Thymoma and Thymic Carcinoma

Protocol applies to thymic epithelial tumors located in any area of the mediastinum.

Protocol revision date: January 2004
No AJCC/UICC staging system

Procedures

- **Biopsy**
- **Resection**

Authors

Alberto Marchevsky, MD
Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California
M. Elizabeth H. Hammond, MD
Department of Pathology, LDS Hospital and University of Utah School of Medicine, Salt Lake City, Utah
Cesar Moran, MD
M.D. Anderson Cancer Center, Houston, Texas
Saul Suster, MD
Department of Pathology, Ohio State University School of Medicine, Columbus, Ohio
For the Members of the Cancer Committee, College of American Pathologists

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 2004

No changes have been made to the data elements of the checklist(s) since the January 2003 protocol.

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to all epithelial thymic neoplasms
No AJCC/UICC staging system

THYMOMA AND THYMIC CARCINOMA: Biopsy

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Fine-needle aspiration biopsy
___ Computed tomography-guided needle biopsy
___ Transthoracic needle biopsy
___ Limited thoracotomy
___ Other (specify): _____
___ Not specified

Tumor Site
___ Thymus
___ Anterior mediastinum
___ Middle mediastinum
___ Posterior mediastinum
___ Other (specify): _____
___ Not specified

* 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.

MICROSCOPIC

Histologic Type

___ Type A thymoma (epithelial, spindle cell, medullary)
___ Type B thymoma, B1 (lymphocyte-rich, lymphocytic, predominantly cortical, organoid)
___ Type B thymoma, B2 (cortical)
___ Type B thymoma, B3 (epithelial, atypical, squamoid, well-differentiated thymic carcinoma)
___ Type AB thymoma (mixed)
___ Type C thymoma (thymic carcinoma), epidermoid keratinizing (squamous cell) carcinoma
___ Type C thymoma (thymic carcinoma), epidermoid nonkeratinizing carcinoma/ lymphoepithelioma-like carcinoma
___ Type C thymoma (thymic carcinoma), sarcomatoid carcinoma
___ Type C thymoma (thymic carcinoma), carcinosarcoma
___ Type C thymoma (thymic carcinoma), clear cell carcinoma
___ Type C thymoma (thymic carcinoma), basaloid carcinoma
___ Type C thymoma (thymic carcinoma), mucoepidermoid carcinoma
___ Type C thymoma (thymic carcinoma), papillary carcinoma
___ Type C thymoma (thymic carcinoma), undifferentiated carcinoma
___ Other (specify): _____
___ Carcinoma, type cannot be determined

*Comment(s)

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to all epithelial thymic neoplasms
No AJCC/UICC staging system

THYMOMA AND THYMIC CARCINOMA: Thymectomy, Other Procedure

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Cervical thymectomy
___ Thoracotomy
___ Video-assisted thoracotomy
___ Other (specify): _____
___ Not specified

***Specimen Size**
*Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm

Tumor Site
___ Thymus
___ Anterior mediastinum
___ Middle mediastinum
___ Posterior mediastinum
___ Other (specify): _____
___ Not specified

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

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MICROSCOPIC

Histologic Type

___ Type A thymoma (epithelial, spindle cell, medullary)
___ Type B thymoma, B1 (lymphocyte-rich, lymphocytic, predominantly cortical, organoid)
___ Type B thymoma, B2 (cortical)
___ Type B thymoma, B3 (epithelial, atypical, squamoid, well-differentiated thymic carcinoma)
___ Type AB thymoma (mixed)
___ Type C thymoma (thymic carcinoma), epidermoid keratinizing (squamous cell) carcinoma
___ Type C thymoma (thymic carcinoma), epidermoid non-keratinizing carcinoma/ lymphoepithelioma-like carcinoma
___ Type C thymoma (thymic carcinoma), sarcomatoid carcinoma
___ Type C thymoma (thymic carcinoma), carcinosarcoma
___ Type C thymoma (thymic carcinoma), clear cell carcinoma
___ Type C thymoma (thymic carcinoma), basaloid carcinoma
___ Type C thymoma (thymic carcinoma), mucoepidermoid carcinoma
___ Type C thymoma (thymic carcinoma), papillary carcinoma
___ Type C thymoma (thymic carcinoma), undifferentiated carcinoma
___ Other (specify): _____
___ Carcinoma, type cannot be determined

Pathologic Staging

___ Stage I: Grossly and microscopically encapsulated
___ Stage IIa: Microscopic transcapsular invasion
___ Stage IIb: Macroscopic capsular invasion
___ Stage III: Macroscopic invasion of neighboring organs
___ Stage IVa: Pleural or pericardial dissemination
___ Stage IVb: Hematogenous or lymphatic dissemination
___ Cannot be determined

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: _____

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Margins
___ Cannot be assessed
___ Margins uninvolved by tumor
Distance of tumor from closest margin: ___ mm
___ Margin(s) involved by tumor
Specify margin(s): _____

Invasion of Pulmonary Parenchyma
___ Cannot be assessed
___ Absent
___ Present
___ Indeterminate

Pleural Invasion
___ Cannot be assessed
___ Absent
___ Present
___ Indeterminate

***Vascular (Small/Large Vessel) Invasion**
*___ Absent
*___ Present
*___ Indeterminate

***Additional Pathologic Findings**
*Specify: _____

***Comment(s)**

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Background Documentation

Protocol revision date: January 2004

I. Biopsy

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. Date of specimen receipt in pathology laboratory
5. Previous/concurrent cytology or biopsy specimen (Note **A**)
6. Other relevant clinical information
   a. History (eg, lung cancer, myasthenia gravis, previous diagnosis, treatment)
   b. Imaging and laboratory findings (eg, computed tomography [CT] scan, magnetic resonance imaging [MRI], positron emission tomography [PET] scan, operative findings)
   c. Clinical findings and diagnosis(es)
   d. Previous or concurrent therapy, including dates (eg, surgery, radiation, chemotherapy, other)
   e. Procedure(s) (eg, CT-guided needle biopsy, mediastinoscopic biopsy, limited thoracotomy)
   f. Findings at procedures (eg, mediastinoscopy, limited thoracotomy)
   g. Anatomic site(s) of specimen(s) (eg, thymus, anterior mediastinum, posterior mediastinum, middle mediastinum)
   h. Other

B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Size (3 dimensions)
   c. Descriptive features
   d. Results of intraoperative consultation
2. Tissue submitted for microscopic evaluation
   a. Entire specimen or selected samples
   b. Frozen section tissue fragment(s) (unless saved for special studies)
3. Special studies (specify)

C. Microscopic Evaluation

1. Tumor, if present
   a. Histologic type (Note **B**)
   b. Extent of invasion, as appropriate
   c. Vascular and lymphatic invasion
   d. Perineural invasion
   e. Other (specify)
2. Additional pathologic findings, if present
3. Status/results of special studies (specify)
4. Comments
   a. Correlation with intraprocedural consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

II. Resection

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. Date of specimen receipt in pathology laboratory
5. Previous/concurrent cytology or biopsy specimen (Note **A**)
6. Other relevant clinical information
   a. History (eg, lung cancer, myasthenia gravis, previous diagnosis, treatment)
   b. Imaging and laboratory findings (eg, CT scan, PET scan, operative)
   c. Clinical findings and diagnosis(es)
   d. Previous or concurrent therapy, including dates (eg, surgery, radiation, chemotherapy, other)
   e. Procedure(s) (eg, thymectomy, cervical or mediastinal; thoracotomy; other)
   f. Operative findings
   g. Anatomic sites of specimen(s)
   h. Other

B. Macroscopic Examination

1. Specimen
   a. Organs/tissues received (documentation of extent of resection)
   b. Unfixed/fixed (specify fixative)
   c. Size of entire specimen (3 dimensions)
   d. Weight
   e. External aspect (Note **C**)
      (1) encapsulated, invasive borders
      (2) attached tissue (eg, parietal pleura, pericardium, diaphragm, chest wall with or without ribs, other)
   f. Documentation of specific areas marked by surgeon
   g. Results of intraoperative consultation
2. Tumor
   a. Location
      (1) thymus
      (2) other (eg, paraesophageal, peribronchial, pericardial, others)
   b. Size (3 dimensions)
   c. Descriptive features
      (1) color
      (2) shape
      (3) circumscription
      (4) cavitation
      (5) other (eg, necrosis, hemorrhage)
   d. Extent of invasion
      (1) structures involved by invading tumor, including vessels and nerves
   e. Additional tumors, if present
      (1) size (range)
      (2) number
      (3) location
   f. Margins (specify distance from closest approach of tumor)
   g. Additional pathologic findings, if present

h. Regional lymph nodes in specimen
   (1) location
   (2) number
   (3) description
      i. matted
      ii. gross metastasis
      iii. size of largest lymph node containing tumor
      iv. extranodal extension of tumor
i. Sections of tissue for microscopic evaluation (Note **D**)
   (1) tumor (at least 1 section per centimeter per maximum tumor diameter)
   (2) tumor interface with adjacent tissues
   (3) tumor invading adjacent tissues; adjacent tissues containing tumor
   (4) tumor capsule (capsule should be histologically sampled in areas of capsular disruption; otherwise, multiple random capsular sections should be made)
   (5) margins
   (6) frozen section tissue fragment(s) (unless saved for special studies)
   (7) specific areas designated by surgeon
   (8) areas with additional pathologic findings
   (9) other organs(s), tissues

3. Special studies (specify)
4. Photography

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **B**)
   b. Site/location
   c. Transcapsular invasion, extent
   d. Vascular invasion (arteriolar or venous)
   e. Lymphatic invasion
   f. Perineural invasion
   g Adjacent structures/organs
2. Margins
   a. Presence
   b. Margin width (in millimeters)
3. Status of area(s) marked by surgeon
4. Additional pathologic findings
5. Non-neoplastic tissues from site of origin (eg, thymus)
6. Regional lymph nodes included in main specimen
   a. Total number examined
   b. Number involved by tumor
   c. Size of the largest metastasis
   d. Extracapsular extension present or absent
   e. Metastases to other organs
7. Additional pathologic findings, if present
8. Results of special studies (specify) (Note **E**)
9. Stage (Note **F**)
10. Comments
    a. Correlation with intraoperative consultation, as appropriate
    b. Correlation with other specimens, including cytology, as appropriate
    c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Cytologic Findings

Pathologists should indicate the nature and clinical significance of any cytologic abnormality as specifically as possible. Fine-needle aspiration biopsies of mediastinal masses have a reasonably high yield for the diagnosis of thymoma and carcinomas. Cell blocks are particularly helpful, as they can be used for immunocytochemical studies.

B. Histologic Type

Levine and Rosai have classified tumors of the thymic epithelium as encapsulated and invasive (malignant) thymomas and thymic carcinoma.[1-4] In general, the Cancer Committee of the College of American Pathologists provides guidelines solely for malignant neoplasms, such as invasive thymomas and thymic carcinomas. Although encapsulated thymomas are benign neoplasms in the vast majority of patients, because they can recur locally in a small number of patients and because distant metastases have been reported in rare patients, they are included in this protocol. Levine and Rosai have subclassified both encapsulated and invasive thymomas, based on histopathologic features, into epithelial, lymphocytic, and mixed lymphocytic and epithelial.[1] More recently, Marino and Muller-Hermelink have proposed a histological classification of thymomas designating them as cortical, mixed (common, with cortical predominance, with medullary predominance), and medullary.[5] This classification is widely used in Europe but is not accepted by most American pathologists because of diagnostic reproducibility problems.[6] Recently, the World Health Organization (WHO) proposed the following grouping of thymomas and thymic carcinomas[7,8]:

Type A Thymoma (spindle cell, medullary)
Type B Thymoma
- B1 thymoma (lymphocyte-rich, lymphocytic, predominantly cortical, organoid)
- B2 thymoma (cortical)
- B3 thymoma (epithelial, atypical, squamoid, well-differentiated thymic carcinoma

Type AB Thymoma (mixed)
Type C Thymoma (thymic carcinoma)
- Epidermoid keratinizing (squamous cell) carcinoma
- Epidermoid nonkeratinizing carcinoma/lymphoepithelioma-like carcinoma
- Sarcomatoid carcinoma
- Carcinosarcoma
- Clear cell carcinoma
- Basaloid carcinoma
- Mucoepidermoid carcinoma
- Papillary carcinoma
- Undifferentiated carcinoma

Type A thymomas are composed of epithelial cells with oval or spindle-shaped nuclei and few lymphocytes. This tumor type corresponds to the designation of epithelial thymomas of the Levine and Rosai classification scheme. Types B1 and B2 thymomas are composed of large numbers of lymphocytes admixed with a fewer epithelial cells. These tumors correspond to the designation of lymphocytic thymomas of the Levine and Rosai scheme. Type B3 thymomas correspond to thymomas with atypical histology, which were not clearly defined by Levine and Rosai. Type AB thymomas correspond to mixed lymphoepithelial thymomas of the Levine and Rosai scheme. Thymic carcinomas include a variety of malignant cytologic features and are designated as Type C thymomas.[9-17]

C. Designation of Areas Suspicious for Invasion

Areas of adherence of the mediastinal mass to other mediastinal structures may be the only indication of tumor capsular penetration and hence the only indication of tumor malignancy. Surgeons should be strongly encouraged to refrain from incising the tumor capsule prior to examination by a pathologist; incisions result in tissue retraction and can compromise margin assessment. Uncertainties regarding the nature and degree of capsular adherence should be discussed with the surgeon(s) who removed the tumor. Any areas of macroscopic adherence or otherwise deemed suggestive of invasion should be marked by the surgeon postexcision and histologically sampled.

D. Number of Sections to Submit

The number of sections submitted varies with the size and character of the specimen and the nature of the underlying neoplastic process. Tumors with a heterogeneous cut surface should be sampled more thoroughly. The capsule of thymomas should be sectioned more thoroughly than the central area of the tumors. One section per centimeter of tumor largest diameter is recommended for most neoplasms.

E. Special Studies in Mediastinal Lesions

Thymomas and thymic carcinomas usually require immunocytochemistry or, less frequently, electron microscopy to establish a diagnosis. The types of special studies that must be obtained vary with the histologic appearance of the tumor as it appears on initial examination. Immunostains for keratin are helpful in distinguishing between thymomas and lymphoid lesions. In selected cases, the use of immunohistochemistry for CD1a and terminal deoxynucleotidyl transferase (TdT) may be helpful in defining the cortical thymocyte phenotype of thymoma, as distinguished from the typical peripheral T-cell phenotype of tumor-infiltrating lymphocytes associated with other tumors. Immunostains for human chorionic gonadotropin, placental alkaline phosphatase, carcinoembryonic antigen, and □-fetoprotein are helpful in differentiating among thymic carcinomas and mediastinal germ cell tumors.

F. Staging of Thymic Epithelial Neoplasms

No TNM protocol has been proposed by the American Joint Committee on Cancer (AJCC) or the International Union Against Cancer (UICC) for the staging of thymic epithelial neoplasms. The scheme developed by Masaoka as modified by Koga et al is frequently used for staging[18-21]:

Stage I	Grossly and microscopically completely encapsulated (including microscopic invasion into the capsule)
Stage IIa	Microscopic transcapsular invasion
Stage IIb	Macroscopic capsular invasion into thymic or surrounding fat, or grossly adherent but not breaking through mediastinal pleura or pericardium
Stage III	Macroscopic invasion of neighboring organs (eg, pericardium, lung, great vessels, others)
Stage IVa	Pleural or pericardial dissemination
Stage IVb	Hematogenous or lymphatic dissemination

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