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Nodal Malignant Lymphoma (with comments on extranodal lymphoma and metastatic cancer)

1. GROSS DESCRIPTION

Specimen

— fine needle aspirate/needle biopsy core/excisional biopsy/regional lymphadenectomy.

Malignant lymphoma presents as persistent, mobile, rubbery and non-tender lymphadenopathy with or without associated systemic symptoms such as weight loss, itch or night sweats. Investigation is by full blood picture (infections/leukaemias), serology (infections/autoimmune diseases), FNA (to exclude metastatic cancer) and biopsy.

The preferred specimen for diagnosis, subtyping and grading of nodal malignant lymphoma is an excisional lymph node biopsy carefully taken by an experienced surgeon to ensure representation of disease and avoidance of traumatic artefact. Submission of the specimen fresh to the laboratory allows imprints to be made to which a wide panel of immunohistochemical antibodies can be applied, some of which are more effective than on tissue sections, e.g. demonstration of light chain restriction. Tissue can also be harvested for molecular and genetic techniques. Morphological classification is generally based on well-fixed, thin slices, processed through to paraffin with high quality 4-μm H&E sections. Core biopsy may be the only option if the patient is unwell or the lesion relatively inaccessible, e.g. mediastinal or para-aortic. Allowances must be made in interpretation for undergrading of nuclear size, sampling error and artefact. Confirmation of lymphomatous (or other) malignancy is the prime objective and further comments on subtyping and grading given with care and only if definitely demonstrable. A positive diagnosis can be given in a significant percentage of cases. Importantly, interpretation should be in light of the clinical context, i.e. the presence of palpable or radiologically proven significant regional or systemic lymphadenopathy and the absence of any obvious carcinoma primary site. Tumour heterogeneity must also be borne in mind. The same principles apply to FNAC, which is excellent at excluding inflammatory lymphadenopathy, e.g. abscess or sarcoidosis and non-lymphomatous cancer (e.g. metastatic squamous cell carcinoma, breast carcinoma or malignant melanoma) and reasonably robust at designating Hodgkin's and high-

grade non-Hodgkin's lymphoma. Morphology is the principal diagnostic criterion when assessing excisional lymph node biopsies, core biopsies and FNAs but is supplemented by immunohistochemical antibody panels targeted at the various diagnostic options, e.g. a small lymphoid cell proliferation (lymphocytic lymphoma vs. mantle lymphoma, etc). In addition, flow cytometry and molecular gene rearrangements are helpful in determining a diagnosis. Limited needle sampling techniques can also be used in patients with a previous tissue biopsy-proven diagnosis of lymphoma and in whom recurrence is suspected. However, possible transformation of grade must be considered and even change of lymphoma type, e.g. small lymphocytic lymphoma to Hodgkin's lymphoma or Richter's transformation to diffuse large B-cell lymphoma. A range of inflammatory nodal disease may also be encountered secondary to chemotherapy and immunosuppression, e.g. tuberculosis.

A systematic approach to excisional lymph node biopsies will allow the majority to be categorized as specific inflammatory pathology, benign or malignant and the latter as haematopoietic or non-haematopoietic. Diagnostic morphological clues to malignant lymphoma are:
Low-power magnification:

— capsular/extracapsular spillage of lymphoid tissue.
— capsular thickening and banded septal fibrosis or hyaline sclerosis.
— loss of sinusoids either with compression or due to a cellular infiltrate
— alteration in follicular architecture with changes in
  a. distribution: proliferation in the medulla
  b. size and shape: relative uniformity of appearance, and
  c. definition: loss of the mantle zone–germinal centre interface/"filling up" of the germinal centre/loss of tingible body macrophages.
— prominent post capillary venules

High-power magnification:

— presence of a background polymorphous inflammatory cellular infiltrate, e.g. eosinophils, plasma cells and histiocytes (epithelioid in character ± granulomas).
— alterations in the proportions of the normal cellular constituents.
— dominance of any mono- or dual cell populations.
— presence of atypical lymphoid cells
  a. nuclei: enlargement/irregularity/hyperchromasia/bi- or polylobation/mummification/apoptosis
  b. nucleoli: single/multiple/central/peripheral/eosinophilic/basophilic/Dutcher inclusions
  c. cytoplasm: clear/vacuolar/eosinophilic/scant/plentiful/paranuclear hof.

A morphological diagnostic short list should be created, e.g. mixed cellularity Hodgkin's disease vs. T-cell lymphoma vs. T-cell-rich B-cell lymphoma and a targeted immunohistochemical antibody panel used. In the majority of cases it will confirm the preliminary diagnosis but will in a minority lead to its modification and either a refinement within or revision of diagnostic category.