HOrthie cell chanoes (oxvyhilic changes

Hashimoto's thyroiditis
Adenomatous goiter
Grave's disease
Radiation
Myxedema
Partial thyroidectomy

Sauamous cells

Cysts

Lateral
Epidermal

Lymph nodes

Metastatic epidermoid carcinoma

Salivary glands

Mucoepidermoid carcinoma

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Fine needle aspiration cytology of lymph nodes

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Fine needle aspiration (FNA) cytology enables a simple and rapid diagnostic approach of patients with lymph node enlargement. The first objective in the assessment of smears from an enlarged lymph node is to distinguish between metastases, infectious diseases, reactive hyperplasia and lymphomas.

The value of FNA for the diagnosis of lymph node metastasis either of an unknown primary or in the follow-up management of a patient with cancer is widely accepted, with an overall sensitivity and specificity of >98% in large series, thus avoiding the need for excisional biopsies in most patients.

The dia~nostic accuracy depends on the cytological expertise and on a good clinicopathological correlation that allow knowledge of the pitfalls and adequate management of the problem cases. Cystic metastasis may constitute an example of such problems, as it may be difficult to identify malignant cells even after fluid centrifugation. These cases are not rare in the neck region and frequently, when considering both the macroscopic characteristics of the cyst fluid and neck ultrasound, it is possible to suspect the true origin of the cyst.

Besides the identification of malignancy, the categorization of the neoplasia is often possible, especially when combining morphology with immunocytochemistry. This is particularly useful for tumors that have specific markers, such as prostate and thyroid carcinomas, and for melanoma which has so many cytological appearances. Positive estrogen receptors in a metastatic carcinoma in cervical or axillary lymph nodes, although nonpathognomonic, also strongly support the breast as the source of the primary tumor.

FNA of lymph nodes may also be very useful for the diagnosis of infectious diseases, either by the morphological identification of microorganisms or, and more importantly, by providing material for microbiological studies. This is particularly pertinent in HIV patients and diminishes the need of surgical biopsy and allows a rapid onset of therapy. When a cytological diagnosis of granulomatous lymphadenopathy is done, one should, however, remember that it does not exclude the possibility of an associated malignancy; therefore, if the clinical and laboratory data are not consistent with a granulomatous disease, a biopsy should be carried out. The same applies to persistent lymph nodes with a reactive morphological and immunophenotypic pattern on smears, consistent with follicular hyperplasia or a paracortical response without any identifiable possible cause in order to avoid false negative diagnoses. Smears from infectious mononucleosis may constitute diagnostic problems as they can be misinterpreted as non-Hodgkin's yinphoma when a large number of blasts are present or as Hodgkin's lymphoma when Reed-Steinberg-like cells are prominent.

The role of FNA for the primary diagnosis of lymphoproliferative diseases is still controversial. The main objections have been the following: i) the inability to evaluate the architectural pattern and thus subclassify non-Hodgkin's lymphomas; ii) a low sensitivity due to diagnostic problems in differentiating reactive hyperplasia from low-grade non-Hodgkin's lymphomas or from lymphocyte predominant Hodgkin's lymphoma; and iii) partial involvement of lymph nodes by some lymphomas, particularly high-grade non-Hodgkin's lymphomas.

Partial involvement of lymph nodes by a malignant disease constitutes a true problem for FNA diagnosis, whether it be a yinphoma or a metastatic deposit, and stresses the importance of practicing cytology in close cooperation with clinicians so that problem cases are readily recognized and a biopsy pertormed.

As for the other arguments against using FNA for diagnosing and classify lymphoproliferative diseases and since the latest yinphoma classification (REAL) is based not in architectural pattern but on cellular morphology, phenotype and genotype of malignant yinphoid cells, all of which can be assessed by cytology, we believe, like others, that FNA with immunocytochemistry, flow cytometry and, in difficult cases, molecular techniques such as polymerase chain reaction (PCR) and *in situ* hybridization (ISH) can confidently make the diagnosis and subclassification of malignant lymphoinas in the majority of cases with a high diagnostic accuracy (>90%). An exception to this statement may be mantle zone lymphomas since it has been suggested that architectural pattern may be of use to further subdivide this type of non-Hodgkin's lymphoma. To achieve good results, not only is expertise in lymph node cytology and pathology necessary but also in the recognition of the cases in which, due to discrepancies in morphology and ancillary techniques, a biopsy is needed.

The entities that cause more diagnostic problems are low grade non-Hodgkin's lymphomas with a mixed cell population *(e.g.,* T-cell rich B-cell lymphoma, CLL/LL with many histiocytes), which often have equivocal results in immunocytochemistry and flow cytometry. Evidence of clonality by POR may be needed to achieve

the diagnosis. T-cell lymphomas constitute a diagnostic challenge for FNA; this diagnosis has to be supported by the identification on flow cytometry of an aberrant phenotype expression and T-cell receptor rearrangement by ISH and should, in our opinion, be confirmed by biopsy.

Hodgkin's disease is usually easy to diagnose by FNA, except for the lymphocyte predominant subtype where we usually see smears with a monomorphic pattern suggesting low-grade non-Hodgkin's lymphomas with a polyclonal phenotype; because of this discrepancy a careful search of Reed-Steinberg cells is advised and, if negative, a biopsy suggested. Immunocytochemistry should always be performed in diagnostic smears for Hodgkin's disease to prevent a misdiagnosis with anaplastic Ki-1 non-Hodgkin's yinphomas, although in many cases this distinction is feasible by morphology. One should think of Ki-1 non-Hodgkin's lymphomas when examining a smear suggestive of Hodgkin's disease that shows too many Reed-Steinberg cells, and should therefore look carefully for cells with the ring nucleus characteristic of this lymphoma. Although some attempts have been made to cytologically subclassify Hodgkin's disease, we do not think this it is prudent or even necessary, since the most relevant prognostic information is the clinicopathological staging. Therapy may be initiated based on FNA diagnosis in cases where node excision is not easily available.

In summary, like Buley, Young and Tani, we think that the accuracy of FNA in the diagnostic workup of lymph node pathology has been greatly enhanced due to ancillary techniques, allowing the diagnosis and subclassification of lymphomas in most cases and thus being sufficient for establishing therapy. Except for difficult cases, which always occur both in cytology and in histopathology, the decision to conduct a surgical biopsy shall be taken, not for the mere confirmation of diagnosis, but with the aim of preserving archival material frozen or in paraffin blocks, for further studies that may contribute to advances in treatment.

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Aspiration cytology of soft tissue tumors

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The preoperative diagnosis of soft tissue tumors (STT) should always be established in a manner that does not compromise the radical surgical treatment. Fine needle aspiration cytology (ENAC), when applied with respect to anatomic compartment boundaries, is the least invasive method to obtain diagnostic material for microscopy and other cell-based techniques (1). Our routine procedure is to identify and mark (by a tattoo) the aspiration site(s), if possible together with the surgeon and/or radiologist.

Often the aspirations are performed under radiographic or ultrasound guidance. We usually aspirate with a 21-gauge needle attached to a 20 nil syringe in a Cameco syringe-holder. We prepare both air-dried and ethanol-fixed cell smears, but also rinse the needle with physiological, phosphate-buffered saline (PBS) to obtain material for cytospins. In order to check the representativity, we routinely perform a Diff-Ouick staining on the spot. This is also very helpful to disclose areas of the tumor that may be totally or partly necrotic. It is, indeed, an advantage if the cytopathologist samples the lesion him- or herself in order to assess the representativity of the cell material. It is more difficult to evaluate a submitted specimen in this respect.

When aspirating pediatric STT tumors, where international protocols demand histopathological diagnoses, we use FNAC to select representative areas for core needle biopsies. The procedure will then also allow us to make a preliminary assessment of the type of