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QUICK COMPENDIUM
OF
SURGICAL PATHOLOGY

Dedication

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QUICK
COMPENDIUM
OF SURGICAL PATHOLOGY

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— S. Ramsburgh, MD

Preface

Readers of this text should understand that it does not represent a compendium of unique, original material. What I have tried to do is assemble in 1 easy-to-use book, the diagnostically relevant information pertaining to many diagnostic entities...information gleaned from diverse sources, most of which are considered “gold standard” books in the field. All of the references used in a given chapter are cited at the end of the chapter. Specific footnotes have not been used in the text, given that each section represents an amalgam of material prepared in conjunction with use of sources listed at the end of the chapter.

Many times I encountered major differences of opinion from one author or editor to another. Some of these differences were on opposite ends of a spectrum. I did my best to resolve as many of these as possible, but often went with the majority opinion. Most of these issues involve differential diagnosis, immunohistochemical stains, or molecular alterations. No text of this type can possibly cover all aspects of all diagnoses, so at times I simply had to stop. Any errors of omission or commission are entirely my responsibility and reflect my own decisions.

I have reviewed the role of both the pathologist and the surgeon concerning both the intraoperative consultation (the frozen section or frozen section diagnosis) and the handling of specimens. Understanding and communication on the part of both surgeon and pathologist is often essential to insure diagnostic accuracy of both frozen and permanent sections. Much of this is a reflection of my observations as both a surgeon and surgical pathologist. I also found *Intraoperative Consultations in Surgical Pathology*, published by the California Society of Pathologists in 1996 under the editorship of Mahendra Ranchod, MB, ChB to be an invaluable resource.

I sincerely hope this text be a helpful reference for those training in anatomic pathology, especially as they prepare for their “Boards.” In addition I would like the text to be of use at pathology sign-out, when questions concerning microscopic variants, immunohistochemical stains, molecular alterations, and possible associated conditions come up between faculty and residents. Finally, the book will hopefully serve as a resource for all physicians who come in contact with pathologic specimens and surgical pathology reports. In particular, surgeons in every subspecialty may find this text useful, not only in terms of interpreting the microscopic description provided in most pathology reports, but also as a rapid source of information concerning diagnoses that may be out of his or her realm of expertise.

This is a surgical pathology text without photomicrographs; most unusual to say the least. This is not an atlas to be pulled from the shelf to match slides to images but rather a resource to be used when the diagnosis is either fairly certain or limited to 2 or 3 pathologic entities and additional clinicopathologic information is desired.

— S. Ramsburgh, MD

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Foreword

Where Worlds Collide: Surgery and Pathology

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The Surgeon and Pathologist

The advanced technology that is so rapidly changing the face of medicine has resulted in an obvious improvement in the quality of care available to patients in every medical discipline. These technological advances, however, have a drawback; the accompanying explosion of knowledge has reached the point that most specialties, even those that work closely together, have become more and more isolated intellectually. Many physicians today not only lack a detailed knowledge of related fields but also an understanding of what their colleagues in those fields can and cannot do. 150 years ago the fields of surgery and pathology were essentially one specialty. Today, there is often limited communication between the two on issues germane to both. As areas of surgical expertise have become more and more specialized, only the pathologist with a particular subspecialty interest has a real understanding of the issues the surgeon faces in a given surgical field. Likewise, as new technologies have come to the aid of pathologists, their diagnostic reports now contain important information not always understood by clinical colleagues.

Interdisciplinary conferences are now common in most academic as well as private institutions and have gone a long way to broadening the knowledge base of both surgeons and pathologists. Unfortunately, many of the most pressing issues facing the pathologist and surgeon, such as intra-operative consultations (frozen section requests), specimen handling, and the wording of diagnostic reports, are still not completely understood by either party. These problems are often compounded by a lack of bilateral communication. Many surgeons no longer routinely discuss with their pathology colleagues the anticipated operative findings, actual intra-operative findings or the concerns the surgeon may have, not only about the diagnosis, but about the adequacy of surgical excision. In a similar vein, because the pathologist does not always understand the surgeon's concerns, he or she may fail to communicate effectively with the surgeon.

In my experience, it is the rare pathologist who does not enjoy the experience of reviewing the pathology of a case with the operating surgeon. This interaction gives the pathologist the opportunity to discuss the nuances of the case in terms of the differential diagnosis and the possible variants of a given diagnosis. It

also gives the pathologist the opportunity to explain the meaning of any words in the diagnostic report that may be confusing to the surgeon. There are many areas in pathology that are somewhat "grey," even to pathologists. Words such as "atypia," "dysplastic," "carcinoma-in-situ," "reactive change," "changes indicative of prior injury" can be confusing to a surgeon, especially in terms of their clinical implications. A joint review forces the pathologist to explain to the surgeon his or her criteria for calling a lesion dysplastic and the implications of that diagnosis in terms of patient management. The surgeon, in turn, will begin to appreciate the distinctions between high-grade and low-grade dysplasia, the difficulty of recognizing a focus of microinvasion in what otherwise appears to be a carcinoma in situ, and the difficulties inherent in calling changes dysplastic rather than reactive. Making these types of pathologic diagnoses with precision requires a great deal of training and years of experience; indeed, the pathologist often makes these types of diagnoses only after consultation with other pathologists. It seems obvious when both surgeon and pathologist are making decisions that affect patient care, that at some point the two should get together and discuss the pathological and clinical implications of their actions as they relate to each other. Sitting over the microscope with a pathologist, even for a brief period of time with a single case, can often give the surgeon an appreciation for the pathologist's concerns about a particular diagnosis. This exchange of information, in and of itself, can markedly expand the surgeon's sense of the adequacy of his or her procedure and the need for follow-up.

The Intraoperative Consultation

From the pathologist's perspective there are several valid indications for an intra-operative frozen section diagnosis:

1. ***When the surgeon needs a diagnosis that will determine immediate surgical management.*** This situation arises most frequently during intra-abdominal or intrathoracic procedures when it has not been possible to obtain a diagnosis prior to the laparotomy or thoracotomy. Examples include abdominal explorations for suspected malignancy, such as an ovarian mass or obstructive biliary lesion. A diagnosis of "positive for carcinoma" may lead to a staging procedure.

Intraoperative Consultation

cedure in the former and possibly a pancreaticoduodenectomy in the latter.

- 2. *When the surgeon needs to know that diagnostic material has been obtained.*** The purpose of this frozen section is not to establish a definitive diagnosis intra-operatively, but rather to ensure that the tissue sample is adequate for eventual diagnosis on permanent section. This situation most frequently arises when a surgeon is attempting to obtain tissue from a site accessible only with difficulty or when tissue is being obtained from a patient who is under general anesthesia. The surgeon must realize that the presence of lesional tissue on a frozen section does not necessarily mean that there is enough tissue for a definitive final diagnosis. This problem may arise in biopsies of large lesions, many of which have a variety of histologic patterns, such as areas of dedifferentiation that can only be accurately assessed after multiple sections from multiple locations have been examined.
- 3. *When the surgeon needs information to facilitate a decision as to the scope of a procedure.*** Typical examples include biopsies of liver nodules or mesenteric lymph nodes in cases of suspected metastatic carcinoma. The rendering of a diagnosis, “positive for carcinoma” in this instance will often result in the surgeon abandoning a proposed procedure; while a diagnosis, “negative for carcinoma,” may lead the surgeon toward a resection.
- 4. *When the surgeon needs to determine the adequacy of resection.*** The surgeon’s best chance of obtaining a complete excision is typically at the time of initial surgery. The ideal way to determine the status of surgical margins is for the surgeon to bring the specimen to pathology and discuss the anatomy with a pathologist. If frozen sections are deemed necessary to determine the adequacy of the surgical margins, the appropriate sections can then be taken by the pathologist in conjunction with the operating surgeon. This insures that the operating surgeon knows exactly where the sections were taken that might prove to be positive. Difficulty arises, however, if the neoplasm is not readily visible. The boundaries of well-differentiated soft tissue tumors are notorious for being hard to see within a soft tissue specimen. The risk of a sampling error that can lead to a report of a negative surgical margin, only to be followed by a permanent section report indicating the margin is

positive, represents a major error and may have significant consequences for the patient, namely that he or she will likely face a second procedure. The risk of this type of error can be dramatically reduced if the surgeon and pathologist work together to examine the fresh specimen and jointly determine where the most appropriate frozen sections should be taken. Even under the best of circumstances, sampling errors occur; if the surgeon is aware of the types of specimens that generate these types of errors, he or she can modify the operative procedure accordingly.

- 5. Finally, *when the presence of lesional tissue must be confirmed.*** Confirmation of lesional tissue is crucial prior to submitting tissue for additional studies (eg, culture, flow cytometry, immunoperoxidase stains on frozen tissue, electron microscopy, gene rearrangement studies or research).

It is important for the pathologist in the rendering of a frozen section report to have some understanding of the actual conduct of the surgical procedure. A case in point is the request for a frozen section of a bronchial margin on a lobectomy or pneumonectomy for malignancy. Another example is a request for a frozen section of pancreatic and biliary margins on a pancreaticoduodenectomy. If the entire specimen is received in pathology with an accompanying frozen section request concerning margins, the pathologist should appreciate that for all practical purposes the surgeon is now in the final phases of the procedure. In the case of the lobectomy or pneumonectomy, the surgeon may well be ready to close the chest. In the case of the pancreaticoduodenectomy, the surgeon has begun the anastomoses to reestablish intestinal continuity. In such cases the pathologist should move immediately to render the frozen section report. This may well mean moving a case to the “front of the line.” The surgeon who learns that the bile duct margin is positive on a pancreaticoduodenectomy after the choledochojejunostomy has been performed is now in a position of having to take down the anastomosis, resubmit a new bile duct margin and re-perform the anastomosis, all of which are time consuming, technically challenging, and usually avoidable. By the same token, the thoracic surgeon who has removed a lung may well have to delay closure of the chest if the frozen section on the bronchial margin takes more than 15 to 20 minutes.

Intraoperative Consultation

To the pathologist, certain frozen sections are considered unnecessary or inappropriate. Occasionally a surgeon will submit a frozen section in “the name of patient care.” The intra-operative frozen section diagnosis supposedly enables the surgeon to relieve the patient’s anxiety or to communicate more effectively with the patient or the patient’s family immediately after surgery. This preliminary diagnosis does not, however, truly serve patient care, and in addition, may differ from the final diagnosis. Most patients understand, if they are told, that some time is required to process and examine tissue adequately. It is the rare patient indeed who will balk at waiting 24 to 36 hours for a pathology report that is complete and carries a very small chance (generally thought to be <1%) of being either falsely positive or falsely negative. Frozen section reports may not carry the same degree of accuracy.

Frozen sections are also occasionally submitted because the surgeon is curious about an incidental, intra-operative finding that has no bearing on the course of the procedure or the patient’s welfare. This represents the single “most inappropriate” request for a frozen section diagnosis.

Sometimes the rendering of a frozen section can actually compromise the accuracy of the final diagnosis. If limited tissue is available and all or most of it is frozen, the inevitable freezing artifacts in the permanent sections may compromise the final diagnosis. Typical examples involve skin biopsies for melanoma and breast biopsies (especially biopsies done under mammographic direction in which there is no grossly discernible lesion). These types of specimens require complete fixation, careful sectioning, and total submission so that all of the material can be examined under the microscope. Frozen section diagnosis in these settings is associated with unacceptably high false-negative and false-positive rates, and the final, permanent sections may be suboptimal.

The most vexing clinical situation in which a surgeon and pathologist can find themselves is the situation in which a definitive diagnosis cannot be made on frozen section and yet the diagnosis will have a major and immediate effect on the intra-operative management of the patient. A diagnosis, “positive for carcinoma,” if incorrect, may lead to an unnecessary major resection or may stop a resection that is indicated. On the other hand, a diagnosis of, “negative for carcinoma,” if incor-

rect, may lead to a futile resection or leave the patient with at least the need for a second procedure. The pathologist feels this dilemma acutely. For their part, surgeons must accept the fact that a frozen section cannot always provide a definitive diagnosis. Consequently, they must be prepared, on occasion, to make intra-operative decisions based largely on gross operative findings and clinical circumstances. When these situations arise, it is of paramount importance that the surgeon and pathologist communicate with each other as openly and honestly as possible. It is never inappropriate for the pathologist to visit the operating room to discuss the problems concerning the frozen section with the surgeon, or for the surgeon, if possible, to leave the operating room and discuss the frozen section findings over the microscope with the pathologist. The pathologist will almost always recommend the least extensive surgical procedure when the frozen section diagnosis is in doubt. The type of consultation outlined above will increase the likelihood that the best course of action will be chosen.

From the surgeon’s perspective, the rendering of a frozen section diagnosis from an appropriate request for frozen section diagnosis always seems to take an eternity. 15 to 20 minutes is the usual amount of time it actually takes a pathologist to render a frozen section diagnosis. The surgeon should also keep in mind that frozen sections occasionally arrive in the pathology suite in bunches and there may be some delay in processing as the cryostats are cleared of cases that were received earlier. In addition, a pathologist will frequently consult with a colleague or may request that deeper sections be cut to further evaluate the lesion. These efforts and occasional technical problems may delay the rendering of a frozen section report beyond the usual time. When these delays are imminent it behooves the pathologist to communicate with the surgeon who is anxiously waiting for the results. Communication between the pathologist and surgeon concerning the status of the frozen section, especially if the diagnosis will be delayed, is as important as it is considerate and is an essential part of the pathologist-surgeon relationship.

The appearance of the surgeon in the pathology suite in an effort to “speed up” the performance of the frozen section only adds more stress to an already stressful endeavor. On the other hand, the presence of the surgeon to assist the pathologist in obtaining,

Intraoperative Consultation | Resected Surgical Specimen

with maximum efficiency, the samples absolutely necessary for frozen section examination (such as a particularly close surgical margin) is always appreciated. In addition, pathologists with few exceptions, always welcome the opportunity to examine tissue with the operating surgeon so that a more in-depth analysis of the diagnostic possibilities can be discussed beyond a simple positive or negative for neoplasm. This type of interchange over the microscope can be of benefit to the surgeon in cases where the diagnosis may be in doubt and can help the pathologist understand how the surgeon will proceed based upon the diagnosis rendered.

Most surgeons understand that occasionally a pathologist will confirm that diagnostic tissue is present but will defer a definitive diagnosis until permanent sections are available for examination. Most institutions report a deferral rate of approximately 5%. Most deferrals involve a few particular kinds of specimens. One example of such a problem lesion is the follicular thyroid nodule. Distinguishing a follicular adenoma from a follicular carcinoma from a follicular variant of a papillary carcinoma from a nodule of thyroid hyperplasia is extremely difficult on frozen section. In this instance, the report will simply read, “Follicular lesion, defer to permanents.” Another specimen that commonly results in deferral is the lymph node suspected of containing lymphoma. Most institutions do not attempt to make a definitive diagnosis on frozen sections of a lymph node in which there is a possibility of lymphoma. These reports typically read, “Lymphoid tissue present, lymphoma work-up pending.”

Occasionally, the diagnosis rendered on a frozen section will not be confirmed when the permanent sections are examined. The discordance rate between frozen section and final diagnosis should be less than 2%. Most reported errors are false-negative diagnoses (a false-negative diagnosis is one in which the frozen section is reported as negative but permanent sections reveal the lesion to be malignant). While this could be the result of an interpretative error, most commonly it is an artifact of sampling. A sampling error occurs when the frozen section is indeed negative but deeper cuts into the specimen (done to create permanent sections) reveal the presence of a neoplasm. False-positive diagnoses (lesions misinterpreted as malignant that are actually benign) are rare. More often a misdiagnosis is the result of incorrect sampling of the spec-

imen, the plane of section of the frozen section, or limitations imposed by the nature of the specimen itself (for example, specimens that are primarily fat, bone or mucoid).

The final consideration for the surgeon in terms of his or her relationship with the pathology department is the importance of providing an accurate clinical history. There is no doubt that the more pertinent clinical history that is provided, the greater the likelihood that the pathologist will not only render an appropriate and accurate frozen section diagnosis but will render an appropriate and accurate permanent section diagnosis. Surgeons need to discard the notion that “too much clinical history” prejudices the pathologist. Such a concept is contrary to the aim of open and honest communication between surgeon and pathologist.

The Resected Surgical Specimen

When appropriate, the processing, sectioning and examination of individual specimens will be discussed in the introduction to each of the following chapters. There are, however, some general considerations that are important to both pathologists and surgeons.

Pathology departments generally have some form of cutting manual that is used as a guideline for processing surgical specimens. These manuals often provide protocols as to how a specimen should be oriented and, more importantly, how it should optimally be sectioned to demonstrate the disease that is present. It is not always necessary for a surgeon to understand the actual intricacies of specimen processing and sectioning, but there are times where the surgeon’s input into the sectioning of a specimen and the subsequent understanding that can be gained is of benefit to both parties.

As mentioned under the topic of the frozen section, surgical margins are of paramount importance to both the pathologist and surgeon. Some surgical margins are very straightforward and essentially never present a problem. Classic examples are the resection margins of colon cancer or a bronchial margin of a lobectomy or pneumonectomy for malignancy. Other specimens, however, can cause very real problems to the pathologist in terms of determining the adequacy of a surgical margin. Typically, for instance, the surgical margins of

Resected Surgical Specimen

a specimen containing a soft tissue tumor are inked. Different colors of ink are used for each margin and are recorded in the gross description. The pitfall of this approach, however, is that a large resection specimen will have large margins. If, for instance, the entire lateral margin of a large specimen is inked one color and tumor is seen microscopically at that margin, the issue immediately becomes exactly where along that margin is it positive. In addition, where does the lateral margin become the superior margin, the superior margin become the posterior margin, etc? As mentioned earlier, this problem can be minimized if the surgeon is in attendance when the section is taken. The surgeon can help the pathologist orient the specimen and can point out the areas where the margins are most likely to be closest to the tumor. Margins submitted and labeled under the direction of the surgeon contribute to a more concise and meaningful final report. Other specimens are simply difficult to orient. What may seem to be a very straightforward pancreaticoduodenectomy specimen to the surgeon can be a very complicated and difficult specimen for the pathologist receiving it in a bucket with landmarks distorted. The surgeon who identifies and labels important structures with marking sutures or who spends a few moments with the pathologist to assist in identifying the bile duct margin, the pancreatic margin, and the presence of worrisome peripancreatic lymph nodes, can be of tremendous assistance and can assure that all of the important information will be provided in the final report.

If a surgical margin is violated, either accidentally or intentionally, prior to its arrival in the pathology department, the ability of the pathologist to assess the margins of the specimen is significantly compromised. Intraoperative disruption of a surgical margin may be unavoidable on occasion, but sharing that information with the pathologist who will process the specimen and pointing out the areas that have been violated will help the pathologist ink and orient the specimen so that appropriate sections can be submitted. Obviously, when tissue needs to be harvested for research purposes or if the surgeon desires to see the gross morphology of the excised lesion, this is best done in the pathology suite under the direction of the pathologist. It is easy to appreciate the frustration felt by the pathologist when a surgical specimen resected for neoplasm is received piecemeal, ruptured, partially “harvested” or extensively cauterized, considering that the most important pathologic feature next to the diagnosis is the adequacy of the surgical margins.

The surgeon who has some knowledge of pathology and understands the issues faced by a pathologist in determining a diagnosis, be it on frozen section or permanent section, will be a better surgeon. The converse is also true. The pathologist who understands the issues faced by the surgeon, in terms of preoperative management, the conduct of the procedure and the postoperative management, will be a better pathologist. The road to this mutual understanding is based on open communication and an appreciation for the needs of each.