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The importance of histopathological evaluation in cancer diagnosis and treatment

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Abstract--Background: Histopathological evaluation is a cornerstone in cancer diagnosis and treatment, providing critical insights into tumor biology, grading, and staging. Accurate histopathology informs clinical decision-making, ensuring tailored therapeutic approaches. **Aim:** This article aims to elucidate the importance of histopathological examination in diagnosing cancer, guiding treatment decisions, monitoring responses, and contributing to research advancements. **Methods:** A comprehensive review of literature was conducted, including prospective and retrospective studies that assess the value of histopathological examination in cancer diagnosis and treatment. **Results:** Histopathological analysis accurately identifies malignancies, guides tumor grading and staging, and detects biomarkers that influence treatment. It also facilitates monitoring of treatment responses and disease progression. Furthermore, it plays a vital role in cancer research and clinical trials, contributing to the development of novel therapies. **Conclusion:** Histopathological evaluation is indispensable for effective cancer management, ensuring precise

diagnoses, appropriate treatments, and improved patient outcomes. Enhanced collaboration between pathologists and clinicians is essential for optimizing cancer care.

Keywords---Histopathology, cancer diagnosis, tumor grading, biomarkers, treatment response, oncology research.

Introduction

Histopathology is a critical diagnostic tool that is used in the assessment of many different illnesses, including cancers. It is generally accepted as the gold standard for diagnosing neoplasia. Since pathologists and physicians are both essential to the diagnostic process, open and efficient communication is required. We hope that this talk will improve the knowledge that physicians have about the need for critically and accurately analyzing histopathology findings. Although the observations made here apply to all histological reports, the histopathology linked to neoplasia will be the particular subject of this discussion. A common reason for requesting a biopsy is to determine whether an animal has cancer. The type or origin of the neoplasia, signs of vascular or stromal invasion, and the biopsy margins are among the architectural details that are analyzed in a biopsy in order to arrive at this conclusion. Other characteristics that may be indicative of malignancy include irregular cell morphologies like anisocytosis, anisokaryosis, multinucleation, abnormal nuclei, elevated mitotic rates, and the presence of necrosis (1). When taken as a whole, these characteristics provide information on the type of cancer, the histological grade (if relevant), and the extent to which neoplastic cells are absent from the biopsy margins. Assessments of histopathology are vulnerable to subjectivity and unpredictability due to the need for extensive knowledge of both the clinical and pathological aspects of diseases. They also strongly rely on experience and talent. Interobserver differences in histopathological assessments of specific disorders, such as mast cell tumors and digital masses, have been documented in study (2, 3), and anecdotal evidence of such variability is common across different types of biopsy. It is best in these cases to ask for a second opinion or reassessment of the tissue slides by a different pathologist, but what does this actually mean in practice?

Using a set of prospective (6) and retrospective (4,5) studies, two referral institutions' veterinary oncologists assessed the value of second-opinion histology. The findings showed that 20 to 34% of the cases had a partial disagreement, which was defined as a change in the grade or subtype or some other minor discrepancy; on the other hand, 10 to 19% of the cases had a complete disagreement, which was defined as a change in diagnosis from benign to malignant or between two different diagnoses. In 17 to 39% of the instances, these differences led to a significant change in the prognosis or course of treatment. Even though selection bias may be the reason for the significant chance of inconsistencies in second reviews compared to first diagnoses, this is still an important factor to consider for clinical diagnosis. The research findings also suggested that the course of the disease was more consistent with the updated histological diagnosis. This alignment could be explained by the fact that when clinicians ask for a second evaluation, the reviewing pathologists usually

receive new clinical data. A diagnosis that more closely matches the animal's clinical state would probably be possible for the reviewing pathologist to evaluate if more clinical history and findings were included. This emphasizes how important it is to provide a thorough clinical history together with histopathology samples. Additionally, the authors advise doctors to speak with the pathologist directly on any discrepancies found between the clinical suspicion and the histological diagnosis of the submitted tissue in order to resolve the issue and request a second review of the sample. It is recommended that readers approach the second review with a critical eye, acknowledging that a diagnosis may change over time in tandem with the course of the disease and that a third or even fourth review may be necessary.

The interpretation of histological margins, which is a crucial component of a histopathology report, can only be done correctly when the tissue has been properly treated. Tissue architecture near the surgical margins may be harmed by improper cutting before tissue submission or by over-ECU treatment, which can impair margin evaluation. When evaluating the margins of a surgically removed tumor, it is necessary to segment the tissue in the regions where the tumor was grossly closest to the "deep" and "lateral" borders. Then, the distance between the cancer cells and the tissue edge of non-neoplastic tissue must be measured under a microscope. The histopathology report then reports this measurement in millimeters along with descriptions like "complete," "complete but narrow," or "incomplete" margins. Histologically "complete" margins may not prevent local tumor recurrence, which presents a therapeutic dilemma. Many aspects of a tumor's biological activities as well as histological assessment can be used to explain this phenomenon. A difference between histopathological margins and local tumor recurrence can be attributed to the following histological factors: (i) tissue shrinkage from formalin fixation and processing; (ii) the determination of relevant surgical planes; and (iii) the impracticability of evaluating each and every tissue edge. In terms of biology, tumor recurrence can occur even in cases when local tumor control is maintained, possibly as a result of metastasis to distant organs or lymph nodes (7,8).

One inevitable result of typical tissue processing techniques is tissue shrinking. Studies using cadavers from cats and dogs have shown that there is a mass size reduction between pre-surgical and histological measures that ranges from 10% to 36% (9,10). Analogously, antemortem investigations have demonstrated a 7–43% reduction in mass size between histological assessments and post-surgical measurements (11, 12). This suggests that a measurement of one millimeter on histology does not necessarily correspond to a measurement of one millimeter in vivo. This could be especially important for tumors like canine oral squamous cell carcinomas or high-grade mast cell tumors, as the measurement of tumor-free margins establishes whether adjuvant therapy is required (7). Using fascial planes as a natural defense against tumor invasion is part of surgical planning. These planes might not, however, be immediately visible during histological examination. Pathologists can be helped in choosing which surgical planes to analyze by accurately identifying pertinent surgical planes by adequate surgical margin tagging and efficient communication between pathologists and physicians (13). It is advised to visit the histopathology laboratory for optimal labeling techniques, as not all commercially available colors for margin inking are judged

advisable based on the authors' experiences. It will be more likely that histological margins will be determined accurately if margins of clinically significant planes are evaluated. It is not feasible to evaluate every edge of the removed tissue using routine sectioning. While different trimming techniques, like the tangential method (14), can reduce errors, it is still not feasible to obtain conclusive evaluations. Depending on the trimming strategy used, reported margins can differ greatly (15). When providing recommendations about malignancies for which incomplete excision could change the prognosis, clinicians should take this constraint into account. Clinicians and pathologists should talk about trimming techniques and the certainty of clean excision.

There is always a chance of local recurrence even in cases where a tumor is completely removed with broad histopathological margins. Although there isn't much research in the veterinary field, melanomas (16) and osteosarcomas (17) preclinical models have shown evidence of "self-seeding" by circulating tumor cells. Furthermore, as demonstrated by human head and neck malignancies, histologically "normal" tissue may still be vulnerable to neoplastic transformation, and local residual tissue may be more prone to recurrence as a result of the field effect (18). Because of these issues with margin assessment, even in cases when histologically tumor-free margins are recorded, there remains a chance of local recurrence for some cancers (20), such as canine high-grade mast cell tumors. When appropriate adjuvant therapy is recommended, clinicians should use their discretion. For the diagnosis of solid tumors in dogs and cats, histopathology remains the gold standard. However, it is important to carefully evaluate histopathological reports within the framework of the clinical situation. Clinicians should provide samples with complete clinical histories and physical examination results to help pathologists formulate clinically relevant assessments and diagnoses. After consulting with the pathologist, a secondary histological assessment may be requested if there are any discrepancies between the clinical and pathological findings. In the end, even though histological margins should be used as a guide, physicians should continue to be on the lookout for tumor recurrence by performing routine recheck exams and keeping an eye on patients depending on the expected course of their condition.

Main Histological Features in Cancers

The main histological features used to identify and classify cancer include:

1. **Cellular Morphology:** Abnormalities in cell shape and size (pleomorphism) are common in cancerous tissues. Features include:
 - **Anisocytosis:** Variation in cell size.
 - **Anisokaryosis:** Variation in nuclear size.
 - **Multinucleation:** Presence of cells with multiple nuclei.
 - **Abnormal nuclear features:** Enlarged nuclei, irregular nuclear contours, and prominent nucleoli.
2. **Mitotic Activity:** Increased mitotic figures, including atypical mitotic figures, indicate higher cellular proliferation rates, which can suggest malignancy.
3. **Architectural Disturbance:** Alterations in tissue organization, such as loss of normal architectural patterns, can be indicative of cancer. This includes:

- **Invasion:** Tumor cells infiltrating surrounding tissues.
 - **Disorganized Growth:** Irregular arrangements of cells, loss of polarity, and disrupted structures.
4. **Necrosis:** The presence of necrotic areas within the tumor can signal aggressive behavior and high-grade malignancy.
 5. **Vascular and Stromal Invasion:** Tumors may invade blood vessels (angioinvasion) or stroma, indicating a higher likelihood of metastasis.
 6. **Tumor Grading:** Tumors are often graded based on histological characteristics, such as cellular differentiation (well-differentiated, moderately differentiated, poorly differentiated).
 7. **Lymphatic Invasion:** Presence of tumor cells in lymphatic vessels can indicate a higher risk of metastasis.
 8. **Desmoplasia:** Increased connective tissue formation around a tumor, often seen in certain types of cancers, indicates a host response to the tumor.

These histological features are crucial for diagnosing cancer, determining its type and grade, and guiding treatment decisions.

The Importance of Histopathological Examination in Cancer Diagnosis and Treatment

Histopathological examination serves as a cornerstone in the diagnosis and management of cancer, providing critical insights that shape clinical decision-making and patient care. By analyzing tissue samples at the microscopic level, pathologists can identify cancerous cells, determine tumor type and grade, and assess the extent of disease, all of which are vital for formulating an effective treatment strategy. This discussion elaborates on the multifaceted importance of histopathological examination in cancer diagnosis and treatment.

1. Accurate Diagnosis of Cancer

The primary role of histopathological examination is to provide an accurate diagnosis of cancer. When a suspicious lesion is detected through imaging studies or physical examination, a biopsy is typically performed to obtain a sample of the affected tissue. Histopathology involves staining these tissue samples and examining them under a microscope, allowing pathologists to evaluate the cellular architecture and morphology. This examination reveals whether the cells are benign or malignant and can differentiate between various types of cancers. For example, certain cancers exhibit distinct histological features, such as the presence of specific cellular arrangements or abnormal nuclear characteristics. The identification of these features enables pathologists to classify the cancer accurately, which is essential for determining the appropriate treatment pathway. Misdiagnosis can lead to inadequate treatment and poor patient outcomes, emphasizing the need for precise histopathological evaluation.

2. Tumor Grading and Staging

Histopathological examination plays a crucial role in grading and staging tumors, both of which are essential for prognosis and treatment planning. Tumor grading involves assessing the degree of differentiation of cancer cells, which reflects how

closely the tumor resembles normal tissue. Well-differentiated tumors tend to grow more slowly and are often associated with better outcomes, while poorly differentiated tumors are typically more aggressive and may require more intensive treatment. Staging, on the other hand, refers to the assessment of the extent of disease spread within the body. Histopathological findings, such as the presence of lymphovascular invasion or perineural invasion, can provide vital information regarding the tumor's aggressiveness and likelihood of metastasis. This information, combined with clinical findings, aids in determining the cancer stage, which is critical for prognosis and treatment strategies. For instance, stage I cancers may be treated with surgery alone, whereas stage IV cancers may necessitate a combination of chemotherapy, radiation, and targeted therapies.

3. Identification of Biomarkers

Histopathological examination facilitates the identification of specific biomarkers that can influence treatment decisions. With the advent of personalized medicine, the understanding of molecular and genetic characteristics of tumors has become increasingly important. Certain histopathological techniques, such as immunohistochemistry, allow for the detection of specific proteins or gene expressions associated with cancer. For example, the expression of hormone receptors (e.g., estrogen and progesterone receptors) in breast cancer can guide the use of targeted therapies such as hormone therapy. Similarly, the presence of specific mutations, such as EGFR mutations in non-small cell lung cancer, can determine the suitability of targeted therapies like tyrosine kinase inhibitors. By identifying these biomarkers through histopathological examination, clinicians can tailor treatment plans to the individual patient, enhancing the likelihood of favorable outcomes.

4. Monitoring Treatment Response and Disease Progression

Histopathological examination is also instrumental in monitoring the response to treatment and assessing disease progression. Following initial treatment, such as surgery, chemotherapy, or radiation, follow-up biopsies may be performed to evaluate the effectiveness of the intervention. Changes in histological features, such as a reduction in tumor cellularity or the presence of necrosis, can indicate a positive response to therapy. Conversely, persistent or evolving histopathological features may suggest treatment resistance or disease progression, prompting reevaluation of the treatment strategy. For instance, the development of new mutations in tumor cells may lead to changes in treatment regimens, necessitating a shift from one therapeutic approach to another. Regular histopathological assessments, therefore, are essential for ongoing management and adjustment of treatment plans.

5. Role in Research and Clinical Trials

Histopathological examination is fundamental in cancer research and the development of new therapeutic strategies. Tissue samples obtained from patients enrolled in clinical trials are analyzed to understand the underlying mechanisms of cancer biology and treatment response. This research can lead to the discovery of novel biomarkers, potential therapeutic targets, and insights into cancer

heterogeneity. Moreover, histopathology contributes to the validation of preclinical models and the efficacy of new drugs. By correlating histological features with clinical outcomes, researchers can identify promising treatment approaches and refine existing ones. This research is critical in the pursuit of improved cancer therapies and better patient outcomes.

6. Ethical and Societal Implications

The implications of histopathological examination extend beyond individual patient care to broader ethical and societal considerations. Accurate cancer diagnosis and treatment are essential for ensuring patients receive appropriate care, thereby reducing the overall burden of cancer on healthcare systems. Moreover, disparities in access to histopathological services can impact cancer outcomes in different populations. Addressing these disparities through improved access to quality histopathological examinations is vital for achieving equitable cancer care. In conclusion, histopathological examination is an indispensable component of cancer diagnosis and treatment. Its role in providing accurate diagnoses, grading and staging tumors, identifying biomarkers, monitoring treatment responses, and facilitating research underscores its significance in the oncology field. As advancements in histopathological techniques continue to evolve, the integration of these methods into routine clinical practice will enhance our ability to provide personalized and effective cancer care, ultimately improving patient outcomes and quality of life. The ongoing collaboration between pathologists, oncologists, and researchers is crucial in harnessing the full potential of histopathology in the fight against cancer.

Conclusion

Histopathological examination is an integral component of cancer diagnosis and treatment, offering invaluable insights that guide clinical practice. The accuracy of histopathology in identifying malignant lesions is crucial, as misdiagnoses can lead to inappropriate treatment strategies and adverse patient outcomes. The ability of pathologists to analyze tissue samples microscopically allows for the differentiation of cancer types, which is fundamental in formulating tailored treatment plans. Additionally, tumor grading—a critical aspect of histopathology—provides information about the aggressiveness of the cancer, which influences therapeutic decisions. For instance, poorly differentiated tumors may necessitate more aggressive treatments compared to well-differentiated ones. The identification of biomarkers through histopathological techniques, such as immunohistochemistry, has revolutionized cancer treatment, allowing for the application of personalized medicine. By recognizing specific protein expressions and genetic mutations, clinicians can select targeted therapies that are more likely to yield favorable outcomes. The ongoing assessment of treatment responses via follow-up histopathological evaluations ensures that treatment regimens can be adjusted based on the patient's response, facilitating more effective management of the disease. Furthermore, histopathology serves as a vital tool in cancer research, enabling the exploration of new therapeutic avenues and the validation of preclinical models. The correlation of histological features with clinical outcomes enhances our understanding of cancer biology, paving the way for the development of novel treatment strategies. Beyond individual patient care,

the implications of histopathological evaluation extend to broader ethical and societal issues, including disparities in access to diagnostic services. Addressing these disparities is essential for ensuring equitable cancer care and improving overall health outcomes across diverse populations. In conclusion, the importance of histopathological examination in cancer management cannot be overstated. It remains the gold standard for diagnosing cancer, informing treatment decisions, and monitoring disease progression. As the field of histopathology continues to advance, its integration into routine clinical practice will further enhance the delivery of personalized cancer care. Continuous collaboration among pathologists, oncologists, and researchers is vital to harness the full potential of histopathology in the fight against cancer, ultimately leading to improved patient outcomes and quality of life.

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أهمية التقييم النسيجي المرضي في تشخيص وعلاج السرطان

الملخص:

الخلفية: يعتبر التقييم النسيجي المرضي حجر الزاوية في تشخيص وعلاج السرطان، حيث يوفر رؤى حيوية حول بيولوجيا الورم، والتصنيف، والمراحل. إن وجود تقييم نسيجي دقيق يسهم في اتخاذ القرارات السريرية، مما يضمن استخدام أساليب علاج مخصصة.

الهدف: يهدف هذا المقال إلى توضيح أهمية الفحص النسيجي المرضي في تشخيص السرطان، وإرشاد قرارات العلاج، ورصد الاستجابات، والمساهمة في تقدم الأبحاث.

الطرق: تم إجراء مراجعة شاملة للأدبيات، بما في ذلك دراسات مستقبلية ودراسات سابقة التي تقيم قيمة الفحص النسيجي المرضي في تشخيص وعلاج السرطان.

النتائج: يحدد التحليل النسيجي المرضي بدقة الأورام الخبيثة، ويرشد تصنيف الورم والمراحل، ويكتشف المؤشرات الحيوية التي تؤثر على العلاج. كما يسهل رصد استجابات العلاج وتقدم المرض. بالإضافة إلى ذلك، يلعب دورًا حيويًا في أبحاث السرطان والتجارب السريرية، مما يساهم في تطوير علاجات جديدة.

الاستنتاج: يعد التقييم النسيجي المرضي ضروريًا لإدارة السرطان بشكل فعال، مما يضمن تشخيصات دقيقة، وعلاجات مناسبة، وتحسين النتائج للمرضى. إن تعزيز التعاون بين أخصائي الأمراض والعيادات أمر ضروري لتحسين رعاية السرطان.

الكلمات المفتاحية: النسيج المرضي، تشخيص السرطان، تصنيف الأورام، المؤشرات الحيوية، استجابة العلاج، أبحاث الأورام.