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FOLLICULAR ADENOMA OF THE THYROID: RETROSPECTIVE REVIEW OF THE CYTOMORPHOLOGIC CHARACTERISTICS IN 104 CASES

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SUMMARY – Thyroid fine-needle aspiration biopsy samples from 104 patients with subsequent histopathologic diagnosis of follicular adenoma of the thyroid formed the basis of this review. Cytomorphologic features for detailed cytologic assessment included cellular patterns, cellularity, colloid content, nuclear enlargement, nuclear pleomorphism, nuclear grooves, nucleoli, marginal vacuoles, macrophages, and Hürthle cells. Of the four cellular patterns assessed, acinar formation was observed in most cases (87%), while the remaining cellular patterns were present in the following order: honeycomb pattern in 65%, single-cell pattern in 57%, and syncytial pattern in 45% of cases. Most of the cases were hypercellular (70%), while colloid content was absent or scanty in 65% of cases. Nuclear enlargement was present in 84%, and nuclear pleomorphism in 75% of cases. Nuclear grooves were detected in 12%, while nucleoli were not identifiable in 66% of cases. Marginal vacuoles were found in 14%, macrophages in 30%, and Hürthle cells in 15% of cases.

Key words: *Thyroid gland, pathology; Thyroid nodule, pathology; Biopsy, needle*

Introduction

The principal procedure for evaluation of patients with thyroid nodules is fine-needle aspiration biopsy (FNAB)[1]. The routine use of FNAB in the assessment of thyroid nodules has reduced the number of patients subjected to surgical treatment for benign disease of the thyroid[2-7]. FNAB is the most accurate and cost-effective method for the evaluation of thyroid nodules[8,9]. Limitations of the procedure are inadequate rate and inability to differentiate follicular adenoma from follicular carcinoma[10-12]. Attempts to overcome these difficulties include repeat FNAB for nondiagnostic cases[13] and analysis of smears to define cytomorphologic criteria for various follicular lesions[14].

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FNAB samples from 104 patients with subsequent histopathologic diagnosis of follicular adenoma were reviewed, and all cases were subjected to detailed cytologic assessment in order to describe the cytomorphologic features of follicular adenoma. The cytomorphologic features of follicular adenoma have been addressed in several articles, but the number of cases studies in each series was small[14-17].

Material and Methods

One hundred and four patients were surgically treated at ENT Department, Sestre milosrdnice University Hospital, and their subsequent histopathologic diagnosis was follicular adenoma of the thyroid. FNAB was preoperatively performed in all these patients. Routine percutaneous ultrasonography guided FNAB was carried out using a 23-gage needle attached to 10-mL syringe. The aspirated material was smeared onto glass slides, air fixed, stained by May-Grünwald-Giemsa method, and exam-

ined under light microscope. All patients presented with a single nodule or multiple nodules. There were 19 males and 85 females, male to female ratio 1:4.1, age range 15-76 (median 45) years.

Detailed morphologic parameters were determined. On review, the following cytomorphologic features were assessed in each individual case: cellular patterns such as acinar formation, honeycomb pattern, syncytial pattern, and single-cell pattern, cellularity, colloid content, nuclear enlargement, nuclear pleomorphism, nuclear grooves, nucleoli, marginal vacuoles, macrophages, and Hürthle cells.

Cellular patterns. Four patterns were assessed and graded as absent (0), present (1), or predominant form (2). The cellular patterns considered for detailed cytologic assessment included acinar formation, honeycomb pattern, syncytial pattern, and single-cell pattern. If the smear showed more than one pattern, each type was noted and graded as above.

Acinar formation included acini or microfollicles and macrofollicles. Acini or microfollicles consisted of a peripheral ring of nuclei surrounding a central syncytium of cytoplasm. Large, intact macrofollicles consisted of spheres of colloid surrounded by nuclei imparting a three-dimensional appearance. Honeycomb pattern was characterized by a uniform monolayer of cells with regular polarity. Syncytial pattern indicated follicular cells in a multilayered, disorganized pattern. Single cells were characterized by noncohesive distribution of follicular cells.

Cellularity. Cellularity was semiquantitatively graded as normal (1), moderate (2), or excessive (3), based on subjective impression.

Colloid content. In May-Grünwald-Giemsa stained smears, colloid content was observed as a bluish or pinkish homogeneous film of variable thickness. Colloid content was graded as absent (0), scanty (1), moderate (2), or abundant (3), based on subjective impression.

Nuclear features. Nuclear enlargement and pleomorphism were semiquantitatively graded as absent (0), mild (1), or high (2), based on subjective impression. Nuclear grooves were seen as a dark linear thickening of nuclear membranes running through longitudinal axis of the nucleus; absence (0) or presence (1) of this feature was noted. Nucleoli were identified as intranuclear structures distinct from chromatin clumping, ill defined, and variable in size. They were graded as not identifiable (0), identifiable (1), or large and prominent (2).

Marginal vacuoles, macrophages, and Hürthle cells. Marginal vacuoles were seen as peripheral cytoplasmic vacuoles. Likewise macrophages and Hürthle cells, they were graded as absent (0) or present (1).

Results

Detailed cytologic assessment of all parameters in 104 reviewed cases is illustrated in Figs. 1-5.

Cellular pattern. Of the four patterns assessed, acinar formation was present in a majority of cases (90/104) and as a predominant form in 44 cases. Honeycomb pattern was observed in 68 cases, and in only 19 cases as a predominant form. Syncytial pattern was present in 46, and single-cell pattern in 59 cases; the two patterns were observed as a predominant form in a similar number of cases.

Cellularity. Most aspirates were cellular and graded as moderate (55/104) or excessive (18/104), while normal cellularity was recorded in 31 cases.

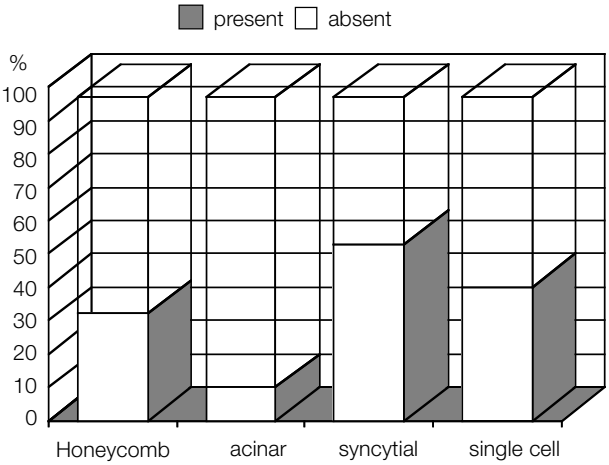

Fig. 1. Cellular patterns

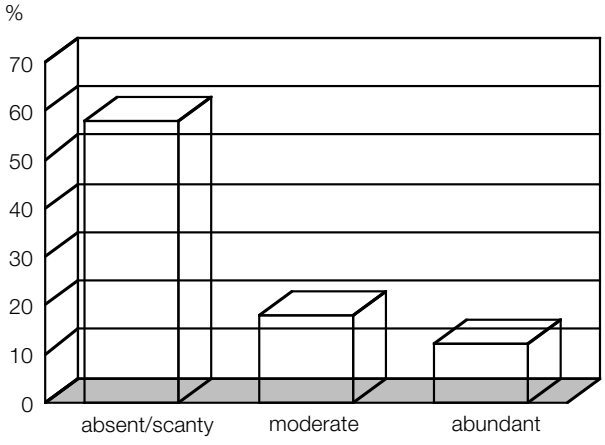

Fig. 2. Colloid content

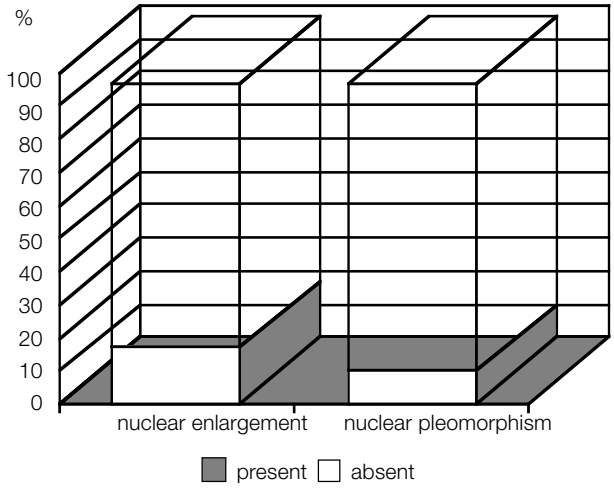

Fig. 3. Nuclear enlargement and pleomorphism

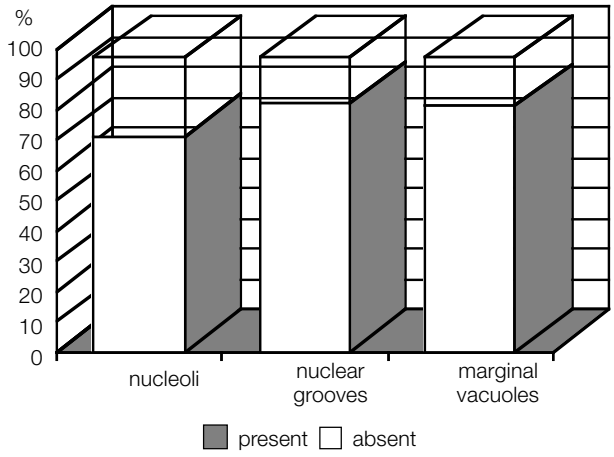

Fig. 4. Nucleoli, nuclear grooves, and marginal vacuoles

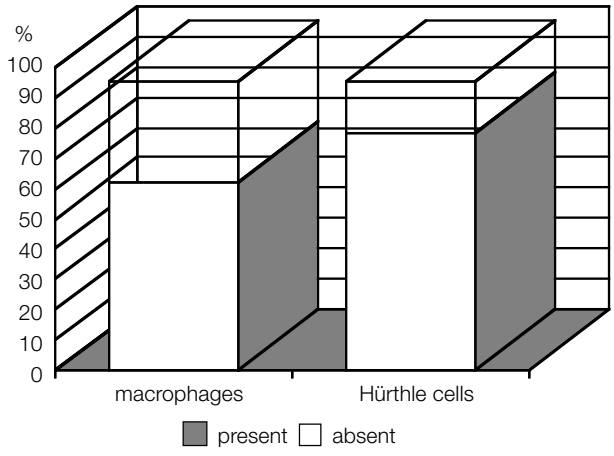

Fig. 5. Macrophages and Hürthle cells

Colloid content. According to selection criteria, colloid was absent in 29, scanty in 35, moderate in 23, and abundant in only 17 cases.

Nuclear features and marginal vacuoles. Most cases showed mild to moderate nuclear enlargement (81/104) and nuclear pleomorphism (73/104). Nuclear grooves were observed in 13 cases. Large and prominent nucleoli were detected in only 11 cases, whereas in a majority of cases they were not identifiable (69/104). Marginal vacuoles were observed in 15 cases.

Macrophages and Hürthle cells. Macrophages were observed in 31 cases, whereas in a majority of cases (73/104) they were absent. Hürthle cells were found in 16 cases.

Discussion

FNAB is a widely used, accurate, and cost-effective method of evaluating a thyroid nodule[8,18]. The selection of thyroid nodule patients for surgical treatment, although improved by FNAB, remains problematic[4]. Careful balance must be sought between reliance on cytologic interpretation to exclude malignancy, and a low but real risk associated with the surgery[19]. With the routine use of FNAB in patients with thyroid nodules, the percentage of patients undergoing thyroidectomy has decreased by 25%, reducing the overall cost of treatment as well as the associated morbidity and mortality[11].

A classic example of the limitation of fine-needle aspiration cytology is the classification of follicular lesions of the thyroid. The only accepted difference between follicular adenoma and follicular carcinoma is capsular or/and vascular invasion. To date, the morphologic characteristics of follicular adenoma of the thyroid have only been analyzed in small series[14-17]. The smears from colloid nodules were originally described as having abundant colloid and scarcity of glandular cells; aspirates with high cellularity and scarcity or absence of colloid were considered to be characteristic of neoplasms[20,21]. In the present, retrospective analysis, follicular adenoma of the thyroid showed excessive cellularity, significantly higher frequency of acinar formation, and scarcity or absence of colloid. In this review, acinar formation was found in approximately 90% of cases, which is consistent with reports from other studies[14,16,17], confirming its high predictive value in the diagnosis of follicular neoplasms of the thyroid[14].

Deshpande et al.[14] believe that the presence of honeycomb pattern in follicular adenoma or nodular goiter has a sound histopathologic basis. In two large cellular pattern

studies[15,22], the honeycomb pattern was found exclusively in nodular goiters, and not in follicular adenomas or carcinomas, as opposed to the high incidence in follicular adenomas reported by others[14,23]. Our results could be considered consistent with the latter. Kini et al.[22] did not find syncytial pattern in any of the follicular adenomas they examined, whereas Ravinsky and Safneck[15] found this pattern in follicular adenomas. Our results are consistent with the latter (45%). We found the single-cell pattern in 57% of cases, in contrast to lower incidence reported by others[14,22].

A previous study[15] has shown mild nuclear enlargement and mild nuclear pleomorphism in all cases, while we found mild to moderate nuclear enlargement and nuclear pleomorphism in most of our cases. Large and prominent nucleoli were observed in 11% of cases, in contrast to their lower incidence reported by others[14,15]. Das et al.[16] report on the presence of marginal vacuoles in 15% of follicular neoplasms, and our result of 14% is consistent with this study. Macrophages were absent in most of our cases, which is in agreement with literature data[15]. Our results on the presence of Hürthle cells were also consistent with those reported from other studies[16,17].

In conclusion, none of the cytomorphologic features assessed was present in all cases of follicular adenoma of the thyroid. The following cytomorphologic features were present in most cases: moderate to high cellularity, absence or scarcity of colloid, acinar formation as a cellular pattern, and nuclear enlargement and nuclear pleomorphism.

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Sažetak

FOLIKULARNI ADENOM ŠTITNJAČE: PREGLED CITOMORFOLOŠKIH OBILJEŽJA U 104 BOLESNIKA

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Razmazi dobiveni aspiracijskom biopsijom tankom iglom u 104 bolesnika s kasnije postavljenom histopatološkom dijagnozom folikularnog adenoma štitnjače tvorili su osnovu ove retrospektivne analize. Podrobna citološka analiza obuhvatila je sljedeća citomorfološka obilježja: staničnu građu, celularnost, sadržaj koloida, veličinu jezgara, pleomorfizam jezgara, jezgrine brazde, jezgrice, marginalne vakuole, makrofage i Hürthleove stanice. Od četiriju analiziranih tipova stanične građe najčešći je bio acinarni tip (87%), zatim slijede građa "poput pčelinjeg saća" (65%), pojedinačne stanice (57%) te sincicijalni tip (45%). U većini slučajeva zabilježena je hipercelularnost (70%), a koloid je bio odsutan ili oskudan u 65% slučajeva. Jezgre su bile povećane u 84%, dok je pleomorfizam jezgara bio prisutan u 75% slučajeva. Jezgrine brazde nađene su u 12% slučajeva, a jezgrice nisu bile vidljive u 66% slučajeva. Marginalne vakuole bile su prisutne u 14%, makrofazi u 0% te Hürthleove stanice u 15% slučajeva.

Ključne riječi: *Štitna žlijezda, patologija; čvor štitne žlijezde, patologija; Biopsija, igla*