

RECOMMENDATIONS FOR THE REPORTING OF PARATHYROID SPECIMENS

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THE ASSOCIATION OF DIRECTORS OF ANATOMIC AND SURGICAL PATHOLOGY

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Introduction for ADASP reporting Guidelines

It has been evident for decades that pathology reports are very variable even within a single institution. Standardization of reporting is the optimal way to insure that information necessary for patient management, prognostic and predictive factor assessment, grading, staging, analysis of outcomes and tumor registries is included in pathology reports. In recent years, two societies (first ADASP and then the CAP), have undertaken to publish guidelines for the reporting of common cancers. The CAP assigned multidisciplinary groups of pathologists, surgeons, radiation and medical oncologists to develop the protocols. They were then reviewed by other pathologists and clinicians. After those reviews the protocols were reviewed by multiple CAP committees and finally approved by the Board of Governors.

The ADASP, in contrast, chose a pathologist expert in each field to assemble a group from within the pathology community (with clinician input if desired) to write specific cancer protocols. These were then approved by the ADASP council and subsequently by the membership. Even though both societies began the process at approximately the same time the streamlined approach adopted by the ADASP enabled them to publish years earlier in pathology journals frequented by anatomic pathologists. While the formats are somewhat different, the contents are essentially the same.

The American College of Surgery (ACS) Commission on Cancer (COC) accredits cancer centers in the USA. Recently, the COC decided to require elements, deemed as essential by the CAP, to be described in all pathology reports in their accredited cancer centers as of January 2004. Importantly they do not require that the specific CAP protocols or synoptic reports be utilized. ADASP has updated all of its protocols to comply with the COC requirements in the form of 37 uniform checklists. The checklists use the staging criteria sited in the American Joint Committee on Cancer (AJCC) 2002 staging manual (sixth edition) but include a variety of other references listed in each of the checklists. Moreover, the checklists are formatted for ease of use. They may be used as templates for uniform reporting and are designed to be compatible with voice activated transcription.

The different elements in these revised ADASP Diagnostic Checklists have been divided into *Required* and *Optional* . The term *Required* in this context only signifies compliance with the COC guidelines. ADASP realizes that specimens and practices vary and it will not be possible to report these elements in every case. However, ADASP hopes that pathologists will find these checklists to be useful in daily clinical practice, while facilitating compliance with the new COC requirements.

The checklists are in standard PDF file format, and may be easily downloaded from the ADASP website. They are not to be reproduced, altered or used for commercial purposes without consent from ADASP.

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INTRODUCTION

Hyperparathyroidism is a common disease, the incidence of which has increased rather dramatically over the past several decades. As a result, surgical exploration of the parathyroid has become a relatively commonplace procedure at most large institutions. Most parathyroid tumors represent either adenomas or hyperplasia. The distinction between these two entities is problematic, and usually requires pathologic examination of more than one gland as well as clinical data. This together with the rarity of other parathyroid neoplasms focuses this protocol on defining the information necessary to distinguish parathyroid adenoma from hyperplasia, and the features most useful in the diagnosis of parathyroid carcinoma.

INFORMATIVE GROSS DESCRIPTION

- A. Specify whether the specimen was received fresh vs. in fixative (type)
- B. Specimen identification-precisely designated site (e.g., left upper parathyroid) and whether biopsy or whole gland
- C. Describe and measure specimen:
 - 1. Weight (include estimate from surgeon of percentage of gland removed, if available)
 - 2. Size in three dimensions
 - 3. Color and consistency
 - 4. Presence of capsule
 - 5. Adherence to other structures
 - 6. Cystic elements

7. Hemorrhage
8. Necrosis
9. Nodularity

D. When frozen section or touch imprint performed, so specify.

E. Paraffin block key

F. When ink is used, so specify

G. Note following if done

1. gross photography
2. tissue processed for ancillary studies or stored for such potential

DIAGNOSTIC INFORMATION

A. Surgical procedure

B. Histological classification

1. Hyperplasia
2. Adenoma
3. Atypical adenoma
4. Carcinoma

Several studies have defined histological features important in the diagnosis of parathyroid carcinoma, including thick fibrous bands, trabecular growth pattern, and high mitotic rate. Similarly, criteria have been developed to distinguish adenoma from hyperplasia (See Appendix).

C. Characteristics of carcinoma

1. features present to make diagnosis
2. grade (no grading currently available)
3. extent
4. margins

D. Lymph nodes

OPTIONAL FEATURES

A. Subtyping tumor (e.g. chief cell vs clear cell)

B. Results of ancillary studies

1. DNA ploidy
2. proliferative activity (e.g., MIB-1, p27)
3. nuclear morphometry
4. genetic abnormalities
5. growth factors and receptors

C. Pathologic stage-proposed system (Table 1)

D. Clinical data

1. patient history, including family history
2. endocrine testing results
 - serum Ca⁺⁺
 - serum PTH
 - other

pre- and postoperative diagnoses

CHECKLIST (Non Formatted)

1. TOPOGRAPHY, PROCEDURE, AND GROSS FEATURES

SITE	PROCEDURE	SIZE	WEIGHT (estimated % of entire gland)
Left upper			
Right upper			
Left lower			
Right lower			
Other			

2. HISTOLOGIC CLASSIFICATION

Hyperplasia _____
 Adenoma _____
 Carcinoma _____
 Other _____

Table 1. Proposed Staging System for Parathyroid Carcinoma (1)

Primary Tumor (T)

T1 < 3 cm.
 T2 > 3 cm.
 T3 tumor of any size with invasion of the surrounding soft tissues, such as the thyroid gland, strap muscles, etc.
 T4 Massive central compartment disease invading the trachea and esophagus, or recurrent parathyroid carcinoma

Nodal Involvement (N)

N0 No regional lymph node metastases
 N1 Regional lymph node metastases

Metastatic Involvement (M)

M0 No evidence of distant metastases
 M1 Evidence of distant metastases

APPENDIX

Although the diagnostic categories of parathyroid nodules are generally limited to hyperplasia, adenoma, and carcinoma, the criteria to make these diagnoses remain elusive and controversial. Depending on the criteria to distinguish adenoma from hyperplasia, the relative incidence of these diagnoses in large series varies dramatically (2-4).

CRITERIA TO DISTINGUISH ADENOMA FROM HYPERPLASIA

1. FAT STAINS

Several studies have utilized fat stains to define functional activity within parathyroid glands, considering intracytoplasmic fat droplets as evidence of functional inactivity and the absence of such fat as indicative of hyperfunction as would characterize hyperplasia and adenoma. Abundant intraparenchymal fat in a normal sized gland suggests that this gland is suppressed and supports the diagnosis of adenoma in another enlarged gland. However, some hyperplastic glands contain prominent parenchymal fat (5).

2. RIM OF NORMAL PARATHYROID TISSUE

A compressed remnant of normal or atrophic parathyroid adjacent to a hypercellular nodule is strongly supportive of a diagnosis of adenoma. However this remnant is not found in association with all adenomas, and a pseudoremnant may be seen in nodular hyperplasia (6).

3. SECOND GLAND

The presence of one or more glands of normal size and cellularity strongly supports the conclusion that an enlarged gland is an adenoma. Conversely, hyperplastic changes within a second gland support the diagnosis of hyperplasia. However, some hyperplastic glands are only slightly enlarged, and the surgical specimen may consist of only a part of the gland, making definition of enlargement difficult. Similarly, histologic changes of hyperplasia may be focal and subtle, and parts of a hyperplastic gland may appear normal (5,7).

With the increased use of intraoperative assays of PTH in minimally invasive parathyroid surgery, only a single gland may be submitted for pathological examination. In such cases, a diagnosis of “hypercellular parathyroid” is recommended, with a note that it is not possible to distinguish hyperplasia from adenoma on the basis of examination of a single gland. In cases where there has been a fall in PTH levels following removal of a single gland, the diagnosis may be “hypercellular parathyroid gland, consistent with adenoma”.

4. WEIGHT AND OTHER FINDINGS

The size, color, consistency, cell types present and their relative frequency are of no value in distinguishing adenoma from hyperplasia (8). However, the presence of two or more enlarged glands generally can be viewed as indicating that these glands are hyperplastic. Careful autopsy studies have demonstrated that the maximal normal total parenchymal cell weight, as estimated by density gradient techniques, is 144 mg, and the corresponding value for total glandular weight (including stromal fat) is 208 mg. The upper limit of a normal parenchymal cell weight for the largest gland in an individual is estimated to be 49 mg, and that for the next largest gland in that person 39 mg. However, the presence of distinct nodularity in any gland, especially those composed of chief cells, should be interpreted as abnormal, even if the weight is within normal limits (9).

CRITERIA TO DISTINGUISH CARCINOMA FROM ADENOMA

1. GROSS APPEARANCE

A gray-white color, hard consistency, and lobulated cut surface have been cited as features more commonly seen in carcinoma than in benign glands (10).

2. THICK FIBROUS BANDS

Thick, intratumoral fibrous bands are present in up to 90% of carcinomas (11). However, similar changes may be seen in association with degeneration within adenomas, usually accompanied by chronic inflammation and hemosiderin deposition.

3. MITOTIC ACTIVITY

Mitotic figures are present in about 80% of cancers, and atypical mitotic figures are considered diagnostic of parathyroid carcinoma. However, mitotic counts of one per ten high power fields may be seen in hyperplasia, have also rarely been described in adenoma (12), and even higher counts have been reported in MEN 2 (13).

4. CAPSULAR INVASION

This is seen in up to 70% of carcinomas, but must be distinguished from entrapment or pseudoinvasion. Direct infiltration of adjacent structures, particularly the thyroid or esophagus, is considered indicative of malignancy, unless there are associated degenerative changes or a history of previous surgery (14).

5. VASCULAR INVASION

This is generally considered a specific histologic finding for malignancy, and is virtually diagnostic if the intravascular tumor is outside the tumor capsule and at least partially attached to the vessel wall, but this is demonstrated in only 10-15% of all carcinomas. As with other endocrine neoplasms, this finding may rarely be seen in otherwise benign parathyroid tumors (14).

6. GROWTH PATTERNS

Most parathyroid cancers have been reported to show a trabecular or rosette-like arrangement of cells, at least focally, as opposed to the nested or diffuse growth of the usual adenoma. However, a trabecular pattern may also be seen in some adenomas and in hyperplastic glands. In addition, trabecular growth was found in only 20% of cases in a recent large series of parathyroid carcinomas, with diffuse or nested growth predominating in the vast majority (15).

7. ADHERENCE

Gross adherence to surrounding soft tissue structures, best appreciated by the surgeon, suggests that the tumor is malignant, but is present in only about 50% of cases of carcinoma (16). Such adherence has not been noted in adenomas with degenerative changes and in cases with previous surgery (5,14).

8. SERUM CALCIUM LEVEL

Although patients with parathyroid carcinoma tend to have more severe metabolic disease manifestations and a significantly higher serum calcium level than patients with adenoma, there is considerable overlap between these two groups (17).

9. METASTASIS

Metastases are unusual at initial presentation, and only 30% of patients diagnosed as having carcinoma manifest metastatic disease during their course (5).

10. RECURRENCE

Although recurrence may indicate that a parathyroid tumor is malignant, it may also occur in incompletely resected benign glands (14).

11. ATYPICAL ADENOMA

Those parathyroid neoplasms that demonstrate some of the above features associated with carcinoma, including the presence of thick fibrous bands, mitotic activity, capsular invasion and a trabecular growth pattern, but which lack unequivocal evidence of malignancy, such as vascular or soft tissue invasion, may be diagnosed as atypical adenoma, implying an unpredictable biological behavior (2).

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