Primary and secondary hyperparathyroidism among vitamin D deficient Hashimoto's thyroiditis patients and the need for a parathyroid scan

Dear Editor,

Vitamin D deficiency/insufficiency is quite prevalent in many countries where has been studied. The reported vitamin D screening and supplementation, during the last years in Greece, in healthy persons without underlying risk factors (such as osteoporosis, osteomalakia, malabsorption syndromes, chronic kidney disease, medications, hyperparathyroidism, pregnant and lactating women, etc) [1], is expected to affect the national health care costs in the near future. Although an inverse relationship between serum 25-hydroxyvitamin D (25(OH)D) and serum parathyroid hormone (PTH) levels is well established, the exact serum 25(OH)D levels that lead to a rise in serum PTH levels remain controversial [1, 2]. The World Health Organization (WHO) and Endocrine Society consider a serum 25(OH)D level <20ng/mL as vitamin D deficiency and a serum 25(OH)D level >30ng/mL as normal because at this level, PTH drops down to normal levels [1-3]. At present, it is believed that if serum 25(OH)D level is below 30ng/mL, the level of PTH should start rising [2, 4].

Aiming to determine the correlation between serum 25(OH)D and PTH levels, we analyzed retrospectively data about intact PTH serum levels, before and after 4 months of cholecalciferol (CF) supplementation, among 186 vitamin D deficient with Hashimoto thyroiditis (HT) Greek Cretan patients (173 females and 13 males; mean age 37.3±5.6 years), enrolled in our previous study [5] which included a total of 218 HT patients. The measurement of serum intact PTH levels was carried out in order to investigate whether the prevalence of patients having both HT and primary hyperparathyroidism differed from the prevalence of patients having primary hyperparathyroidism in the general population. Diagnosis of HT was made by determining the elevated anti-thyroid peroxidase (anti-TPO) or/and anti-thyroglobulin (anti-TG) and ultrasound patterns (diffusely enlarged thyroid gland with heterogeneous echotexture of the gland parenchyma with or without hypervascularity in color Doppler study). Serum levels of 25(OH)D and intact PTH were measured with a chemiluminescent microparticle immunoassay method (CMIA) (Architect i1000 System®, Abbott, USA). In our study a 25(OH)D level <10ng/mL was considered as severe vitamin D deficiency, 10-19.9ng/mL as moderate vitamin D deficiency, 20-29.9ng/mL as mild vitamin D deficiency (or insufficiency), and ≥30ng/mL as vitamin D sufficiency. The normal range for intact PTH was 15-68pg/mL. Statistical analyses were performed using GraphPad Prism 3.0 (GraphPad Software, Inc., California, USA). The relations between continuous variables were investigated using Pearson's correlation analysis, but paired t tests were used to analyze mean differences between the initial and post 4 months values for the measured parameters. Chi-square (χ^2) test was used to compare observed and expected frequencies. All P-values were two tailed, and P-values below 0.05 were considered statistically significant.

All 186 HT patients were euthyroid (with or without medication) and vitamin D deficient. All patients were normocalcemic and their estimated glomerular filtration rate (e-GFR) was normal. Among the 186 vitamin D deficient HT patients, 58.6% (109/186) had moderate vitamin D deficiency, 33.3% (62/186) had mild vitamin D deficiency, 8.1% (15/186) had severe vitamin D deficiency and 97.8% (182/186) had elevated serum intact PTH levels. The four of 186 patients with normal serum intact PTH levels had mild vitamin D deficiency. The mean value of intact PTH was 102.5±15.2pg/mL. There was a significant negative correlation between serum 25(OH)D levels and intact PTH levels (Pearson r=-0.83, P<0.00001) in our study population, which meant that intact PTH levels tended to be higher with lower serum 25(OH)D levels. Neck (parathyroid glands) and abdomen ultrasound did not reveal findings suggestive of primary hyperparathyroidism (PHP) in any of our patients. Cholecalciferol supplementation with target serum 25(OH)D levels ≥40ng/mL resulted in a significant increase in serum 25(OH)D levels from 14.6±7.2ng/mL to 45.7±4.3ng/mL (or 213%, P<0.0001) and a significant reduction in serum intact PTH levels from 102.5±15.2pg/mL to 56.3±18.4pg/mL (or -45%, P<0.0001). Only ten of the 182 patients failed to achieve normal serum intact PTH levels after CF supplementation despite the increase of serum 25(OH)D levels ≥40ng/mL. Four of these ten patients were diagnosed after six months follow-up with laboratory findings suggestive of classic (hypercalcemic) primary hyperparathyroidism (cPHP), were subjected to parathyroid scintigraphy (PS) and eventually were operated (single parathyroid adenoma). Six of the ten patients with elevated serum intact PTH levels after CF supplementation still remain normocalcemic and are being monitored in our hospital as we monitor the patients with normocalcemic primary hyperparathyroidism (nPHP) [4]. Thus, in our study population (186 vitamin D deficient HT patients), the prevalence of patients with diagnosed cPHP was 2.15% (4/186), but the prevalence of patients with secondary hyperparathyroidism was 92.5% (172/186). The results of our study revealed that vitamin D deficiency is a usual cause of secondary hyperparathyroidism in HT patients and that in all cases of elevated serum PTH levels, serum 25(OH)D levels must be measured and corrected whenever necessary. The coexistence of cPHP with vitamin D deficiency is a masked form of cPHP responsible for normal serum calcium levels which is uncovered after vitamin D restoration. Moreover, a preoperative assessment of vitamin D status in all patients with PHP is necessary decreasing probably the risk of postoperative hypocalcemia and "hungry bone syndrome" among vitamin D-deficient patients undergoing parathyroidectomy [6, 7].

Also, patients with persistent isolated increases of PTH without previous measurement of serum 25(OH)D levels may be subjected to unnecessary PS within the framework of their management.

It is known that imaging parathyroid glands with PS has no place in the diagnosis of primary, secondary or tertiary hyperparathyroidism or in the decision for surgical treatment [8]. Parathyroid scintigraphy is a useful preoperative non-invasive technique for the localization of the pathological parathyroid glands [8]. The inability of sonography to image parathyroid adenomas in four patients with cPHP was probably due to coexisting HT [9]. Although the underlying mechanism that possibly links HT to cPHP is not quite clear, the prevalence of cPHP in our study population (186 vitamin D deficient HT patients) was 2.15%, significantly higher than the prevalence of cPHP in the general population, which is about 0.3% (χ^2=21.296, df=1, P<0.0001) [10]. Another prospective study contacted in central Serbia revealed a 1.89% occurrence of cPHP in 2267 HT patients [10].

In conclusion, the patients with HT must be investigated mainly for secondary hyperparathyroidism due to vitamin D deficiency/insufficiency.

The authors of this study declare no conflicts of interest

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