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Evaluation of Risk Factors for Malignancy Obtained by Means of Fine Needle Aspiration Biopsies in Thyroid Nodules and Surgical Outcomes of Patients with Bethesda Category III (AUS/FLUS)

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Abstract
Background: The nodules diagnosed as the “atypia of undetermined significance" category are a heterogenous group with an indeterminate risk of malignancy. This study aimed to perform a detailed cytological examination of the preparations to determine the cytomorphological criteria that may be useful to distinguish benign cases from malignant ones, correlate them with ultrasonographic findings, and compare them with the final pathological result in surgically treated patients.
Methods: The preparations of patients classified as Bethesda 3 were re-evaluated; presence or absence of one of 11 parameters (hypochromasia, oval nucleus, colloid, intra-nuclear pseudo-inclusions, nuclear grooving, nuclear moldering, isolated nuclear enlargement, nuclear irregularity, nuclear size, microfollicular pattern, distinct nucleoli) and correlating with surgical outcomes by adding ultrasonographic findings to statistically significant parameters.
Results: Two hundred and six fine needle aspirations (FNA) procedures were classified as Bethesda 3. A total of 53 patients underwent surgery; 28 (52.8%) of them were benign, and 25 (47.1%) were malignant. Thirty-two (15.5%) accepted direct surgery; 53 patients underwent repeat FNA at 3-6 month intervals and those with malignancy and repeated Bethesda 3 interpretation were operated. One hundred twenty-one (69.5%) patients who did not undergo biopsy were invited for ultra-sonographic controls at 3-6 month intervals. Among the 11 cytomorphologic parameters evaluated, 7 were found to be statistically significant ($p<0.05$) with malignancy. When at least 3 of these parameters were positive, the malignancy rate was 92%. Malignancy was present in 19 (61.3%) of the patients with high risk nodules (TIRADS ≥ 4), compared to only 6 (35.8%) of the low-risk (TIRADS ≤ 3); there was a significant correlation between the presence of malignancy and TIRADS score ($p=0.015$). The preparations that displayed nucleus atypia were closely associated with the ultrasonographically high-risk group.
Conclusion: The parameters indicating nuclear atypia, presence of more than 3 cytomorphological factors, TIRADS score ≥ 4 were significantly associated with malignancy; nuclear atypia were closely associated with the ultrasonographically high TIRADS. No significant correlation was found between the presence of "microfollicular pattern" and malignancy.
Key words: atypia of undetermined significance, fine needle biopsy, nuclear atypia, microfollicular atypia, TIRADS