakness, depression, bone pain and fracture (high incidence in earlier series), renal colic and nephrolithiasis (up to two thirds of patients in earlier studies, but probably decreasing with routine biochemical screening and earlier detection), peptic ulcer disease, and recurrent pancreatitis.
  - Palpable neck masses more common than in hyperplasia or adenoma.
- Etiology is unknown:
  - Most cases are sporadic.
  - Loss of the retinoblastoma (Rb) tumor-suppressor gene may play an important role in the development of parathyroid carcinoma, and its absence may be helpful in distinguishing parathyroid adenoma from carcinoma.
  - Some cases occur in hyperparathyroidism-jaw tumor syndrome, MEN, or familial isolated hyperparathyroidism.
  - External beam irradiation to the neck may be a possible risk factor.
  - Rare cases occur in patients with secondary hyperparathyroidism, possibly linking the development of parathyroid carcinoma from parathyroid adenoma or hyperplasia.
  - May be associated with hyperparathyroidism-jaw tumor syndrome (HPT-JT):
    - Autosomal-dominant disorder with germline mutation in HRPT-2 gene on chromosome 1q25-31
    - Characterized by:
      - Parathyroid adenoma or carcinoma
      - Fibro-osseous lesions of the jaw (e.g., ossifying fibroma of mandible or maxilla): 30% of cases

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Fig. 33-23. Parathyroid carcinoma in a patient with severe hyperparathyroidism.

A, Axial T2-weighted MR image shows a demarcated 2.5-cm mediastinal mass (*) that represents a parathyroid carcinoma. B, Axial T2-weighted MR image of another patient with hypercalcemia shows a nonhomogeneous mass in the right tracheoesophageal groove. The margins are slightly unsharp. This is a parathyroid carcinoma. C, Axial T2-weighted MR image shows a large mass in the right tracheoesophageal groove in this patient with severe hypercalcemia. At surgery, this was a parathyroid carcinoma. (From Som PM, Curtin HD: Head and neck imaging, ed 5, Philadelphia, 2011, Elsevier, Fig. 41-110, p 2674.)

- Renal cyst, hamartoma, carcinoma: 20% of cases
- Approximately 80% of patients develop hyperparathyroidism.
- Usually presents late in adolescence
- Hypercalcemia tends to be severe.
- Higher incidence of parathyroid carcinoma in comparison with patients with MEN-1 and MEN-2A

- Renal lesions may include:
  - Renal cysts, polycystic renal disease, renal hamartoma
  - Papillary renal cell carcinoma, renal cortical adenomas, Wilms tumor

**Radiology**
- Imaging procedures are of similar utility as in para-

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CHAPTER 33 Neoplasms of the Parathyroid Glands

Pathology

• Pathologic findings potentially associated with parathyroid carcinoma are listed in Table 33-2.

Gross

• Average size is larger than parathyroid adenomas; mean weight 6.7 g (range 1.5 to 27 g), although smaller tumors are being identified more often in recent years.
• May be encapsulated or infiltrative

Fig. 33-24. Parathyroid carcinoma.
Parathyroid carcinoma appearing as a large tumor with areas of cystic degeneration associated with large nodules of viable tumor; the capsule is grossly thickened.

Fig. 33-25. Parathyroid carcinoma.
Parathyroid carcinoma appearing as an irregular, infiltrative, indurated, white neoplasm adherent to the adjacent thyroid lobe (on the left). Difficulties in dissection a parathyroid lesion from adjacent structures is suggestive, although not definitively diagnostic, for carcinoma. Histologic confirmation is always required for a diagnosis of parathyroid carcinoma.

• Brown to gray-white, carcinomas may have a smooth, firm cut surface indistinguishable from an adenoma or may be distinctly indurated.
• Difficulty in dissection of the tumor and adherence to and invaded into the thyroid gland are common intraoperative observations.

Histology

• Histologic criteria in diagnosing parathyroid carcinoma are detailed in Table 33-2.
• Many parathyroid carcinomas are encapsulated, and usually the capsule of a carcinoma is thicker than that seen in most adenomas:
  • Some adenomas with reactive and degenerative changes have thick and uneven capsules.

Some parathyroid carcinomas like this one are more advanced at presentation with extensive invasion of surrounding tissues. Cases such as this one are rare today as a result of routine biochemical screening of most populations in developed countries.
SECTION 9  Parathyroid Glands

Fig. 33-28. Parathyroid carcinoma.
Parathyroid carcinoma with acellular fibrous bands coursing through the neoplasm dividing the tumor into multiple nodules.

Fig. 33-29. Parathyroid carcinoma.
Parathyroid carcinoma showing vascular invasion within an endothelial-lined blood vessel.

Fig. 33-30. Parathyroid carcinoma.
Parathyroid carcinoma (P) with perineural invasion (arrows). The neoplastic proliferation includes rather bland-appearing and uniform nuclei, but the presence of neurotropism represents invasive growth diagnostic for carcinoma.

Fig. 33-31. Parathyroid carcinoma.
Parathyroid carcinoma characterized by hypercellularity and trabecular growth.

TABLE 33-2  Pathologic Features Associated with Malignancy in Parathyroid Neoplasms

<table>
<thead>
<tr>
<th>Features Definitively Diagnostic for Malignancy</th>
<th>Features Worrisome for But Not Definitively Diagnostic for Malignancy</th>
</tr>
</thead>
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<tr>
<td>Inv. growth including:</td>
<td>Large size (mean weight 6.7 g)</td>
</tr>
<tr>
<td>• Invasive growth into:</td>
<td>Adherence to surrounding structures (e.g., thyroid tissue, others)</td>
</tr>
<tr>
<td>• Surrounding soft tissues</td>
<td>Irregular contour; lack of distinct encapsulation</td>
</tr>
<tr>
<td>• Surrounding viscera or vital structures (thyroid gland, larynx, trachea, esophagus, pharynx, carotid artery,</td>
<td>Thick capsule</td>
</tr>
<tr>
<td>• recurrent laryngeal nerve)</td>
<td>Intralesional fibrous bands</td>
</tr>
<tr>
<td>• Vascular invasion</td>
<td>Mitotic activity (especially &gt;5 per 10 HPF)</td>
</tr>
<tr>
<td>• Perineural invasion</td>
<td>Coagulative tumor necrosis</td>
</tr>
<tr>
<td>• Metastatic disease:</td>
<td>Diffuse cellular atypia</td>
</tr>
<tr>
<td>• Regional lymph nodes</td>
<td>Diffuse sheet-like monotonous small cells with increased N:C</td>
</tr>
<tr>
<td>• Distant sites</td>
<td>Macronucleoli in many tumor cells</td>
</tr>
<tr>
<td>• Spindling of tumor cells</td>
<td>Trabecular growth</td>
</tr>
<tr>
<td>• Macronucleoli in many tumor cells</td>
<td>Spindling of tumor cells</td>
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Even focally, should raise suspicion for the diagnosis of carcinoma.

- Nuclear palisading may be prominent in trabecular areas.
- Spindling of cells is also a feature more often seen in carcinomas than in benign proliferations.
- Trabecular pattern and spindle-shaped cells, although worrisome for a possible diagnosis of carcinoma, are not definitive diagnostic features for carcinoma.
Parathyroid carcinoma characterized by a monotonous but crowded proliferation of cells with large nuclei and very large eosinophilic nucleoli (macronucleoli); these findings seen in some parathyroid carcinomas are not typically present in benign parathyroid lesions (i.e., adenoma, hyperplasia); mitotic figures can be seen (middle upper, upper right).

- Nuclear pleomorphism is less common than in adenomas, which often contain scattered foci with enlarged atypical nuclei:
  - Monotony of nuclear size and shape is frequently present in carcinomas.
  - Pleomorphism, when present, is usually more diffuse than in adenomas.
- Mitotic activity is identified in most, but not all, of parathyroid carcinomas:
  - Presence of atypical mitoses is virtually diagnostic of malignancy.
  - Although a high mitotic rate is a helpful feature, the presence of mitotic activity exceeding 1 per 10 high-power fields in a minority of parathyroid adenomas and in parathyroid hyperplasia may be seen.
  - Overlap in mitotic activity between all parathyroid proliferative diseases (i.e., adenoma, hyperplasia, and carcinoma) makes mitotic activity a useful finding only when coupled with other features of malignancy.
- Capsular invasion may be obvious in some cases, or may be represented only by irregular tongues or islands of parathyroid tissue protruding into the capsule; invasion beyond the capsule is indicative of malignancy.
- Entrapped islands of parathyroid parenchymal cells in benign disease should be distinguished from these invasive foci by their rounded contours and lack of desmoplastic reaction.
u1300 • Fibrous bands extending from a thickened capsule frequently divide the tumor into irregular compartments and/or nodules.

u1305 • Angioinvasion is diagnostic of carcinoma but is present in a minority of cases;

u1310 † Usually found within vessels in the thick tumor capsule.

u1315 † Artifactualy displaced clumps of tumor cells in vascular spaces should be distinguished from true invasion by their frequently degenerated appearance and by their lack of attachment to the vessel wall.

u1320 • Perineural invasion, although rarely seen, is also virtually diagnostic of malignancy.

u1330 • Immunohistochemistry:

u1335 † Positive for cytokeratins, chromogranin as well as for parathyroid hormone.

u1340 † Loss of (nuclear) parafibromin staining is commonly but not invariably identified:

u1345 – Only about 50% of carcinomas lack parafibromin staining.

u1350 – Some carcinomas may show positive parafibromin staining.

u1355 – Loss of parafibromin reported in sporadic adenomas (unassociated with hyperparathyroidism-jaw tumor syndrome).

u1360 † High frequency of cyclin D1 expression (reported in more than 90% of cases):

u1365 – May result from loss of parafibromin expression.

u1370 – May reflect increased cellular proliferation.

u1375 – High levels of expression also present in hyperplasia (approximately 61%) and adenomas (approximately 39%) so not uniquely seen in carcinoma.

u1380 † Galectin-3 reactivity frequently seen:

u1385 – More than 90% of cases reported positive.

u1390 – Seen in less than 5% of parathyroid adenomas.

u1395 † Diffuse strong staining for protein gene product 9.5 (PGP9.5) frequently found.

u1400 † Ki67 (MB1) proliferative index may be increased:

u1405 – An index greater than 5% should raise suspicion for carcinoma but the diagnosis of carcinoma requires confirmatory diagnostic findings.

u1410 – Proliferative indices in differentiating adenoma from carcinoma are of limited utility given overlapping findings in these lesions.

u1415 † Loss of immunoreactivity for retinoblastoma (Rb) protein.

u1420 † Negative for thyroglobulin and TTF-1.

u1425 • Cytogetic and molecular biology:

u1430 † Mutations of tumor suppressor gene HRPT-2 may be important in the pathogenesis of parathyroid carcinoma:

– Inactivation of germ line mutations in HRPT-2 believed to play a significant role in the development of parathyroid carcinoma:

* Located on 1q25
* Encodes parafibromin known to function in the suppression of cyclin D1
* Implicated in the hyperparathyroidism-jaw tumor syndrome
* Identified in two thirds of cases of sporadic occurring parathyroid carcinoma
* Practically never found in parathyroid adenomas.

† Allelic loss of the retinoblastoma (Rb) tumor-suppressor gene is common:

– May play an important role in the development of parathyroid carcinoma.

– Loss of immunoreactivity for Rb protein reported in 20% to 100% of parathyroid carcinomas.

– Absence may be helpful in distinguishing parathyroid adenomas from carcinomas but not considered sufficiently reliable in differentiating adenoma from carcinoma.

† Somatic mutation in MEN-1 gene:

– Found in 13% of carcinomas
– Suggests a role in the development of parathyroid carcinoma.

† Allelic loss of the p53.

† Reduced expression of cyclin-dependent kinase inhibitor protein p27 commonly identified:

– In contrast, adenomas show higher labeling index.

**Differential Diagnosis**

• Parathyroid adenoma (see Table 33-1)
• Parathyroid hyperplasia (see Table 33-1)
• Parathyromatosis:

† Represents microscopic foci of hyperplastic parathyroid tissue in the soft tissues of the neck in association with primary chief cell hyperplasia.

† May be the cause of recurrent disease after an apparently complete resection of the grossly evident hyperplastic glands.

† Should not be mistaken for invasion as seen in parathyroid carcinoma; differentiating features may include:

– Absence of associated fibroblastic reaction or infiltrative contour.

– Absence of an intravascular location of these nests.

– Absence of other histologic features of carcinoma should help exclude malignancy.

• Metastatic carcinoma from another site.
**SECTION 9 Parathyroid Glands**

**Treatment and Prognosis**
- Surgery is the primary treatment modality with recommended treatment including en bloc resection, to include the ipsilateral thyroid lobe, strap muscles, recurrent laryngeal nerve, trachea, or esophagus if involved.
- Offers the best chance for cure
- Up to 50% of patients are cured by en bloc resection.
- Prophylactic lymphadenectomy not recommended due to the low rate of nodal disease (reported to be 6%);
- Neck dissection warranted if there is clinical evidence of neck (nodal) disease
- Adjuvant radiotherapy may improve local control and limit the occurrence of local relapse, especially when the carcinoma is incompletely excised with involvement of resection margins.
- Efficacy of chemotherapy not proven
- In general, parathyroid carcinomas are generally indolent behaving:
- 5-year survival from 60% to 85%
- 10-year survival from 40% to 79%
- Recurrences generally manifest within 3 years of the first surgery with locally recurrent disease:
- Recurrence rates range from approximately 33% to 50%
- Lower rates of recurrence reported (8%) with en bloc resection
- Higher recurrence rates reported (51%) when treated by parathyroid gland excision
- Metastatic disease occurs rather late in the course of disease:
- Found in approximately one third of patients
- Usually occurs several years after primary diagnosis
- Sites of metastases include regional lymph nodes, mediastinum, lungs, liver, and bones.
- Surgical resection of metastatic or locally recurrent disease is frequently helpful due to the rather indolent nature of parathyroid carcinoma:
- Patients usually survive for several years after recognition of tumor recurrence.
- Recurrence and/or metastatic disease often manifest with recurrent hypercalcemia:
- Lifelong monitoring for recurrent and/or metastatic disease most effectively accomplished with serum calcium levels.
- Major difficulty in management of recurrent disease is severe hypercalcemia and its complications.
- Death is related to excessive hormonal production with subsequent hypercalcemia rather than directly to tumor burden.
- Prognosis has been shown to be related to tumor stage:
  - Stage I: invasion of surrounding soft tissues; 90% disease-free survival
  - Stage II: vascular invasion; 46% disease-free survival
  - Stage III: invasion of vital organs or regional lymph node metastasis; 50% disease-free survival
  - Stage IV: distant metastases; no disease-free survival

**SECONDARY NEOPLASMS**

**Definition:** Contiguous involvement from tumors in adjacent structures or metastatic neoplasms from distant sites involving the parathyroid gland.

**Clinical**
- Usually asymptomatic; may present with a neck mass; other symptoms may include hoarseness, dysphagia, and neck pain; rare cases have been associated with clinical hypoparathyroidism due to massive replacement of multiple glands.
- May result from direct extension, especially from thyroid or laryngeal tumors, or from metastatic spread.
- Metastasis to parathyroid glands is rare; among the more common primary malignancies that may metastasize to the parathyroid glands include:
  - Breast carcinoma (most common)
  - Hematologic malignancies

**Fig. 33-39. Metastatic breast carcinoma.**

Metastatic breast carcinoma to the parathyroid gland. Residual parathyroid parenchyma is present in the center of the image surrounded by a malignant glandular lesion. The patient had a known history of breast carcinoma that was widely metastatic, including the parathyroid gland. Immunohistochemical staining (not shown) included reactivity for mammaglobin, BRST-2, and GATA-3.
CHAPTER 33 Neoplasms of the Parathyroid Glands

Pathology

Malignant melanoma
Lung carcinoma
Renal cell carcinoma
Sarcomas

Differential Diagnosis

Parathyroid carcinoma:
- Reactivity for parathyroid hormone, chromogranin

Treatment and Prognosis

- Treatment based on primary site of origin
- Prognosis poor, related to dissemination of primary disease

FURTHER READING

References may be accessed online at ExpertConsult.

References:

- Malignant melanoma: S100 protein, HMB45, melan A, tyrosinase, MITF1, Sox10, vimentin
- Lung carcinoma: Napsin A, TTF1
- Renal cell carcinoma: RCC antibody, CD10, PAX2, PAX8, CAIX
- Prostate carcinoma: PSA, PAP, prostein

Pathology

- Found in 11.9% of cancer patients in autopsy studies
- May involve one or multiple glands
- A variety of organ-specific markers may be helpful in the diagnosis of a metastatic tumor to the parathyroid gland
- Presence of specific immunomarkers helpful in distinguishing between primary and secondary neoplasms:
  - Breast carcinoma: mammaglobin, BRST2, GATA-3
  - Hematologic malignancies: CD45 (leukocyte common antigen), B-cell (CD20, others), T-cell (CD3, others)
CHAPTER 33  Neoplasms of the Parathyroid Glands 1517.e1

FURTHER READING
Parathyroid Adenoma


Balogh ZW, LiVolli VA: Onclocytic lesions of the neuroendocrine system, Semin Diagn Pathol 16(2):190, 1999.


Rosai J, DeLellis RA, Carcangiu ML, et al: Parathyroid adenoma and variants. In Silverberg SG, editor: Tumors of the thyroid and

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**Parathyroid Carcinoma**


Secondary Neoplasms


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