Frozen section and the thyroid

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Lettura magistrale

Certain philosophical and practical principles need to be accepted by endocrinologists, internists, surgeons and pathologists as we enter the 21st century.
These include:

– The primary approach to a single or dominant nodule in the thyroid of a euthyroid patient is FNA.
– FNA can be diagnostic in papillary cancer, (including some examples of the follicular variant), medullary carcinoma and anaplastic carcinoma.
– If FNA is diagnostic, appropriate therapy should be undertaken *without* further diagnostic tests, i.e., total or near total thyroidectomy for papillary or medullary cancer. If clinician does not trust (enough to act upon) the cytodiagnosis, he/she should find a cytopathologist he/she can trust!
– Most thyroid nodules are follicular in pattern. In many cases, one can define nodular goiter on FNA due to colloid, etc., and this is reassuring to patient and clinician. If however, the nodule is follicular (or Hürthle cell) and cellularity and scant colloid, etc., a neoplasm is suspected, the cytologist cannot distinguish benign from malignant lesions in the two categories on FNA. FNA samples the center of the tumor and a diagnosis of malignancy is based on invasion at or beyond the level of the capsule. Hence, in these cases, the diagnosis must await histologic evaluation of the resected nodule.
– Because invasion is an encapsulated follicular or Hurthle cell tumor may be focal, generous sampling of the capsule is required to find it or its absence. In most pathology labs, sampling the whole or even one half the capsule of a follicular tumor is prohibitively expensive of technical and time resources. In addition, FNA artifacts (enhanced by artifacts of freezing) could lead to over-diagnosis.
– These then are our recommendations (and the surgeons who do the majority (95%) of thyroid surgeries at University of Pennsylvania Medical Center follow these):
a) If FNA is definitely diagnostic (e.g. papillary cancer) proceed with surgical procedure deemed appropriate for that diagnosis
b) If FNA diagnosis is follicular or Hurthle cell neoplasm, do not freeze:
• sampling
• post FNA artifact
• Most (80-85%) are benign
c) If FNA diagnosis is follicular lesion, suspect follicular variant of papillary carcinoma - can freeze lesion and perform intraoperative cytology examination:
if nuclei are perfect or/and
if on frozen, sclerosis is seen -
you can make a definitive frozen section
bord diagnosis and surgery can proceed.
d) We will **always freeze tissue other than the primary intrathyroidal** nodule, e.g., lymph nodes, parathyroids for identification, etc.

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Epidemiology and Natural History of Differentiated Thyroid Cancer

If one examines epidemiologic factors in the development of thyroid cancer, differences between follicular and papillary cancer appear.
Follicular Carcinoma:

Iodine Deficiency
Cytogenetic changes: 3p-
Papillary Carcinoma:
Radiation
Genetic
Iodine Excess
? Thyroiditis

The Natural History of Differentiated Thyroid Cancer depends on whether the lesion is papillary or follicular. If the latter, differences exist between minimally invasive versus angioinvasive lesions.
Papillary carcinoma (usual type - over 80%) is characterized by:
Lymphatic invasion
Lymph node metastases
"Multifocality"
Long natural history
Rare and late distant metastases (Lung)

Follicular carcinoma if minimally invasive (capsule of tumor only; no vascular invasion) is probably extremely benign (90% survival at 10 years or better); however, good data are not available.
Angioinvasive encapsulated follicular carcinomas have a 30-50% metastatic rate at 10 years (to lung, bone, brain). There appears to be a correlation between number of vessels invaded and prognosis. These are real cancers and need to be treated aggressively.

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Prognostic Factors in Differentiated Thyroid Cancer

In general, many large series have shown that age, size of tumor, sex and extrathyroidal extension (ETE) are correlated with prognosis. Hence, older age, large size, male sex and ETE are bad.
Recently, at least for papillary cancer subtype (as defined by histology) may correlate with prognosis: hence tall cell variant, columnar cell variant and diffuse sclerosing type are aggressive tumors.
Other histologic parameters which may affect prognosis include: lymphoid reaction to tumor, vascular invasion

and "dedifferentiated areas." More studies are needed to test validity of these features.

For follicular carcinoma, number of vessels invaded appears to correlate with prognosis. "Dedifferentiated" foci, spontaneous necrosis and easily found mitoses also may portend aggressive behavior.

Recent studies have shown other parameters may influence prognosis: DNA ploidy (S-phase confusing results), ret/PTC (conflicting results), p53 mutations (very rarely seen in differentiated thyroid cancers).

Immunostains for CEA, LeuM, Leu7, S 100, and EMA have been valued by some authors and debunked by others.

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