Recommendations for Reporting of Extra-Adrenal Paragangliomas

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The Association of Directors of Anatomic and Surgical Pathology (ADASP) has proposed recommendations for surgical pathology reporting of malignant tumors. Recommendations for reporting of extra-adrenal paragangliomas are outlined herein.

The Association of Directors of Anatomic and Surgical Pathology (ADASP) has requested various committees to propose recommendations for the content and scope of the surgical pathology report for common or uncommon tumors. The following recommendations were developed by an *ad hoc* committee composed of Ernest E. Lack, MD, (Chair), Ricardo V. Lloyd MD, PhD, J. Aidan Carney, MD, PhD, James M. Woodruff MD, and a group of pathologists with expertise or special interest in paragangliomas. These recommendations are reviewed and approved by the council of the ADASP and then circulated to the entire membership of the ADASP for their input. Thus, an interim consensus on reporting is reached among those with interest and expertise in a particular area or field of pathology; clearly, it is recognized that classification of tumors, diagnostic criteria, and terminology may undergo change in the future.

The purpose of the recommendations herein is to provide an informative report that has clinical relevance and can be easily and accurately interpreted by clinicians. The recommendations made are suggestions only and their adoption is voluntary. Future developments in any particular field of tumor pathology may require changes in these recommendations. In special clinical circumstances direct recommendations based upon the ADASP proposals may not be applicable. The recommendations put forth by the ADASP council and approved by the general membership are intended as an educational resource rather than a mandate.

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Guidelines

Extra-adrenal paragangliomas are rare neoplasms that arise in a wide variety of anatomic sites. Knowledge of the widespread anatomic distribution of the tumors and familiarity with variations in their histologic patterns will help in achieving accurate histopathologic diagnosis of these tumors. The following guidelines are offered to facilitate generation of a comprehensive surgical pathology report, realizing of course that minor or major modifications are appropriate depending upon the features of an individual tumor. Pheochromocytomas are arbitrarily regarded as adrenal medullary paragangliomas and recommendations for reporting of adrenal tumors are covered elsewhere. Explanatory notes are appended.

Patient Information

1) Clinical and demographic data
   a. Name, sex, age, date of birth, and medical record number.
   b. Attending physician and/or surgeon.
   c. Date of surgery and date of receipt of the surgical specimen in the laboratory.
   d. History and/or endocrinologic data, and preoperative as well as postoperative diagnosis (see A).
2) Tumor site: the precise anatomic location of the tumor should be stated. Terminology of the extra-adrenal paragangliomas should be based upon anatomic site of origin (*e.g.*, urinary bladder paraganglioma, gallbladder paraganglioma, carotid body paraganglioma). Information regarding multicentricity or bilaterality should be included (*e.g.*, bilateral carotid body paragangliomas-familial or sporadic occurrence) (see B).
3) Surgical procedure: the report should indicate whether the surgical specimen was a biopsy, partial excision or complete excision of the lesion, or part of a more extended surgical procedure, whether a biopsy or subtotal excision was performed (or if resection was done by laparoscopy).
4) Specimen processing: The date, time and state (fresh or in fixative) of the specimen should be

noted on receipt in the laboratory. It may be desirable to indicate in the report the approximate time elapsed between surgical removal of the specimen and receiving it for examination in the surgical pathology laboratory.

5) Gross examination
   a) Ideally, the specimen should be given to the pathologist by the surgical team with appropriate orientation of the specimen and identification of any relevant attached tissues or organs.
   b) Record tumor size (three dimensions in cm.) and weight (g) following removal of extraneous tissue (see C).
   c) Specify any other tissue or organs present.
   d) Accurate and complete gross description of the external and internal (cut) surface of the tumor, noting its color and presence of necrosis or hemorrhage.
   e) Specimen photography, special studies and tumor dispersal (tumor bank, immunohistochemistry, electron microscopy, DNA quantitation, cytogenetics or other) should be recorded.
   f) Record results of intraoperative consultation including frozen section and/or smear/imprint preparations.
6. Microscopic examination and diagnosis
   a) Histologic type of tumor with brief reference to clinical and/or endocrinologic data, if pertinent.
   b) Presence and estimated extent of tumor necrosis.
   c) Presence and approximate quantitation of mitotic activity.
   d) Prognostic features as appropriate, *e.g.*, invasion of adjacent tissues or organs, presence of vascular/lymphatic invasion.
      Record status of surgical margins.
   e) Status of regional lymph nodes where pertinent, *e.g.*, total number with metastatic tumor if present.
   f) Record whether outside consultation is requested or desired and indicate source of consultation.
   g) Record in rare instances whether the tumor has composite features with a component of ganglioneuroma or malignant peripheral nerve sheath tumor. Some tumors may have areas focally resembling ganglioneuroblastoma or even neuroblastoma (see D).

Explanatory Notes

A) Clinical and/or endocrinologic date
   Clinical and endocrinologic information may be helpful in evaluation of extra-adrenal paragangliomas. Paragangliomas may be familial, transmitted as an autosomal dominant trait. Some tumors may be part of the multiple endocrine neoplasm (MEN) syndrome type 2a or 2b (tumors of the sympathoadrenal neuendocrine system, most notably pheochromocytomas) (1). In contrast to pheochromocytomas in MEN syndrome type 2a and 2b, where adrenal medullary hyperplasia is usually the precursor lesion, there is little to no comparable information about extra-adrenal paragangliomas. Extra-adrenal paragangliomas can also occur as part of a complex including gastric stromal sarcoma, pulmonary chondroma and other tumors (2).
   Paragangliomas of the sympathoadrenal neuroendocrine system may be associated with signs and symptoms of excess catecholamine secretion. Paragangliomas arising in the head and neck region are more closely aligned with the parasympathetic nervous system and are characteristically not functionally active with excess catecholamine secretion (rare exceptions exist) (1). Aorticopulmonary paragangliomas (including cardiac paragangliomas) also may be functionally active, but some of these tumors have closer alignment with the sympathetic nervous system. A history of previous surgery may be important, particularly tumors of other endocrine organs.

B) The prognosis of extra-adrenal paragangliomas can be very difficult to predict, but the anatomical location of an extra-adrenal paraganglioma has some influence on biologic behavior of the neoplasm. Carotid body paragangliomas, for example, have a relatively low rate of malignant behavior [2–3% higher in some studies (12%)]. Extra-adrenal retroperitoneal paragangliomas, on the other hand, tend to have a higher incidence of clinically malignant behavior, exclusive of some sites such as urinary bladder (1).

C) Accurate weight of tumor may be important. The approximate weight of a tumor procured in the operating room for investigative purposes should be noted. The preferred practice is to examine intact fresh tissue sent directly to sur-

TABLE 1. Diagnostic Checklist for Extra-Adrenal Paragangliomas

Anatomic site
Pathologic diagnosis, with terminology based upon anatomic site of origin
Type of resection
Tumor size (cm.) and weight (gm)
Gross description, external and cut surfaces
Results of intraoperative consultation
Microscopic examination: presence and quantitation of mitotic figures
Presence and approximate extent of necrosis
Invasive growth (blood vessels, adjacent tissues/organs)
Special studies: EM; frozen tissue; immunohistochemistry
DNA quantitation cytogenetics, other
Unusual pathologic features

gical pathology where essential weight and dimensions can be obtained before portions of tumor are designated for other research purposes.

D) Composite pheochromocytoma and extra-adrenal paraganglioma are rare neoplasms which share a common embryogenesis from neural crest. The histologic behavior of paragangliomas with microscopic features resembling ganglioneuroblastoma, or rarely neuroblastoma, is probably similar to paragangliomas in general, and these tumors do not seem to have the biologic potential or prognostic features of childhood neuroblastoma. The neuronal or ganglionic differentiation *in situ* may represent the neuronal phenotype of paraganglionic cells explanted *in vitro*. The biologic behavior of the rare composite tumors with malignant peripheral nerve sheath component is usually aggressive.

REFERENCES

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Book Review

Lack EE: Pathology of the Pancreas, Gallbladder, Extrahepatic Biliary Tract, and Ampullary Region, 608 pp, New York, Oxford University Press, 2003 ($198.50).

To "keep the production costs low," many American medical publishers often illustrate their well-written books with substandard illustrations. This amazing book proves them wrong and shows that even here (i.e., not only in Hong Kong or the UK!) it is possible to produce a reasonably priced monograph, amply illustrated with high-quality color photographs. I am also urging my colleagues and residents, who rely exclusively on thick multiauthored compilations, passing for textbooks, to see how much more one could get from a detailed single-authored monograph. I would also urge all those contemplating writing a book to study this one, emulate it, and/or use it as a prototype for their own future work.

This is a scholarly contribution to surgical pathology of a rather complex anatomic region. It was written by a seasoned pathologist who obviously has a passion for his subject. He took time to study this field by perusing numerous papers, and above all constructed the corpus of the book on his own experience and problems encountered in daily practice. He must have interacted well with other clinicians because the book has a definitive clinical tilt, with frequent references to radiology and surgery. The correlation of pathologic and clinical data is one of the strong points, and such discussions can be found in almost every chapter.

The author displays his incredible erudition or almost every page, but the thing that I liked the most are discussions of important original articles and especially those advocating controversial or contradictory approaches. This adds to a balanced presentation, which is almost always followed by the author's own take on the problem under discussion.

The author also happens to be a very good (and sometimes rather witty) writer and stylist and a master photographer. The color microphotographs and macrophotographs complement and amplify the text and are almost as important as the written words. An artist provided numerous, very informative original color illustrations. To add a touch of class, the author has included even photographs of 'human interest,' such as the official portrait of Sister Mary Joseph (of the umbilical metastasis fame), or the classic book of Brunner (known for the duodenal glands), and amusing snippets from the literature.

I recommend this book to all clinicians dealing with biliary and pancreatic disease, but, above all, I endorse it as the best book on these topics for practicing pathologists and residents. I have consulted it in my surgical pathology practice and found it very useful. My colleagues and residents liked it also, and I hope you will like it as well. On the other hand, if your budget is limited, do not forget to suggest it to your central library.

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