

RECOMMENDATIONS FOR THE REPORTING OF BONE TUMORS

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 the 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, 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 of recognized authorities 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 elected 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 which protocols or synoptic reports are 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 cited 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.

Abstract

The diagnosis of a bone tumor is often an arduous task, even for the most experienced orthopedic pathologist. As a starting point, the classification of bone tumors is based on a histogenetic perspective encompassing the type of matrix produced (or not produced) by the tumor. In general, the surgical pathology report should include data pertinent to the treatment and prognostication of an individual patient, and the report should be delivered to the clinician in a clear and concise fashion. Reporting of most bone tumors is similar and includes such information as the type of surgery employed, anatomic site, histologic type and grade of the tumor (if applicable), and the adequacy of surgical margins. Special emphasis is needed for those tumors with distinct and well-established prognostic and therapeutic features such as osteosarcoma and Ewing's sarcoma/PNET. Our recommendation will emphasize a standardized protocol for these sarcomas especially in light of evidence that post chemotherapeutic tumor necrosis is of prognostic significance.

It is also important to note that radiographic imaging plays a very important, often critical, role in allowing the pathologist the opportunity to reach the best final diagnosis. This is especially true when a malignant interpretation is contemplated and in subtyping lesions. We recommend close collaboration between musculoskeletal radiologists, clinicians, and pathologists, when dealing with complicated neoplasms of bone.

I. Gross Description:

Many of the resection specimens for skeletal neoplasms are complex, such that each should be thoughtfully approached and dissected with attention to providing as much information as possible concerning diagnosis, grade and stage.

- A. State how the specimen was identified. (patient's name, medical record, surgical pathology number, etc.)
- B. Specify whether the specimen was received fresh or in fixative.
- C. Specify type of specimen, for example, fine or core needle biopsy, incisional biopsy, curettage, excision (segmental resection/en block), limb salvage, amputation, or complex resection (e.g. hemipelvectomy).
- D. Specimen Description and Dissection (by specimen type):

Core needle biopsy or incisional biopsy:

1. Give general gross description.
2. If sufficient tissue is present take sample for possible ancillary studies.
3. Submit specimen for formalin fixation. It requires at least 3 hours fixation. Core needle biopsies if properly fixed may be decalcified overnight with 5% diluted formic acid. - If core is 5 mm or thicker, divide.
4. In general, if ancillary studies are anticipated, then a minimum of three cores may be needed.

Provided adequate material is available for morphology (touch imprint of the biopsy can assist in this determination), additional cores can be triaged for cytogenetics, molecular diagnostics and electron microscopy in appropriate media.

Curettage:

1. Give overall measurements
2. Describe gross characteristics, i.e., color, consistency, presence of: bone, cartilage, fibrous tissue, necrosis, hemorrhage, myxoid change, cystic change, etc.
2. Attempt to separate calcified tissue (needed for decalcification) from soft tissue fragments.
3. If curetting was for therapeutic reasons, sample extensively, i.e. about one section per centimeter.

Segmental/en block resection:

1. Measure the specimen.
2. Orient according to radiographic/clinical information.
3. Assess soft tissue margins, preferably ink margins, and sample margins using perpendicular sections from those areas where there is gross or radiographic suspicion of involvement.
4. Examine for lymph nodes and submit for histologic examination.
5. Remove all soft tissues to expose tumor.
6. Cut bone along a plane determined by radiographs to expose most of the bone tumor (in general sectioning parallel to the long axis of the bone is preferred as it more adequately shows anatomic relationships relative to tumor).
7. Alternatively freeze entire specimen. Cut on a band saw and gently remove bone dust from cut surface with a surgical scrub brush. (It should be noted that this may negatively impact cytomorphology).
8. Inspect cut surfaces, measure the tumor and describe its extent.
9. Assess distance from resection margins.

10. Sample bone resection margins. This can be done by scooping marrow from the end margin before any manipulation of the tumor.
11. Describe status of the cortex, i.e., endosteal scalloping, permeation of the cortex, penetration, breakthrough, soft tissue extension, etc.
12. Describe characteristics of the tumor. i.e., color, consistency, cystic change, presence *of* necrosis, hemorrhage, etc.
13. For many specimens, a radiograph or a photograph of the cut surface is often helpful for orientation and educational purposes. Cut additional 5-6 mm thick slabs parallel to the initial bisected cut.
14. Sample an entire cut surface of the most representative slab of tissue.
15. Section orientation is often best illustrated by a map based on a diagram, photograph or specimen radiograph.
16. Cut additional random sections from the opposite (peripheral) sides of slab, and/or cut additional sections for the remaining slabs.

Amputation or Limb Salvage Specimens:

1. Examine surgical margins of resection; take sections as appropriate.
2. Identify and dissect major groups of lymph nodes
3. Inspect major vessels (arteries and veins) and nerve trunks. Take samples if involvement by tumor is suspected.
4. Open major joints and describe presence or absence of tumor involvement. Identify the location of biopsy site.
5. Dissect specimen and remove the soft tissues.

6. Describe the tumor stating its epicenter and its relation to the cortex, periosteum, joint, location in bone, (epiphysis, metaphysis or diaphysis). Specify precisely, too, whether the tumor is primarily on the surface, in the medullary cavity, or intracortical and if there is soft tissue extension.
7. Examine the specimen for co-existent and/or satellite lesions.

Examination for chemotherapeutic effect:

For osteosarcomas and Ewing's sarcoma, quantification of the extent of necrosis as an index of chemotherapeutic effect is indicated. This approach may also be appropriate for malignant fibrous histiocytoma of bone, as survival rates, therapy, and therapeutic response appear similar to osteosarcoma. Necrosis is usually expressed as a percent of total tumor area. Prognostically significant necrosis, according to most series, appears to be roughly defined at between 90% and 97% of the microscopic tumor mass. Tumors demonstrating such massive necrosis were associated with a favorable prognosis while those with less necrosis were associated with poor survival.

Defining tumor necrosis is quite difficult and can be subjective. However, specific guidelines can be applied to certain osteosarcoma subtypes. Chemotherapy tumor necrosis in osteoblastic and chondroblastic osteosarcomas is probably best defined by cell dropout (empty lacunae). Additionally, "ghost cells," remnants of neoplastic cells appearing as minute pyknotic structures or ill-defined basophilic areas, are often within the lacunae of post-chemotherapy chondroblastic osteosarcomas. Fibroblastic and small cell osteosarcomas as well as Ewing's sarcoma most often exhibit a tumor necrosis characterized by cellular portions of the tumor which have been largely replaced by fibrous and granulation tissue with chronic inflammatory cells. Post-chemotherapy specimens of telangiectatic

osteosarcoma usually reveal residual cystic spaces filled with blood and scattered hemosiderin deposition. Residual atypical cells may be evident.

In all these specimens, there may exist a population of cells which most assuredly exhibit chemotherapy effect, although the significance of these changes is uncertain. Such cells often show marked nuclear atypia with a smudgy chromatin pattern and cytoplasmic vacuolization. In an attempt to reduce the subjectivity of determining tumor necrosis, we recommend that such cytologic changes not be considered necrosis. Taking into account all the subtypes of osteosarcoma and Ewing's sarcoma., post-chemotherapy tumor necrosis is best assessed by the presence or absence of neoplastic cells.

Distinguishing spontaneous tumor necrosis from post-chemotherapy tumors necrosis may not always be possible but it is our contention that features such as absence of tumor cells accompanied by fibroblastic ingrowth and hemosiderin deposition are the result of chemotherapy and not spontaneous tumor necrosis.

We recommend the following guidelines for the evaluation of post-chemotherapy osteosarcoma and Ewing's sarcoma specimens.

1. An entire representative slice of the tumor should be sampled completely using a grid pattern diagram or radiograph indicating the site for each numbered block.
2. Additional blocks taken in a plane perpendicular to the previous ones are to determine the extent of the tumor in 3-dimensions.
3. The numbered multiple blocks systemically are obtained not only from the main tumor, but also from areas that maybe "shielded" from chemotherapy effect such as soft tissue extension and tumor/nodal

tissue interface, cortex, subcortical marrow, peri-cartilaginous regions, and areas surrounding hemorrhagic necrosis and ligaments.

Resection specimens from tumors other than osteosarcoma or Ewing's sarcoma:

Resection specimens from tumors other than osteosarcoma or Ewing's sarcoma may be processed similarly but tumor "mapping" of an entire representative slice of *tumor* is probably unnecessary. Instead, we would recommend an analogous approach similar to tumors from other anatomic sites: Representative sampling of the tumor (1 section per 1 cm) with meticulous attention to unusual appearing areas, satellite lesions, anatomic relationships, and surgical margins.

Tissue for Ancillary Studies:

Current classifications of bone tumors are largely based on light microscopic features, occasionally supported by electron microscopic and/or immunohistochemical evidence when deemed necessary. Recent advances in our understanding of the molecular biology and cytogenetics of sarcomas (especially Ewing's/PNET) have already begun to impact surgical pathology reports. It is probably prudent, when possible, for the pathologist to set aside "fresh" tissue for such studies (if available); recognizing that light microscopy must take precedence over any ancillary technique. For the present, we believe that cytogenetic studies are most appropriate for the differential diagnosis of "small blue cell neoplasms," including Ewing's /PNET. No diagnostically specific chromosomal abnormalities have been identified in osteosarcoma.

References:

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Final Anatomic Diagnosis Checklist

NEOPLASTIC BONE

Accession No.:

Part No(s).

Date:

Patient Name:

ORGAN,

SITE,

OPERATION

Bone

(Skull)

Cranium

Facial Bones

Jaw (Gnathic Bones)

Mandible

Maxilla

Long Bones

(Upper Limb)

Scapula

Humerus

Radius

Ulna

Short Bones

(Hand)

Carpals

Metacarpals

Phalanges

Long Bones

(Lower Limb)

Femur

Tibia

Fibula

Patella

Short Bones

(Foot)

Tarsals

Metatarsals

Phalanges

Thorax

Clavicle

Ribs

Manubrium

Sternum

Right

Left

Other _____

Epiphyseal

Metaphyseal

Diaphyseal

Fine Needle Biopsy

Core Needle Biopsy

Incisional Biopsy

Excisional Biopsy

Curettage

Segmental Resection

En-Block Resection

Ray Resection

Amputation

Complex Resection

Forequarter

Hindquarter

Hemipelvectomy

Other _____

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Final Anatomic Diagnosis Checklist

NEOPLASTIC BONE

Spine

(Vertebral Column)

Cervical
Thoracic
Lumbar
Sacrum
Coccyx

Pelvis

Ilium
Ischium
Pubis

Metastatic Sites

Lymph Nodes
Regional
Distant
Lung
Other Sites _____

-Primary Tumor Diagnosis

Adamantinoma

Conventional
Osteofibrous-dysplasia-like (well-differentiated)

Angiosarcoma

Chondrosarcoma

Conventional
Clear Cell
Dedifferentiated
Mesenchymal
Peripheral Juxtacortical (Periosteal)

Myxoid
Arising in association with osteochondroma

Other _____

Chordoma

Conventional
Chondroid
Dedifferentiated

Ewing's Sarcoma/Peripheral Neuroectodermal Tumor (PNET)

Fibrosarcoma

Conventional
Periosteal

Giant Cell Tumor of Bone (*specify*: Conventional, Malignant)

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Final Anatomic Diagnosis Checklist

NEOPLASTIC BONE

Hemangioendothelioma

Epithelioid

Hemangiopericytoma/Solitary Fibrous Tumor

Leiomyosarcoma

Liposarcoma

Malignant Fibrous Histiocytoma

Malignant Mesenchymoma

Malignant Peripheral Nerve Sheath Tumor

Osteosarcoma

Conventional

Chondroblastic

Fibroblastic

Osteoblastic

Mixed (*specify cell types* _____)

Low Grade Central

Intraosseous, well differentiated

Giant Cell Rich

Small Cell

Telangiectatic

Epithelioid

Osteoblastoma-like

Chondroblastoma-like

Associated with (*specify* Fibrous Dysplasia, Paget's disease of Bone, _____)

Post-Radiation

Surface

Parosteal

Dedifferentiated Parosteal

Periosteal

High Grade Surface

Rhabdomyosarcoma

Other: _____

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Final Anatomic Diagnosis Checklist

NEOPLASTIC BONE

-Lymph Nodes, *(specify site)*

A. Number examined: _____

B. Number positive: _____

C. Comment: _____

-Additional Tumor Features: *Optional*

A. Cystic Change: Identified Not Identified

B. Presence of Necrosis: Not Identified < 25% 26 – 75% > 76%

C. Hemorrhage: Identified Not Identified

-pTN Stage: *Required*

A. Primary Tumor:

pTX Primary tumor cannot be assessed

pT0 No evidence of primary tumor

pT1 Tumor 8 cm or less in greatest dimension

pT2 Tumor more than 8 cm in dimension

pT3 Discontinuous tumors in the primary bone site (skip metastasis)

B. Regional Lymph Nodes:

pNX Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 One (1) or more regional lymph node metastasis

C. Distant Metastasis:

pMX Distant metastasis cannot be assessed

pM0 No distant metastasis

pM1A Distant metastasis in lung only

pM1B Distant metastasis in bone only

pM1C Distant metastasis in other sites with or without bone or lung

Reference:

1. AJCC Cancer Staging Manual. Lippincott-Raven Press, 6th edition, 2002 (pg. 187-192).