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PATHOLOGI ANATOMICAL FEATURES OF ONCOLOGICAL DISEASE

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Annotation

Histopathology plays an essential role in oncology, both in the initial tissue diagnosis of the tumour and later in the detailed examination of the surgical specimen. The information gained from the macroscopic and microscopic examination of the specimen will guide further treatment and establish prognostic and predictive markers for the patient. Pathologists will often demonstrate the morphology of tumours to the members of the multidisciplinary team (MDT).

Key words: cancer, tumour, biopsy, carcinoma, tumour morphology, sarcoma.

This is an excellent opportunity to question the pathologist on morphological descriptions and it provides a teaching experience for medical students through to senior consultants. Mutual understanding of working practices and interpretation of results among all members of the MDT improves team working and patient care.

Molecular genetic analysis is also an important and rapidly developing area of histopathology with tissue used for diagnostic and prognostic purposes. It is beyond the scope of this chapter to list all the molecular investigations available, as these are covered in specific chapters.

It is not essential for an oncologist to have a detailed knowledge of histopathology, but a general understanding of pathological terms, tumour morphology, laboratory techniques and limitations is helpful. This chapter describes:

specimen types,

important microscopic descriptions of tumours,

essential and practical immunohistochemical results and

important aspects of working with pathologists within busy MDTs.

Before obtaining a biopsy, the risks and benefits for the individual patient should be considered, especially when deciding which site is likely to most easily give a complete and accurate diagnosis, balancing the risk of failing to get a tissue diagnosis with the possible morbidity of the procedure. The patient will almost certainly be very anxious and any delays from repeated negative biopsies will not only make this worse but also delay treatment decisions. Sometimes a biopsy may not be necessary if treatment options are very limited.

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Biopsy procedures oft en have an associated risk of morbidity; for instance, up to 5% of patients may require a therapeutic chest drain after a lung biopsy and liver biopsy may have a mortality rate of up to 1%. When requesting a pathology report, it is important for the requesting clinician to put all relevant clinical details on the request form including radiological information, symptoms, tumour markers, suspected diagnosis and previous cancer diagnosis (if relevant) to allow the pathologist to perform the most helpful tests as rapidly as possible. Advances in both pathology and oncology have changed working practices significantly. Th ere are now more tools available to pathologists to guide treatment decisions (e.g. ER/PgR and HER2 testing in breast cancer and diff erentiating adenocarcinoma from squamous cell carcinoma in non-small-cell lung cancer (NSCLC)) and in elucidating a primary tumour when none may be apparent clinically (e.g. by immunohistochemistry). Additional genetic tests (e.g. epidermal growth factor mutation testing in NSCLC) have also changed working practices and a tissue diagnosis may now be needed when none was needed previously, with more tissue required for all the necessary tests. This means good teamwork to ensure that the most appropriate tissue is available to make an accurate, complete and timely diagnosis. The pathologist will receive a variety of different types of specimen, each of which has advantages and limitations for making a diagnosis.

Exfoliative cytology (non-gynaecology). Exfoliative cytology specimens include pleural and peritoneal fluids, urine, cerebro-spinal fluid (CSF), sputum, bronchial washings and brushings. These samples are relatively rapid to process, although not as rapid as FNAC, and the cellularity depends on the disease process involved. In skilled hands, high sensitivity and specificity can be obtained and immunohistochemistry can be performed using the cell block method, which may, however, be more diffi cult to interpret than a core biopsy. Samples can also be sent for flow cytometry if required. The disadvantages are also similar to those of FNAC specimens. It may be difficult to accurately subtype tumours on cytological grounds alone and poor cellularity of the sample may be a problem.

Frozen section. A frozen section is useful for a rapid answer to an issue that arises during an operation. There may, for instance, be a suspicious peritoneal nodule during an anterior resection of a colonic carcinoma, or a need to examine margins to establish complete surgical excision. Frozen sections can provide a rapid result, but the morphology of cells in frozen section specimens differs from that in conventional paraffin-embedded, haematoxylin

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and eosin-stained slides. False positive and negative results are possible and in a difficult case the pathologist would issue a cautious report while awaiting more definitive paraffin sections.

Tissue core, endoscopic and excision biopsies. This is the commonest type of specimen. Depending on the size of the tissue, the sample tends to be fixed in formaldehyde for a period ranging from a few hours to overnight. The morphology from a good-quality long core of tissue is oft en excellent, enabling the pathologist to assess the overall architecture and cytonuclear features. It is possible to perform histochemical stains (for example, to look for mucin) and also immunohistochemical stains. Tissue can also be prepared for flow cytometry and sent for molecular analysis if required. The drawback of most core biopsies is that the fixation and processing of the tissue can delay the reporting of the specimen, although it can usually be diagnosed and reported on the day after reaching the processors that enable a much more rapid assessment of the laboratory. There are now microwave tissue and a ‘same-day’ diagnosis, but their cost prohibits their use in many pathology laboratories. Another problem may be the quality of the sample, and a tumour in a difficult anatomical location may produce fragmented, small-volume cores leading to a cautious or unhelpful pathology report.

Large cancer resections. Following fixation in formaldehyde for at least 24 hours, the pathologist will examine the gross morphology carefully and decide on the appropriate tissue blocks of tumour, background, margins and lymph nodes. These will be processed overnight and cut and stained into slides the following day. The advantage of this specimen is that there will usually be abundant tissue to examine. Gross photographs of the specimen are taken and, with appropriate consent, tissue can easily be collected for research or for the local cancer bank.

The following section is a brief overview of the histological appearances of some of the common tumour subtypes.

Squamous cell carcinoma. Squamous epithelium may be simple or stratified; the latter covers many parts of the body, including skin, oral cavity, oesophagus, cervix, vagina and anal canal. The epithelium is typically robust and can withstand mechanical stresses placed on it. Dysplasia of the squamous epithelium may progress to invasive squamous cell carcinoma that invades through the basement membrane into the underlying supporting connective tissue. The usual appearance of the tumour depends on the degree of diff erentiation. There are different grading systems, but typically high-grade squamous tumours will exhibit reduced keratinisation and intercellular bridging and increased cytonuclear pleomorphism and mitotic activity. There are several variants of squamous cell carcinoma, including basaloid and spindle cell types.

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Adenocarcinoma. Adenocarcinomas arise from glandular epithelium, of which there are many different types and functions in the body. Some glandular epithelia have a secretory or absorptive role, while others, such as ciliated columnar epithelium, have a propulsion role. The sheer number and diversity of adenocarcinoma cannot be covered in this chapter. They are found in a wide variety of sites including breast, lung, colon, stomach, pancreas, prostate, kidney, liver, ovary, uterus and thyroid, among many others. When a lung biopsy of a mass shows an adenocarcinoma, the pathologist must use a combination of histological appearance, immunohistochemistry and clues from the clinical history and radiology to determine whether it is a primary lung adenocarcinoma or a metastasis. Many adenocarcinomas show similar morphology to each other, but some show subtle clues as to their primary site:

1. a cord-like pattern of lobular carcinoma of breast or the trabecular appearance of hepatocellular carcinoma;

2. comedonecrosis (central necrosis in a rounded epithelial island) as seen in some breast and salivary duct carcinomas;

3. central necrosis (‘dirty necrosis’) seen in the enteric-type epithelium of colonic adenocarcinoma;

4. signet ring adenocarcinomas are a feature of diff use gastric adenocarcinoma, but can also occur in tumours from other locations;

5. prominent perineural invasion is oft en seen in adenoid cystic carcinoma of the salivary glands and in prostate adenocarcinoma;

6. a papillary growth pattern is seen in several types of adenocarcinoma, such as kidney, ovary and thyroid;

7. cribriform (‘sieve-like’) architecture is seen in prostate, breast and some endometrial adenocarcinomas. Other adenocarcinomas show distinctive cytonuclear features that can point to a primary site.

1. The cytoplasm of clear cell renal cell carcinoma is distinctive, but clear cell adenocarcinoma variants are also present in the ovary and endometrium and several other sites.

2. The optically clear nuclei of thyroid papillary carcinoma, so-called ‘Orphan Annie’ nuclei .

Malignant melanoma. The diagnosis of malignant melanoma can be tricky for the pathologist. In the primary cutaneous form, the diagnosis is relatively straightforward when there are nests of atypical melanocytes displaying epidermal pagetoid spread and an infi ltrative

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pattern in the dermis. Melanin pigment may be abundant and the cells can show pleomorphism. Th e problem is that there are a significant number of histological variants of melanoma, with some displaying small bland nuclei and others a prominent spindle cell component. The latter would fall into a wide differential diagnosis including spindle cell squamous carcinoma, cutaneous sarcomas or an atypical fibroxanthoma. Metastatic deposits of malignant melanoma can occur in various clinical situations and anatomical sites, can show a wide variety of cellular appearances and oft en require immunohistochemistry for diagnosis. Pathologists always have melanoma in their differential for a tumour of unknown origin.

Small cell carcinoma. This is a poorly differentiated neuroendocrine carcinoma which can be found in many diff erent parts of the body, with the lung being the commonest primary site. The tumour is often found centrally in the lung, and morphology shows a solid distribution of cells, although other patterns can be seen, including rosettes, ribbons and tubules. Th e cells have a distinctive small size with very dark (hyperchromatic) nuclei. Th e chromatin pattern is granular and there is minimal cytoplasm present. Nuclei may show moulding and in small endoscopic biopsies the nuclei may become elongated and distorted, causing diagnostic problems. In necrotic areas nuclear debris may be smeared into blood vessel walls a phenomenon known as the Azzopardi effect. In a limited and partly crushed endoscopic biopsy, immunohistochemistry for neuroendocrine markers would be essential to confirm the diagnosis because lymphoma would be in the differential.

Lymphoreticular tumours. There is great morphological diversity in the histopathology of lymphomas. From a broad division into non-Hodgkin and Hodgkin lymphoma, the pathologist has a low to high power approach when assessing the microscopy. On low power the lymphoid infiltrate is divided into nodular/follicular or diffuse, and on high power the individual cell morphology is assessed. For example, a nodular/follicular architecture composed of small cleaved centrocytes would suggest grade 1 follicular lymphoma, while a diff use population of large atypical blasts would suggest a diff use large B cell lymphoma.

Soft tissue and bone tumours. Malignant soft tissue and bone tumours are uncommon and the average pathologist will see only a small number of cases per year. Their appearance will depend on the anatomical site, the cell of origin and the degree of diff erentiation. For example, a differentiated leiomyosarcoma should show some morphological similarities to normal smooth muscle. Poorly diff erentiated sarcomas are oft en a diagnostic challenge and may require immunohistochemistry to identify the original cell type. Sarcomas are usually

diagnosed and treated by a dedicated MDT and so if sarcoma is suspected, it is better to refer to the sarcoma MDT who will arrange for the biopsy to be performed in a way that will not affect subsequent management .

In conclusion, diagnosing and treating cancer is a complex process requiring the experience and skills of multiple medical and health professionals, often referred to as the oncology team. Biomarker testing allows the pathologist to provide a definitive diagnosis. After cancer is diagnosed, the pathologist determines the grade and stage of the cancer which helps with treatment planning and assessing the prognosis.

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