PRINCIPLES OF MICROSCOPIC DIAGNOSIS Diagnosis of m

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Neoplasia is a broad term that includes benign and malignant tumours and precursors of malignancy . The word ‘cancer’ is not precise, derives from observations of the similarities - between crabs and tumours by ancient Greek physicians such as Hippocrates and usually refers to all malignancies (rather than carcinoma alone). Classification of a tumour as malignant implies that it can behave aggressively . The main features of malignancy are metastasis and invasion and there are charac - teristic architectural and cytological abnormalities. However, the criteria for a diagnosis of malignancy di ff er between anatomical sites and between tumour types. Sometimes, the traditional concept of benign and malignant is not applicable and instead there is a classification that identifies a spectrum of tumours from well di ff erentiated to poorly di ff erentiated or from low grade to high grade depending on known clinical behaviour. Microscopic features of malignancy /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Microscopic evidence of aggressive behaviour by the tumour is usually su ffi cient for a malignant label. For example, metastasis to another organ such as lymph nodes or liver is diagnostic of malignancy . Invasion of surrounding structures, perineural invasion (Figure 11.10) and vascular spread or invasion (Figure 11.11) strongly suggest malignancy . Other microscopic features that are typical of malig nancy include derangement of the usual tissue architecture, an increase in the number of mitotic figures, atypical mitotic figures and necrosis (tissue death) (Figure 11.12) . Changes in . cytological changes, the appearances of individual cells, i.e include nuclear enlargement, an increase in the nuclear: cytoplasmic ratio, nuclear pleomorphism (variation in nuclear appearance) and n uclear hyperchromasia (dark colour) 11.13a) . Multiplicity , irregularity and enlargement of nucleoli may also be apparent (Figure 11.13b). However, none of these features is diagnostic of malignancy in isolation. or a histological diagnosis of malignancy vary The criteria f according to the site and type of tissue. Carcinoma is by far the most common type of malignancy , and in many settings Nerve Tumour Necrosis Viable tumour - (Figure is diagnosable when epithelial cells invade beyond their nor - mal boundaries. However, the categorisation of some types of non-epithelial proliferations (e.g. lymphoid or mesenchy - chitec - mal) as malignant may rely on cytological and/or ar tural features rather than on invasiveness. In some cases, e.g. phaeochromocytoma, reliable histological distinction between e.g. gas - benign and malignant is not possible. In other cases, trointestinal stromal tumours (GISTs), there are risk catego - ries based on combinations of histological features that help to predict the likelihood of aggressive behaviour rather than . Additional techniques such

benign or malignant designations as immunohistochemistry and clonality studies occasionally help to confirm or support a diagnosis of neoplasia or malig - nancy (see Immunohistochemistry: tumour pathology and Diagnostic molecular pathology). The term ‘dysplasia’ usually indicates that microscopic fea - e is tures similar to those of carcinoma are present but that ther no invasion. The term ‘intraepithelial neoplasia’ is analogous to dysplasia. Examples include cervical intraepithelial neopla - sia (CIN) and gastrointestinal dysplasia (Figure 11.14). Grad - ysplasia may be as low grade/high grade or as mild/ ing of d moderate/severe while grading of intraepithelial neoplasia may be numerical (e.g. CIN 1, CIN 2 and CIN 3).

Metastasis Invasion Of surrounding tissue Vascular (intraluminal tumour and/or tumour in blood vessel wall) Perineural Architectural abnormalities Necrosis Numerous mitotic /f_i gures Atypical mitotic /f_i gures Nuclear abnormalities Pleomorphism Enlargement Hyperchromaticity Chromatin clumping Nucleolar enlargement and multiplicity Figure 11.10 Perineural invasion. A nerve is almost surrounded by adenocarcinoma. Figure 11.11 Vascular invasion. Aggregates of carcinoma cells are present within blood vessels. The tumour is poorly differentiated. Figure 11.12 An area of necrosis in a poorly differentiated carcinoma.

malignancy . These include contamination of a specimen with tumour from elsewhere, interchanging of specimens, observer error and histological mimicry . A false-negative diagnosis, i.e. a failure to diagnose malignancy when present, may reflect absence of tumour in the specimen or failure of the pathologist to recognise the changes as neoplastic. Several conditions can resemble malignancy histologically . For example, radiation e ff ect can produce cytological atypia that mimics malignancy , and the epithelial changes in regen - erating tissue adjacent to a mucosal ulcer may show features reminiscent of neoplasia. The risk of interpretative error by the histopathologist is likely to be lower if there is thor ough training of pathologists, regular updating of knowledge, dis - cussion of di ffi cult cases with colleagues and avoidance of excessive workloads. The surgeon also helps to minimise errors by supplying good clinical details. Summary box 11.6 Causes of false-positive diagnoses of malignancy /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF

(b) Figure 11.13 Cellular features of malignancy. (a) A neuroendocrine carcinoma showing nuclear pleomorphism (variation in shape) and variation in nuclear size. There are several mitotic /f_i gures (arrows). A malignant melanoma showing nuclear pleomorphism and prominent nucleoli (arrow) (courtesy of Dr E Husain, Aberdeen Royal In /f_i rmary Aberdeen, UK). Figure 11.14 A colonic biopsy from a tubular adenoma with low- grade dysplasia. A non-dysplastic crypt is apparent at lower right. The remaining crypts mostly show features of dysplasia, including nuclear strati /f_i cation (multilayering), nuclear enlargement and nuclear hyperchromaticity (dark colour). Interchanged samples Contamination Interpretative error Treatment-induced change, e.g. radiotherapy Ulceration

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