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Fine needle aspiration with cytology analysis and thyroglobulin level of the aspirated biopsy (FNAB-Tg), is an important tool to assess metastasis to cervical lymph nodes (CLN) in patients with papillary thyroid cancer (PTC) who have suspicious lymph node features on ultrasound. Despite the great diagnostic accuracy of the FNAB-Tg, studies failed to define the best cutoff value for FNAB-Tg. In our study, we describe a novel way in performing the Tg washout and process it locally at our laboratory (tertiary care center). We used the FNAB-Tg to serum thyroglobulin level (FNAB-Tg/ Tg serum) ratio to help overcome the heterogeneity in both cutoff values and the assays used to detect thyroglobulin level. We conducted a retrospective analysis of 22 PTC or suspected PTC patients, who have suspicious cervical lymph nodes on ultrasound. All patients underwent fine-needle aspiration, with cytology analysis and FNAB-Tg from the suspicious CLNs. FNAB-Tg was obtained in all subjects using the following method: Blood samples are drawn from the patient's peripheral vein and placed in two yellow top tubes (3 ml of blood in each tube). 1 ml of normal saline (NS) is added to Tube # 1 (Tg Serum tube). The suspected lymph node aspirate is obtained via US-guided FNA. It is washed in 1 ml of NS and added to tube #2 (FNAB-Tg washout tube). Both tubes are sent to our local laboratory for Tg assay. The FNAB-Tg/ Tg serum ratio is calculated. If FNAB-Tg/Serum-Tg ratio >3, this is suggestive of CNL metastasis. We compared our results to the histopathology reports after neck dissection. 59% (13/22) patients had cytology results consistent with metastatic PTC. 12 out of these 13 patients had an FNAB-Tg/serum Tg ratio >3 and one had FNAB-Tg/serum TG ratio < 3, though the FNAB-Tg was 4474 ng/ml and serum Tg was 2444 ng/ml. Metastatic PTC to these CLNs was confirmed on pathology report from total thyroidectomy or neck dissection. Six patients of the 22 studied (27%) had negative cytology with FNAB-Tg/serum Tg ratio > 3. 5 of these patients underwent neck dissection in our institute and confirmed to have metastatic PTC to these CLNs. One patient elected to have surgery in his home country and the pathology report is not available at this time. Three patients of the 22 studied (14%) had negative cytology and FNAB-Tg/serum Tg ratio <3. 2 of them underwent thyroid surgery or neck dissection and the final pathology report was concordant with the FNAB-Tg results. The FNAB-Tg/serum Tg ratio is a novel method to overcome the differences in cutoff values and assays used to measure the Tg level both in serum and FNAB. An FNAB-Tg/serum Tg ratio >3 is more accurate than cytology in detecting cervical lymph node metastasis in patients with papillary thyroid cancer (PTC). In our study, 27% of CLN metastasis would have been missed if FNAB cytology was used alone. This will help to optimize the surgical approach in patients with PTC before initial surgery or for suspected recurrence.

Thyroid THYROID CANCER

Trabecular Bone Score in Women With Differentiated Thyroid Cancer

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Introduction: Thyrotropin stimulating hormone (TSH) suppression in patients with differentiated thyroid cancer (DTC) aims to decrease the growth and proliferation of thyroid cancer cells. However, the effect of TSH suppressive therapy on bone microarchitecture remains undefined. **Methods:** Cross-sectional study including 43 women with DTC undergoing TSH suppressive therapy (sTSH) compared to 20 women also on levothyroxine therapy but with TSH in the low-normal range (nTSH) since the thyroid surgery. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA), and trabecular bone score (TBS) was evaluated using the TBS iNsight software. The relationship between suppressive therapy-related parameters and bone parameters was investigated. **Results:** The TBS mean values were not significantly different in the sTSH and nTSH groups (1.273 ± 0.12 vs 1.307 ± 0.14 , $p = 0.7197$). In both groups, postmenopausal women had degraded microarchitecture (TBS 1.216 ± 0.11 vs 1.213 ± 0.09 , $p = 0.9333$), while premenopausal women had normal microarchitecture (1.328 ± 0.11 vs 1.401 ± 0.12 , $p = 0.195$). The percentage of all postmenopausal women with degraded TBS was 54.7%, while the percentage of osteoporosis diagnoses was 16.1%. Body mass index (BMI) and menopausal status were the only variables associated with TBS and BMD. **Conclusion:** Long-term TSH suppressive therapy does not seem to be associated with deterioration of the trabecular microarchitecture in premenopausal women. However, lower TBS values were observed in postmenopausal women of both groups, even in those with nonsuppressive therapy. These data show that treatment with thyroid hormone in DTC can be detrimental to bone quality in postmenopausal women, regardless of whether TSH levels are maintained chronically suppressed or in the low-normal range.

Thyroid THYROID CANCER

Ultrasensitive Detection of BRAF Mutations in Circulating Tumor DNA of Patients With Metastatic Thyroid Cancer

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Background: Liquid biopsy is a promising technology that can offer various advantages for molecular testing over tissue-based approaches. Most studies trying to address the utility of liquid biopsy in thyroid cancer have failed so far to

achieve satisfactory rates of detection of relevant mutations. In this study, we examined a newly developed approach for ultrasensitive detection of oncogenic mutations in thyroid cancer using BRAF mutation as a proof-of-concept. In an exploratory analysis, we also correlated our findings with clinical outcomes and with levels of standard of care biomarkers. **Methods:** We included a group of patients with metastatic thyroid carcinoma. Cell free DNA (cfDNA) was isolated from an average of 2 ml of plasma and from matched formaldehyde fixed paraffin tissue blocks (FFPB) that were obtained from prior surgery. Extracted DNA was subject to preamplification of mutant copies using Q5 High-Fidelity PCR kit. Digital droplet PCR was performed on pre-amplified purified DNA where BRAF mutated allele frequencies (AF) were measured using BioRad ddPCR Qx200. **Results:** Thirty-three patients were included in our study with a median age at diagnosis of 62. Our method achieved a sensitivity of detection of 47.6% and a specificity of 80%. Mutant BRAF V600E was detected in cfDNA of 54.5% of patients (n=18) compared to 80.8% in isolated DNA from matched FFPB. Median overall survival (OS) was shorter in patients with wild type (WT) BRAF in both ctDNA and tissue (127m vs 218m, p=0.015; 116m vs 223m, p=0.004). Thyroglobulin (Tg) levels did not correlate with BRAF mutations either quantitatively or qualitatively. In the papillary thyroid carcinoma-classic variant cohort (n=20), however, patients with cfDNA mutant BRAF were more likely to have elevated Tg (90.9% versus 44.4% respectively, p=0.05). **Conclusions:** Our study provided a proof of concept for a newly developed technique to provide high sensitivity of mutation detection in thyroid cancer. The achieved sensitivity of detection is the highest to date using liquid biopsy in this tumor type. While we addressed only BRAF mutations in our study, the same approach can potentially be used for other mutations as well, likely changing the paradigm for use of liquid biopsy in thyroid cancer.

Thyroid

THYROID CANCER

Ultrasound Guided Percutaneous Ethanol Ablation of Benign Thyroid Nodule: A Study From a Tertiary Hospital in Eastern India

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Introduction: Ultrasound guided percutaneous ethanol injection (PEI) of benign thyroid nodule is an easy and effective procedure particularly in cystic and predominantly cystic nodule. **Aims:** To evaluate efficacy and safety of PEI in managing purely cystic and mixed cystic and solid thyroid nodules. **Materials and Methods:** Patients of either sex presented with solitary purely cystic benign thyroid nodule, solitary benign mixed with predominantly cystic (>50% of total volume) thyroid nodule, solitary benign mixed with predominantly solid (>50% of total volume) thyroid nodule, solitary solid thyroid nodule were included in this study. Patients who had a nodule BETHESDA 3 and above, pregnancy, patients with critical or terminal illness, patients with other malignancies, multinodular lesions of thyroid, patients with raised T3, T4 and/ or suppressed TSH level were excluded from the study. One hundred

sixty patients presenting with thyroid nodule were initially evaluated with thyroid function test and USG. Only those patients with euthyroid solitary thyroid nodules are subjected for fine needle aspiration (FNA). Nodules under BETHESDA 2 are considered for US guided percutaneous ethanol injection (PEI). One hundred twenty-three patients were excluded because of various reasons. Finally ethanol ablation was done in 37 patients. Benign, purely cystic and mixed thyroid nodules were aspirated under ultrasonography guidance. Sterile absolute alcohol (99.99%) (50% of volume aspirated/ maximum 10 ml) was injected and reviewed after 2, 5 and 7 months. In case of solid nodule alcohol (50% of nodule volume) was injected. A reduction in volume is calculated at each follow up visit. An adequate response is considered as ≥ 50 percent reduction in size from baseline after 7 months. If the reduction is $< 50\%$, then a second session of absolute ethanol injection is given. Again, patients were similarly followed up after 2, 5 and 7 months. **Results:** Thirty seven patients underwent PEI. Thirty three patients were considered for final analysis (4 lost to follow up). Response rate of PEI for purely cystic nodule was 100.0% and the overall response rate for mixed nodule was 53.57%. None of the solid nodule responded to PEI even after second session. Among the responder in the mixed nodules, 93.33% responded after first session of PEI. Minor complications like headache occurred in 54.1% patients in the first session. Transient pain at injection site were complained by 86.5% and 37.8% patients in the first and second session respectively. Nausea and vomiting were complained by 18.9% and 16.2% patients in the first and second session respectively.

Conclusions: PEI is an effective and safe for purely cystic and mixed thyroid nodules. It is a relatively safe and less invasive procedure from management of benign solitary cystic and mixed thyroid nodules.

Thyroid

THYROID CANCER

Unmet Information Needs Among Hispanic Women With Thyroid Cancer

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Background: Despite thyroid cancer being the second most common cancer in Hispanic women, little is known about access to and utilization of medical information resources by Hispanic women with thyroid cancer. **Methods:** Hispanic women who had diagnoses of thyroid cancer reported to the Los Angeles Surveillance Epidemiology and End Results (SEER) registry in 2014-2015, and who had previously completed our thyroid cancer survey in 2017-2018, were offered follow-up surveys in both English and Spanish (N=273; 80% response rate). Acculturation, which is the process by which individuals adopt the language, values, attitudes, and behaviors of a different culture, was assessed with the Short Acculturation Scale for Hispanics (SASH). Health literacy was assessed with the validated single-item question of "How confident are you filling out