Adrenal Gland

Protocol applies to adrenal cortical carcinoma. Pheochromocytoma, neuroblastoma, and other adrenal medullary tumors of childhood are excluded.

Protocol revision date: January 2005
No AJCC/UICC staging system

Procedures

- **Cytology** (No Accompanying Checklist)
- **Incisional Biopsy**
- **Excisional Biopsy**
- **Adrenalectomy**

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the “Surgical Pathology Cancer Case Summary (Checklist)” portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with the document. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

Summary of Changes to Checklist(s)

Protocol revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2005
Applies to adrenal cortical carcinomas only
No AJCC/UICC staging system

ADRENAL GLAND: Resection

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Subtotal adrenalectomy
___ Total adrenalectomy
___ Other (specify): _____
___ Not specified

Laterality
___ Right
___ Left
___ Not specified

Tumor Size
Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm
___ Cannot be determined (fragmented specimen)

Tumor Weight
Specify: ___ g

MICROSCOPIC

Pathologic Staging

Primary Tumor
___ I: Confined to gland, 5 cm or less
___ II: Confined to gland, greater than 5 cm
___ III: Extraglandular extension without other organ involvement
___ IV: Distant metastasis or extension into other organs
___ Cannot be determined

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Regional Lymph Nodes
___ Cannot be assessed
___ No regional lymph node metastasis
___ Regional lymph node metastasis
Specify: Number examined: ___
Number involved: ___

Distant Metastasis
___ Cannot be assessed
___ Distant metastasis
*Specify site(s), if known: _____

Margins
___ Margins uninvolved by tumor
___ Margin(s) involved by tumor
Specify margin(s): _____
___ Cannot be determined

***Venous (Large Vessel) Invasion**
*___ Absent
*___ Present
*___ Indeterminate

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Tumor necrosis
*___ Hyperplasia
*___ Adenoma
*___ Other (specify): _____

***Comment(s)**

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Background Documentation

Protocol revision date: January 2005

I. Cytologic Material

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (Note **A**)
   b. Relevant findings (eg, hormonal and imaging studies) (Note **B**)
   c. Clinical diagnosis
   d. Procedure (eg, fine-needle aspiration [FNA])
   e. Anatomic site(s) (eg, right/left adrenal gland, related sites)

B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of slides received
   c. Quantity and appearance of fluid specimen
   d. Other (eg, cytologic preparation from tissue)
   e. Results of rapid smear review
2. Material submitted for microscopic evaluation (eg, direct smear, cytocentrifuge preparation, touch or filter preparation, cell block)
3. Special studies (Note **C**)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present
   a. Histologic type, if possible (Note **D**)
   b. Other descriptive features (eg, nuclear atypia, necrosis)
3. Additional pathologic finding, if present
4. Results/status of special studies (specify) (Note **C**)
5. Comments
   a. Correlation with intraprocedural consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

II. Incisional Biopsy (Any Surgical Approach Less Than Complete Adrenal Excision)

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure

4. Other clinical information
    a. Relevant history (Note **A**)
    b. Relevant findings (eg, hormonal and imaging studies) (Note **B**)
    c. Clinical diagnosis
    d. Procedure (eg, fine-needle biopsy, core biopsy, incisional biopsy)
    e. Operative findings
    f. Anatomic sites (eg, right/left adrenal gland, related sites)

B. Macroscopic Examination

1. Specimen
    a. Organ(s)/tissue(s) (specify)
    b. Unfixed/fixed (specify fixative)
    c. Number of fragments
    d. Dimensions
    e. Weight, if appropriate
    f. Orientation, if indicated by surgeon
    g. Descriptive features
    h. Results of intraoperative consultation
2. Tumor(s), if identified
    a. Location
    b. Dimensions
    c. Descriptive features (eg, hemorrhage/necrosis)
    d. Relationship to margins, if appropriate
3. Additional pathologic findings, if present (eg, hyperplasia)
4. Tissue submitted for microscopic evaluation
    a. Tumor
    b. Margin(s), if appropriate
    c. Nodules
    d. Other lesions
    e. Frozen section tissue fragment(s) (unless saved for special studies)
5. Special studies (specify) (Note **C**)

C. Microscopic Evaluation

1. Tumor, if present
    a. Histologic type (Note **D**)
    b. Descriptive features (eg, nuclear atypia, necrosis) (Note **E**)
    c. Venous/lymphatic vessel invasion
2. Additional pathologic findings, if present (eg, hyperplasia)
3. Results/status of special studies (specify) (Note **C**)
4. Comments
    a. Correlation with intraoperative consultation, as appropriate
    b. Correlation with other specimens, as appropriate
    c. Correlation with clinical information, as appropriate

III. Complete Excision (Including Laparoscopically Removed Glands)

A. Clinical Information

1. Patient identification
    a. Name
    b. Identification number
    c. Age (birth date)
    d. Sex
2. Responsible physician(s)
3. Date of procedure

4. Other clinical information
    a. Relevant history (Note **A**)
    b. Relevant findings (eg, hormonal and imaging studies) (Note **B**)
    c. Clinical diagnosis
    d. Procedure (eg, laparoscopically removed gland) (Note **F**)
    e. Operative findings
    f. Type of specimen (adrenal excision with or without surrounding soft tissues)
    g. Anatomic site(s) of specimen (eg, right/left adrenal gland, related sites)

B. Macroscopic Examination

1. Specimen
    a. Organ(s)/tissue(s) included
    b. Unfixed/fixed (specify fixative)
    c. Dimensions
    d. Weight
    e. Orientation, if indicated by surgeon
    f. Descriptive features
    g. Results of intraoperative consultation (Note **C**)
2. Tumor(s)
    a. Dimensions (3)
    b. Weight (Note **G**)
    c. Descriptive features (eg, color, consistency, hemorrhage, necrosis)
    d. Extent of invasion (Note **H**)
3. Margins, relationship to and distance from tumor, as appropriate
4. Regional lymph nodes, if submitted
    a. Number
    b. Location, if designated by surgeon
5. Additional pathologic findings, if present
6. Tissue(s) submitted for microscopic evaluation
    a. Tumor, adequate sampling of all areas
    b. Nodules
    c. Margins of resection
    d. All lymph nodes
    e. Other lesions
    f. Frozen section tissue fragment(s) (unless saved for special studies)
    g. Other organs/tissues (eg, liver biopsy)
7. Special studies (specify) (Note **C**)

C. Microscopic Evaluation

1. Tumor
    a. Histologic type (Note **D**)
    b. Descriptive features (eg, nuclear atypia , mitotic rate, necrosis) (Note **E**)
    c. Extent of invasion (Note **H**)
    d. Venous/lymphatic vessel invasion
2. Margins, as appropriate
3. Regional lymph nodes (Note H)
    a. Number (location, if possible)
    b. Number involved by tumor
4. Additional pathologic findings, if present (eg, hyperplasia)
5. Result/status of special studies (specify) (Note **C**)
6. Other organs/tissues
7. Comments
    a. Correlation with intraoperative consultation, as appropriate
    b. Correlation with other specimens, as appropriate
    c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Relevant History

Endocrine manifestations, such as hypertension, change in body habitus, feminization, or virilism, are important. Also of import are family history, previous surgery for adrenal tumors (both benign and malignant) or other endocrine organs, other tumors that may metastasize to the adrenal gland, and endocrine or other therapies. Hyperplastic adrenal tissue may re-grow if previously excised incompletely.

B. Endocrine Status

Laboratory findings are important in the evaluation of an adrenal mass that is not obviously a high-grade carcinoma because the absence of evidence of hormonal excess in the presence of an enlarged adrenal gland usually indicates that the tumor is an incidental finding ("incidentaloma") and not a functioning adenoma.[1]

C. Special Procedures

Special procedures may include frozen sections, cytologic imprints, immunohistochemical stains, histochemical stains, electron microscopy, flow cytometry, molecular studies, and cytogenetic studies. If such studies are performed in another laboratory, either extrainstitutional or intrainstitutional, the laboratory should be identified.

D. Histologic Type

The following histologic classification of adrenal tumors has been modified from Page et al.[2]

Histologic Classification of Adrenal Tumors

Cortical Tumors
- Adenoma
- Carcinoma
- Myelolipoma
- Miscellaneous

Medullary Tumors[#]
- Pheochromocytoma[#]
- Neuroblastoma[#]
- Ganglioneuroblastoma[#]
- Ganglioneuroma[#]

[#] Not covered in protocol.

E. Histologic Grade

Adrenal cortical tumors are not usually graded on histologic grounds. Severe nuclear atypia, high mitotic count, vascular invasion, tumor necrosis, and other microscopic features may, in combination, support a diagnosis of adrenal cortical carcinoma over adenoma and should be recorded, but no precise clustering of histologic features is considered diagnostic of malignancy. However, when several malignant features are present together (eg, highly atypical nuclei, sheet-like growth, necrosis, and many mitoses), the risk of distant metastases is increased.[3-6] In some studies, specific combinations of features, such as mitotic rates of 6 or more per 50 high-power fields (HPF) along with atypical mitosis and venous invasion, have been found to correlate with metastasis or recurrence of adrenal cortical carcinomas.[4] Other studies have shown that mitotic rates greater than 20 per 50 HPF are associated with decreased survival, suggesting that a high mitotic index may be an important adverse prognostic factor.[5]

Although this protocol does not cover medullary tumors, it should be noted that pheochromocytoma is usually diagnosed preoperatively by pharmacologic means. No pathologic criteria for differentiation of benign from malignant pheochromocytomas have been defined. Metastatic disease is considered the only irrefutable proof of malignancy.

F. Laparoscopic Surgery

An entire adrenal tumor may be removed laparoscopically, but with this technique, the gland may become fragmented. This anatomic information, including maximal diameter of the resected tumor, should be provided by the surgeon.

G. Weight

Accurate weights of adrenal cortical neoplasms are important.[6] Although tumor mass cannot be used as the sole criterion for malignancy, adrenal cortical neoplasms weighing less than 50 g are almost always benign, whereas the weight of malignant tumors is usually greater than 100 g.

H. Staging

The staging system proposed by MacFarlane[7] and modified by Sullivan et al[8] and Henley et al[9] is most commonly used for adrenal cortical carcinomas. The American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) have no published TNM staging system for malignancies of the adrenal gland.

Stage	Extent	Size
I	Confined to gland	5 cm or less
II	Confined to gland	Greater than 5 cm
III	Extends out of gland without involving adjacent organs	Any
IV	Distant metastasis or involvement of adjacent organs	Any

Tumors of the Adrenal Gland and Extra-Adrenal Paraganglia[10] proposes the following staging system.

Primary Tumor (T)

T1 Tumor 5 cm or less, no invasion
T2 Tumor greater than 5 cm, no invasion
T3 Tumor of any size, locally invasive but not involving adjacent organs
T4 Tumor of any size with invasion of adjacent organs

Regional Lymph Nodes (N)

N0 Negative regional nodes
N1 Positive regional nodes

Distant Metastasis (M)

M0 No distant metastasis
M1 Distant metastasis

Stage Definitions

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1,T2	N1	M0
	T3	N0	M0
Stage IV	Any T	Any N	M1
	T3,T4	N1	M0

References

1. Kloos RT, Gross MD, Francis IR, Dorobkin M, Shapiro B. Incidentally discovered adrenal masses. *Endocrine Reviews*. 1995;16:460-484.
2. Page DL, DeLellis RA, Hough AJ Jr. *Tumors of the Adrenal; Atlas of Tumor Pathology.* 2nd Series, Fascicle 23. Washington, DC: Armed Forces Institute of Pathology; 1986.
3. Hough AJ, Hollifield JW, Page DL, Hartmann WH. Prognostic factors in adrenocortical tumors: a mathematical analysis of clinical and morphologic data. *Am J Clin Pathol*. 1979;72:390-399.
4. Weiss LM. Comparative histologic study of 43 metastasizing and non-metastasizing adrenocortical tumors. *Am J Surg Pathol*. 1984;8:163-169.
5. Weiss LM, Medeiros LJ, Vickery AL. Pathologic features of prognostic significance in adrenal cortical carcinoma. *Am J Surg Pathol*. 1989;13:202-206.
6. Medeiros LJ, Weiss LM. New developments in the pathologic diagnosis of adrenal cortical neoplasms: a review. *Am J Clin Pathol*. 1992;97:73-83.
7. MacFarlane DA. Cancer of the adrenal cortex: the natural history, prognosis, and treatment in a study of fifty-five cases. *Ann R Coll Surg Engl*. 1958;23:155-186.
8. Sullivan M, Boileau M, Hodges CV. Adrenal cortical carcinoma. *J Urol*. 1978;120:660-665.
9. Henley DJ, van Heerden JA, Grant CS, Carney JA, Carpenter PC. Adrenal cortical carcinoma: a continuing challenge. *Surgery*. 1983;94:926-931.
10. Lack E. *Tumors of the Adrenal Gland and Extra-Adrenal Paraganglia.* AFIP Fasicle No. 19. Third Series. Washington DC: American Registry of Pathology; 1997.

Bibliography

Dehner LP. Neoplasms of the adrenal cortex: preoccupation bordering on obsession [editorial; comment]. *Am J Clin Pathol*. 1994;101:557-558.

Katz RL, Patel S. Mackay B, Zornoza J. Fine-needle aspiration cytology of the adrenal gland. *Acta Cytol*. 1984;28:269-282.

Lack EE, ed. *Pathology of the Adrenal Glands. Contemporary Issues in Surgical Pathology.* Vol. 14. New York: Churchill Livingstone; 1990.

Lloyd RV. *Endocrine Pathology.* New York: Springer-Verlag; 1990.