EnM
ENDOCRINOLOGY AND METABOLISM

Editorial

Endocrinol Metab 2013;28:94-95
http://dx.doi.org/10.3803/EnM.2013.28.2.94
pISSN 2093-596X · eISSN 2093-5978

# Natural Course of Benign Thyroid Nodules

Kyung Won Kim

Department of Internal Medicine, Seoul National University Hospital Healthcare System, Seoul National University College of Medicine, Seoul, Korea

Thyroid nodules are very common and are observed during ultrasonography (US) in 50% of the adult population. Although most thyroid nodules are benign, some nodules have malignant potential. Therefore, the ultimate goal is to diagnose biologically significant cancers, while exposing the fewest number of patients with benign disease to unnecessary diagnostic testing and thyroid surgery. In initial evaluation, current guidelines (American Association of Clinical Endocrinologists, American Thyroid Association [ATA], and National Cancer Institute) recommend fine needle aspiration (FNA) in indicated nodule to rule out malignancy [1]. After an FNA result is determined to be benign, serial US follow-up is recommended at 6 to 18 month intervals in order to minimize missed malignancy [1]. Through serial US, we can detect the size changes or shape changes of nodules. If significant interval growth is identified, repeat FNA is recommended in current guidelines [1]. An expert group suggests that the discordance between US appearance and cytology is indication for repeat FNA [2]. If nodule size remains stable, the guidelines recommend that FNA-proven benign thyroid nodules be followed-up by US every 3 to 5 years, with no endpoint specified [3].

Thyroid nodules diagnosed as benign require follow-up because of a low but not negligible false-negative rate with FNA [3]. Selective repeated FNA has been suggested in cases of size increment, suspicious imaging features or clinical suspicion. Malignancy is believed to produce more prominent growth than a benign nodule, although benign nodules can also grow with time [4-6]. Thus, nodule growth is not in and of itself pathognomonic of malignancy. Also, nodules that appear benign on US can transform to show suspiciously malignant US features on follow-up US [7]. Thus, it is very important to know the benign course of FNA-proven benign thyroid nodules, which may avoid an unnecessary repeat FNA. Little is known about the natural history of benign thyroid nodules.

In this issue, Lim et al. [8] reported that FNA-proven benign thyroid nodules can experience changed US features or volume in the natural. During follow-up of 202 benign nodules for 21.7±10.7 months, the mean volume change was +0.16±1.71 mL (range, -6.9 to +8.4), and the percentage of volume change compared with the initial volume was +10.5±54.3% (range, -98.5 to +378.6). The frequent US changes were cystic component change (7.4%), change of margin (6.9%) and change of calcification pattern (6.0%). The margin change from well-defined smooth to ill-defined was the most frequent margin change ($n$=8, 4.0%). The new appearance of macrocalcification was the most frequent among the changes of calcification pattern ($n$=9, 4.5%). The echogenicity and the ratio of the anteroposterior to transverse dimensions were nearly unchanged morphological findings. Among them, the proportion of nodules with newly developed US changes suggesting malignancy was less than 5%. When using the ATA recommendation as criteria for nodule growth, 19 nodules (9.4%) were increased, 167 (82.7%) were unchanged, and 16 (7.9%) decreased in volume. One patient was diagnosed with thyroid cancer and had a nodule that changed to suspicious for malignancy.

**Corresponding author:** Kyung Won Kim
Department of Internal Medicine, Seoul National University Hospital Healthcare System, Seoul National University College of Medicine, 152 Teheran-ro, Gangnam-gu, Seoul 135-874, Korea
**Tel:** +82-2-2112-5632, **Fax:** +82-2-2112-5635, **E-mail:** kwkimin@gmail.com

Unfortunately, Lim et al. [8] was conducted in a tertiary referral center where patients with a typical benign nodule may not be referred. Only a few patients underwent thyroid resection in this study. As a result, diagnosing a benign nodule was based on FNA results, which have a 5% false-negative rate. In spite of these limitations, this study is meaningful to clinicians because most thyroid nodules are benign and are observed via US. According to these results, the authors suggest that frequent follow-up US is needed for cases with suspicious US findings because of low malignancy detection rate. This is consistent with findings of another report [9].

Further studies are needed to demonstrate the most important marker in predicting malignancy during follow-up and when clinicians can cease long-term routine follow-up of an FNA-proven benign nodule.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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