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CYTOLOGICAL CHARACTERISTICS OF NODULES IN THE THYROID GLAND

Summary: Fine- Needle Aspiration Biopsy (FNAB) plays an important role in the evaluation of the nodules in the thyroid gland and the selection of patients for surgical treatment. However, it needs to be interpreted together with all the other factors that are of importance for the assessment of the thyroid nodule's true nature. Cytological findings can be classified into 8 diagnostic categories: benign colloid nodules, cystic lesions, different types of thyroiditis, cellular microfollicular lesions, Hürthle-cell lesions, primary malignant tumors, other lesions and the non-diagnostic category. FNAB is very successful in the diagnosis of benign cystic lesions of the thyroid gland, Hashimoto's thyroiditis, anaplastic and papillary carcinoma of the thyroid gland, while it is less successful in the diagnosis of medullary carcinoma, lymphoma, and metastasized tumors. Follicular carcinoma of the thyroid gland cannot be cytologically differentiated from follicular adenoma, and Hürthle-cell carcinoma cannot be cytologically differentiated from Hürthle-cell adenoma of the thyroid gland.

Key words: Thyroid gland, thyroid nodule, fine-needle aspiration biopsy, cytology.

Solitary thyroid nodule is a clinical term signifying an isolated palpable formation in the thyroid gland with the remaining tissue of the thyroid gland normally or diffusely enlarged.[1] Bearing in mind the limited precision of the palpatory finding a great number of solitary nodules diagnosed only through clinical examination in fact represents polynodal goiter, with the remaining nodules being impalpable as they are small in dimension or are inaccessible for palpation. An actual solitary nodule is in its histological structure most often a tumor or a solitary cyst, and less frequently a pathohistological substrate of a different nature, for instance thyroiditis. Approximately 3/5 of solitary nodules are follicular adenomas, 1/5 are cysts and 1/5 of them are thyroid gland carcinomas [1].

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Fine Needle Aspiration Biopsy – FNAB of the thyroid gland nodule is a widely accepted and diagnostically useful procedure which has an exceptional value in the evaluation of thyroid nodules and the selection of patients for surgical treatment. [1, 2] The evaluation is aimed at discovering relatively rare carcinomas of this organ amongst otherwise very frequently occurring nodules in the thyroid gland.[1] The real diagnosis can be reached by taking into consideration numerous relevant elements of the clinical picture, the laboratory analyses, ultrasonography, scintigraphy, and cytological findings.

The FNAB method is simple, minimally painful and without any risk of creating serious complications. It is carried out in ambulatory settings and, if needed, may be repeated a number of times. [3] If the suspicious formation in the thyroid gland is small or positioned deeply within the gland the biopsy needs to be performed under control of ultrasound. [4]

The material obtained by punction (FNAB) is smeared over a slide, dried and stained. Several staining methods are used in practice: the hematoxylin-eosin smear (HE), the Papanicolaou stain, May-Grünwald-Giemsa staining and the Diff-Quik stain[5]. Based on the smear it possible to establish a diagnosis in 80-85% of the cases, while biopsy needs to be repeated in the remaining cases[1].

The cytological findings can be classified into 8 diagnostic categories: benign colloid nodules, cystic lesions, different types of thyroiditis, cellular microfollicular lesions, Hürthle-cell lesions, primary malignant tumors, other lesions and the non-diagnostic category [6].

BENIGN COLLOID NODULES

This category includes the solitary colloid nodule, which is the dominant nodule within the polynodal goiter of the thyroid gland, and macrofollicular adenoma. [6] The cytological diagnosis of goiter, i.e. of colloid adenoma is established when there is a presence of diffusely distributed colloid, which sometimes has the appearance of a mosaic, and individual and grouped follicular cells with a centrally positioned, round, dark nucleus with no signs of atypia. Smears obtained from goiter with regressive changes, which are most often the focal points of bleeding, in addition to already described elements also display the presence, to a lesser or greater degree, of mac-rophages with hemosiderin in the cytoplasm.[6]

CYSTIC LESIONS

In this group we most often find benign colloid nodules, and less commonly neoplasms, amongst which papillary carcinoma of the thyroid gland is most frequent.

The smear shows a dominant presence of individual and grouped macrophages with abundant, foam-like cytoplasm and/or granules of hemosiderin in the cytoplasm in an area of a great quantity of inactive and predominantly coagulated colloid. The benign cystic lesion is characterized by regularly shaped follicular cells, while in papillary carcinoma follicular cells with hypochromatic nuclei can be found. [2,6]

DIFFERENT TYPES OF THYROIDITIS

In day-to-day medical practice Hashimoto's Thyroiditis is the one diagnosed most frequently. This diagnosis is established by analyzing a smear that is usually rich in cells and contains a smaller amount of colloid as well as grouped, regularly shaped and often oxyphilic transformed follicular cells with abundant eosinophilic cytoplasm and moderately apparent signs of atypia and also numerous dispersed lymphoid elements and a large quantity of cell debris. [7]

CELLULAR MICROFOLLICULAR LESIONS

This category includes microfollicular adenoma, follicular carcinoma of a low level of malignity and hyperplastic microfollicular lesions in polynodal goiter and Hashimoto's thyroiditis.

Cytological differentiation of follicular adenoma from follicular carcinoma of the thyroid gland, despite numerous attempts of definition with the help of immuno-histochemistry (e.g. galectin-3 and CD44v6)[8] still remains impossible. A hypercellular smear with irregular smaller and larger groups of thyrocytes, displaying at least minimal signs of anisomorphism is best described as a "follicular lesion". After a surgical procedure and a detailed histological examination of a greater number of sections it is possible to establish a definite diagnosis.

HüRTHLE-CELL LESIONS

Oxyphilic lesions of the thyroid gland include Hürthle-cell adenoma, Hürthle-cell carcinoma, and hyperplastic Hürthle-cell nodules in Hashimoto's thyroiditis and polynodal goiter. The smear is characterized by large, polygonal cells with abundant granulated cytoplasm and enlarged, centrally and eccentrically positioned nuclei, with visible nucleoli. Cells with two nuclei are also frequent. [9]

Differential diagnosis between oxyphilic lesions and Hashimoto's thyroiditis may be difficult, especially if groups of oxyphilic cells dominate the smear and if there aren't many lymphocytes and much cell debris, characteristic of Hashimoto's thyroiditis. [7]

PRIMARY MALIGNANT TUMORS

This diagnosis includes: papillary carcinoma, microfollicular carcinoma of a high level of malignancy, insular carcinoma, medullary carcinoma, anaplastic carcinoma of the thyroid gland and lymphoma.

Papillary carcinoma is the most frequent malignant tumor of the thyroid gland. The smear of the papillary carcinoma is rich in cells which may be grouped into papilloform structures or be distributed individually. Tumor cells are larger than normal follicular cells and are of a mildly irregular shape. Characteristic light colored, hypochromatic nuclei are apparent in HE stained smears or smears made using the Papanicolaou method. [2]. Intranuclear cytoplasmatic inclusions and nuclear grooves are often present.

Anaplastic carcinoma of the thyroid gland is formed *de novo* or via anaplastic transformation of preexisting papillary or follicular carcinoma of the thyroid gland. The smears show an abundance of blood, necrotic debris, many neutrophils and markedly atypical epithelial cells of variable form with a high nucleocytoplasmic index and frequent aberrant mitoses. Polygonal, spindle shaped cells and giant cells are dominant. [10].

Medullary carcinoma of the thyroid gland originates from C-cells secreting calcitonin. Cells of various shapes, individual or those with a tendency to grouping, are visible in the smear: from polygonal to rounded to elongated cells. The quantity of amyloid varies. [2, 10] In order to confirm the diagnosis of medullary carcinoma it is useful to stain with calcitonin using the immunoperoxidase technique.

Lymphomas of the thyroid gland are mainly non-Hodgkin lymphomas, originating from B- lymphocytes. They are almost always accompanied by Hashimoto's thyroiditis, which is why differentiation between these two entities is difficult in practice. As far as cytology is concerned, a monotonous lymphoid population with apparent mitoses and very rare follicular cells is present in lymphoma. [11]

OTHER LESIONS

Graves' disease and metastasized thyroid gland carcinoma are in this group.

In Graves' disease, as far as cytology is concerned, the so called "hyperactive" colloid is usually apparent with numerous groups of mildly enlarged thyrocytes which may display moderately apparent elements of anisomorphism.

The metastases most frequently found in the thyroid gland are metastases of: renal, lung, breast and esophageal carcinomas and metastases of malignant melanoma. [12] Cytological identification of the tumor's origin is more reliable if it correlates with clinical data and if the smear contains characteristic cells of the primary tumor (e.g. cells with markedly light colored cytoplasm in renal carcinoma or the presence of mucus in adenocarcinoma cells).

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