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What a High Prevalence of Autoimmune Thyroiditis and Thyroidectomy in Women

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Thyroidal disorders are found among the most common causes of patients' visits to internal medicine polyclinics. Most of them are probably related with autoimmune thyroiditis (AT) and/or multinodular goiter (MNG) because micro-nodulation is a common feature of AT. We have taken 430 consecutive patients applying for check up procedure to detect prevalences of thyroidal disorder and operations. Student t-test has been used as the method of statistical analysis. Thirteen cases had been operated for MNG, one of female operated twice, one for papillary carcinoma of thyroid and one for Graves' disease. So operation rates for MNG have been 5.26 (12/228) and 0.9% (2/202) among female and males, respectively. When we compared these rates with the chance of having a thyroid cancer for either sex, the difference in women has been found as statistically significant ($p < 0.01$), whereas not in men ($p > 0.05$). Additionally 40 cases with abnormal thyroid function tests have been detected. Thirty three of them have been diagnosed as AT (82%) and 85% of the AT cases have been female. As a conclusion, AT and MNG operations have high prevalences in women and most of the MNG are probably related with AT. Whereas thyroid cancer is a rare event and it accounts for rather few deaths. Thus thyroid nodules should be evaluated by experienced physicians on gland. By this way, high prevalence of MNG operations and their costs and complications can be reduced in women.

Key words: Autoimmune thyroiditis, multinodular goiter, thyroid cancer, thyroidectomy

INTRODUCTION

It seems that thyroidal disorders are found among the most common causes of patients' visits to internal medicine polyclinics. Probably the most commonly seen thyroidal problems are related with Autoimmune Thyroiditis (AT) and/or multinodular goiter (MNG).

AT is an organ specific disease characterized by lymphocytic infiltration of the gland and production of autoantibodies directed against thyroid specific antigens (Dayan and Daniels, 1996). It is subdivided into Hashimoto's thyroiditis (chronic lymphocytic thyroiditis), Graves' disease and painless thyroiditis, which is also called as postpartum thyroiditis if it develops after birth. Patients may apply to clinicians with hypoor hyperthyroidism and/or goiter especially with micronodulation (Yeh *et al.*, 1996). Ophthalmopathy is more common with Graves' form of the disease and main diagnostic criterium is the presence of thyroidal autoantibodies, thyroid peroxidase (TPOAb) and/or thyroglobulin (TgAb), in serum. Presence of any or both of them together with an abnormal serum thyroid stimulating hormone (TSH) concentration is usually enough for the diagnosis.

Prevalence of palpable thyroid nodule is 2.1-4.2% but when ultrasonography (US) is used, it can reach up to 67% in society (Pedrazzini, 2005). There are many patients taking oral L-thyroxine regimen to suppress growth of the nodules and again there are many patients who have already been operated for MNG, mostly for the risk of malignancy. However, thyroid cancer is a rare event and is only seen as 1% of all malign tumours. The medium incidence is 2.1 for 100,000 men and 5.19 for 100,000 women per year (Pedrazzini, 2005). Here, we have tried to understand the prevalences of thyroidal disorder and operations and necessities of the MNG operations in society.

MATERIAL AND METHODS

We have taken consecutive patients applying for check up procedure to internal medicine polyclinic of the Dunlupinar University between August and December, 2005, randomly. Their medical histories, including any operation or drug usage, have been learnt. As the check up procedure, routine hematologic and biochemical tests, urinalysis, serum levels of TSH and free thyroxine (fT4), hepatitis markers, electrocardiography and a posterior-anterior chest X-ray graphy have been performed in all cases. Additional TPO and TgAbs and thyroid US have been taken from the abnormal thyroid function having cases and US-guided fine-needle

aspiration biopsy (FNAB) of thyroidal nodules have been performed to rule out malignancy, just in suspected cases. AT is diagnosed by the presence of TPO and/or TgAbs together with an abnormal TSH concentration in serum. The normal ranges of TSH and fT4 have been accepted as 0.4- 4.5 mU L⁻¹ and 8.7-22.6 nmol L⁻¹, respectively. Additionally cases with abnormal thyroid function tests have been subdivided into subclinical hypothyroidism (an elevated TSH alone), subclinical hyperthyroidism (a suppressed TSH alone), obvious hyperthyroidism (a suppressed TSH together with an elevated fT4) and obvious hypothyroidism (an elevated TSH together with a decreased fT4). ELISA method (the Trinity Biotech Captia) has been used to detect the TPO and TgAbs in serum. Prevalences of thyroidal operations for MNG have been detected for male and females and the results have been compared with the risk of thyroid cancer separately for either sex. Student t test has been used as the method of statistical analysis.

RESULTS

Four hundred and thirty consecutive patients have been taken into the study (Table 1). It has been learnt that 13 of them had been operated for MNG, even one female operated twice and all of the 14 operations had been performed to avoid from cancer in the absence of any already presenting evidence of malignancy. Additionally, one operation for papillary carcinoma of thyroid and one for Graves' disease have been detected. So operation rates for MNG have been 5.26 and 0.9% in female and males, respectively. When we compared these rates with the chance of having a thyroid cancer for either sex separately (2.1 for 100.000 men/year and 5.19 for 100.000 women/year are multiplied by 70, as an expected mean period of life span), the difference in women has been found as statistically significant ($p < 0.01$), whereas not in men ($p > 0.05$). Totally the 15 operated cases have been on L-thyroxine treatment, now. We couldn't find any knowledge about the autoimmune nature of the thyroid disease of the 14 operated cases, except operated for Graves' disease. Additionally eight cases with obvious hyperthyroidism, ten with subclinical hyperthyroidism, seven with subclinical hypothyroidism and 15 cases with obvious hypothyroidism have been detected among the 430 cases (Table 2). Thirty three of the 40 cases have been diagnosed as autoimmune thyroiditis. If we add the

Table 1: Sexual distribution and mean age of the study cases

	Female	Male
Number	228	202
Percentage (%)	53.02	46.97
Mean age	44.46±15.27	41.40±14.39

Table 2: All types of thyroidal disorder and operations detected among the study cases

	No. of cases/Total No. according to sexes (Female/Male)/Mean age			Prevalence (%)
	Operated *MNG	13	†12/†2	
Operated Graves' disease	1	1/0	62	0.23
Operated papillary carcinoma of thyroid	1	0/1	54	0.23
Obvious hyperthyroidism	8	5/3	42.37	1.92 (8/415)
Subclinic hyperthyroidism	10	4/6	55.70	2.40 (10/415)
Subclinic hypothyroidism	7	5/2	43.85	1.68 (7/415)
Obvious hypothyroidism	15	15/0	42.40	3.61 (15/415)
Autoimmune thyroiditis	34	29/5	43.98	8.17 (34/416)
All thyroidal disorders	55	41/14		12.79

*Multinodular goiter: †p<0.01, ‡p>0.05

Table 3: Sexual distributions of patients with autoimmune thyroiditis

	Female	Male
Number	29	5
Percentage (%)	85.29	14.70
Mean age (year)	44.34	48.20

Table 4: Clinical presentation types of patients with autoimmune thyroiditis

	No. and sex (F/M)		(%)
Obvious hypothyroidism	14	(14/0)	41.17
Subclinic hypothyroidism	12	(10/2)	35.29
Subclinic hyperthyroidism	2	(0/2)	5.88
Obvious hyperthyroidism	6	(5/1)	17.64

Table 5: Ultrasonographic properties of patients with abnormal thyroid functions

	Thyroiditis	Thyroiditis plus partial hyperplasia	Thyroiditis plus *MNG	Thyroiditis plus nodule	*MNG	Normal
No. of cases	24	1	5	2 of cases	5	4
Percentage	58.53	2.43	12.19	4.87	12.19	9.75

*Multinodular goiter

operated one case of Graves', the prevalence of AT has been 82.92% among all of the cases with abnormal thyroidal functions and 85% of the AT cases have been female. Totally five ultrasound-guided FNAB have been performed in five cases among the 40 patients and in none of the results has contained any malignant property. The prevalence of AT has been found as 8.17% among the 416 study cases (Table 3 and 4). Even two cases of the autoantibody negative but abnormal thyroid function having eight cases have been reported as AT, ultrasonographically (Table 5).

DISCUSSION

Iatrogenic destruction of the thyroid and AT represent the most common causes of adult hypothyroidism in iodine-sufficient areas (Vanderpump *et al.*, 1995). AT mainly affects the middle age and elder females. In a previous study, we had detected the prevalence of AT as 13.79% in adult population in Turkiye (Helvacı *et al.*, 2005), but it has only been detected as 8.17%, here, which may be secondary to the fact that some of the operated cases of our study had actually been AT, since AT accounts for most of the goiter cases in adults (Vanderpump *et al.*, 1995).

The prevalence of palpable thyroid nodule is 2.1-4.2% but when the US is used, it may reach up to 67% in society and as already mentioned above, an important percentage of them has probably been related with AT. The incidence of thyroid nodules increases with gender and age. The role of genetic factors is estimated as being around 80%. The remaining 20% are related to environmental factors, some of them being still unknown (Leclere, 2005). Admit these external factors, the iodine deficiency is predominant and should be theoretically easy to avoid. On the other hand, the thyroid cancer is a rare event and it only accounts for 1% of all malign tumours. The medium incidence is 2.1 for 100,000 men and 5.19 for 100,000 women per year. So thyroid cancer is one of the few malignancies that are more common in females than in males (M:F sex ratio, 0.36) and it comprises 2.1% of cancers in women. As an important fact, it is known that diagnostic practices (f.e., histological examination of resected goiters or at autopsy) can influence apparent rates of incidence. Additionally, the prognosis of thyroid cancer is good (mortality/incidence ratio, 0.25, worldwide) so it only accounts for 0.5% of all cancer deaths (Parkin *et al.*, 2002). In a prospective cohort study of 89,835 Canadian women, aged between 40 and 59 years, only 169 incident thyroid cancer cases have been

observed during a mean period of 15.9 years (Navarro *et al.*, 2005). As another important fact, the prevalence of thyroid microcarcinomas found at autopsies is even 100-1000 times higher than in clinical cancer and they seem to be more prevalent between the ages of 40-59 years and all microcarcinomas have been of the papillary type (Kovacs *et al.*, 2005). It is already known that there is an overlap in morphological features, immunohistochemical staining pattern and most importantly, molecular profile between papillary thyroid carcinoma and Hashimoto's thyroiditis. Although considered a 'benign' condition, Hashimoto's thyroiditis almost always harbours a genetic rearrangement that is strongly associated with and is highly specific for papillary thyroid carcinoma. Submicroscopic foci of papillary thyroid carcinoma must be present in Hashimoto's thyroiditis, although the clinical behaviour is still benign (Arif *et al.*, 2002). In addition to that, in another study it has been detected that p63 is commonly expressed in papillary thyroid carcinoma and in Hashimoto's thyroiditis. Given the debated association of papillary thyroid carcinoma with Hashimoto's thyroiditis, it is possible that p63 expression may be a potential pathobiologic link between these two disorders. The finding of p63 in benign squamoid nests supports a possible interrelationship between these structures and both Hashimoto's thyroiditis and papillary carcinoma of thyroid (Unger *et al.*, 2003). Here, we have detected the prevalences of thyroid operations for MNG as 5.26% in females and 0.9% in males and it has been learnt that all of these operations have been performed for MNG in the absence of any already existing criterium, supporting malignancy. As a result of the detected significant difference between the rates of MNG operation and chance of having a thyroid cancer in females, we think that such a high prevalence of thyroidal operations in women could not be accepted due to complications, which may be high if this procedure is not carried out by surgeons experienced on endocrine surgery including postoperative permanent recurrent laryngeal nerve palsy, transient hypocalcemia, hemorrhage requiring reoperation and incision infection, surgery-induced stress on patients, cost-effectiveness and life long requirement of L-thyroxine treatment.

As a conclusion, AT and operations for MNG have high prevalences in women and most of MNG are probably related with AT. Whereas the thyroid cancer is a rare event and it accounts for rather few deaths.

Additionally the prevalence of thyroid microcarcinomas found at autopsies is even 1000 times higher than clinical cancer. Thus thyroid nodules should be evaluated by experienced physicians on the gland. By this way, the high prevalence of MNG operations and their costs and complications can be reduced in women.

REFERENCES

- Arif, S., A. Blanes and S.J. Diaz-Cano, 2002. Hashimoto's thyroiditis shares features with early papillary thyroid carcinoma. *Histopathology*, 41: 357-362.
- Dayan, C.M. and G.H. Daniels, 1996. Chronic autoimmune thyroiditis. *N. Eng. J. Med.*, 335: 99-107.
- Helvacı, M.R., E. Gulcan, B. Akcay and M. Seyhanlı, 2005. Is there any increased risk of coronary artery disease in autoimmune thyroiditis? *Endokrinolojide Yonelisler*, 6: 173-176.
- Kovacs, G.L., G. Gonda, G. Vadasz, E. Ludmany and K. Uhrin *et al.*, 2005. Epidemiology of thyroid microcarcinoma found in autopsy series conducted in areas of different iodine intake. *Thyroid*, 15: 152-157.
- Leclere, J., 2005. Multinodular goiters. *Rev. Prat.*, 55: 167-173.
- Navarro, S.A., A.B. Miller and T.E. Rohan, 2005. Risk factors for thyroid cancer: A prospective cohort study. *Intl. J. Cancer*, 116: 433-438.
- Parkin, D.M., F. Bray, J. Ferlay and P. Pisani, 2002. Global cancer statistics. *CA Cancer J. Clin.*, 55: 74-108.
- Pedrazzini L., 2005. Treatment of patient having thyroid nodules: Dimension of disease, diagnostic choices and guide-lines. *Minerva. Endocrinol.*, 30: 59-69.
- Unger, P., M. Ewart, B.Y. Wang, L. Gan, D.S. Kohtz and D.E. Burstein, 2003. Expression of p63 in papillary thyroid carcinoma and in Hashimoto's thyroiditis: A pathobiologic link? *Hum. Pathol.*, 34: 764-769.
- Vanderpump, M.P., W.M. Tunbridge, J.M. French, D. Appleton and D. Bates *et al.*, 1995. The incidence of thyroid disorders in the community: A twenty-year follow-up of the Whickham Survey. *Clin. Endocrinol.*, 43: 55-58.
- Yeh, H.C., W. Futterweit and P. Gilbert, 1996. Micronodulation: Ultrasonographic Sign of Hashimoto's Thyroiditis. *J. Ultrasound. Med.*, 15: 813-819.