Ultrasonography Should Be Accepted as a Diagnostic Criterion for Autoimmune Thyroiditis until Demonstration of New Antithyroidal Antibodies

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Article:

Abstract: Autoimmune Thyroiditis (AT), together with iatrogenic destruction of gland are the most common causes of hypothyroidism in society. Its diagnosis is mainly dependent upon presence of thyroidal autoantibodies in serum and ultrasonography (US) is only accepted as a supporting tool of diagnosis for today. Ambulatory 161 patients with AT and 206 cases referring to general internal medicine polyclinic for any complaint other than AT have randomly been taken. US could be performed for 114 cases with AT and 59 cases without AT. Sensitivity and specificity of TPO and TgAbs and US for diagnosis of AT and positive and negative predictive values of US have been calculated. Sensitivities of TPO and TgAbs and US for diagnosis of AT have been 85, 73 and 80% and specificities of them 91, 87 and 69%, respectively. Additionally positive and negative predictive values of US have been calculated as 83 and 65%, respectively. So US has a statistically significant role for the diagnosis of AT (p=0.0001). Although demonstrated thyroidal autoantibodies are necessary tools for diagnosis of AT, US has a statistically significant role, too and it should be accepted as one of the diagnostic criteria until demonstration of new thyroidal autoantibodies. By this way, many unnecessary radionuclear imaging, fine-needle aspiration biopsy and even operations could be prevented in a significant percentage of cases, in whom AT is highly suspected by the ultrasonographic findings, but couldn’t absolutely be diagnosed by already known thyroidal autoantibodies for today.

Key words: Autoimmune thyroiditis, thyroid peroxidase antibody, thyroglobulin antibody, ultrasonography

INTRODUCTION

Autoimmune thyroiditis (AT) is an organ specific disease, characterized by lymphocytic infiltration of the gland and production of autoantibodies, directed against thyroid specific antigens\[4\]. Iatrogenic destruction of the gland and AT represent the most common causes of adult hypothyroidism in iodine-sufficient areas\[2\]. 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. These subtypes may convert to each other by time. Patients may come with hypo- or hyperthyroidism and/or goiter, especially with the micronodulation\[11\]. AT accounts for 40% of goiter cases in young adults\[6\]. Ophthalmopathy is more common with Graves’ form of the disease.

Presence of thyroid peroxidase (TPO) and/or thyroglobulin (Tg) antibodies together with an abnormal serum thyrotropin (TSH) concentration in serum is usually enough for the diagnosis of AT and positivities of TgAb in 60% and TPOAb in 95% of cases with AT have been reported. Until now not any other thyroidal autoantibody could be demonstrated and ultrasonography (US) is only accepted as a supporting tool of the diagnosis for today. We have tried to understand the diagnostic significance of US for AT, here.

MATERIALS AND METHODS

Ambulatory 161 patients with AT and 206 cases referring to general internal medicine polyclinic for any complaint or disease other than AT have randomly been taken into the study. AT is diagnosed by the positivity or positivities of the thyroidal autoantibodies together with an abnormal thyrotropin concentration in serum. Ultrasonographic images have been obtained by using Toshiba Power Vision 8000 device. ELISA method (The Trinity Biotech Captia) has been used to detect the serum positivities of the TPO and TgAbs. US could be performed for 114 cases with AT and 59 cases without AT by the same physician who had been blind for the study. Sensitivity and specificity of TPO and TgAbs and US for the diagnosis of AT have been defined as true positive/ true positive + false negative and true negative/ true negative + false positive, respectively. Positive and
negative predictive values of US have been defined as true positive/true positive + false positive and true negative/true negative + false negative. McNemar test has been used as the statistical method.

RESULTS AND DISCUSSIONS

One hundred and fortytwo of 161 patients with AT have been female with a mean age of 45.70 +/- 13.81 years (range 17-83) and 19 of them have been male with a mean age of 48.30 +/- 12.76 years (range 15-69). So 88.19% of cases with AT have been female (Table 1). One hundred and fourteen of 206 cases without AT have been female with a mean age of 47.61 +/- 15.50 years (range 18-83) and 92 of them have been male with a mean age of 52.07 +/- 17.70 years (range 6-87). TPOAb has been found as positive in 138 cases (sensitivity 85%) and TgAb in 119 cases (sensitivity 73%) with AT. On the other hand, TPOAb has been detected as negative in 188 cases among all 206 cases without AT (specificity 91%) and TgAb as negative in 181 of them (specificity 87%). US has given a result of AT in 92 of 114 cases with AT (sensitivity 80%) and a result excluding AT in 41 of 59 cases without AT (specificity 69%) (p=0.0001). The positive and negative predictive values of US have been calculated as 83 and 65%, respectively (Table 2).

AT is the most common cause of hypothyroidism, mainly affecting middle age and elder females. Thus an abnormal thyroid tropin is usually accepted as a proof of AT in iodine-sufficient areas[9]. Autopsy studies, performed in England and USA, have shown that various degrees of thyroiditis is present in 40-45% of female and 20% of male[10]. The main diagnostic criteria of AT is the presence of thyroidal autoantibodies in serum, but although the presence of high suspicion about the others, there are only two thyroidal autoantibodies demonstrated for now. Prevalences of the two autoantibodies may reach up to 33% in females older than 70 years[11]. We have observed that 88% of cases with AT have been female with a mean age of 45 years and again the mean age of male has been 48 years, here. So AT is an eight times more commonly seen autoimmune disease in females and again it is more commonly seen around the fifth decade of life. Positivities of TgAb in 60% and TPOAb in 95% of cases have been reported before. Whereas in our study, TPOAb has been found as positive in 85% and TgAb in 73% of AT cases.

It is believed that autoimmune procedure is initiated by the activation of thyroid antigens specific CD4(+) T lymphocytes (T-helper). Although the antigen specific T-helpers could be isolated in thyroid tissues of Graves’ patients, they couldn’t be detected in Hashimoto’s thyroiditis[12]. Activation mechanism of T-helpers is still unknown. Currently two hypotheses are thought about this activation mechanism. According to the first hypothesis, infections by some viruses or bacteria, carrying proteins similar with the thyroidal ones, may activate the thyroid specific T-helpers. This way is dependent upon the fact of molecular similarity. Representation of intracellular proteins to T-helpers by thyroid epithelial cells is the second hypothesis. This hypothesis is also supported by the fact that although thyroidal cells of AT patients represent major histocompatibility complex-class II (MHC-class II) proteins (HLA-DR, HLA-DP vs HLA-DQ), normal thyroidal cells don’t represent them[13]. These proteins are required for representation of antigens to T-helpers. Once activated, self-reactive T-helpers may cause production of thyroidal antibodies by stimulating autoreactive B lymphocytes. Until now three antigenic targets have been detected on thyroid. They are thyroglobulin (storage protein of thyroid hormones), thyroid microsomal antigen (thyroid peroxidase enzyme as the rate-limiting step of thyroid hormone synthesis) and receptor of thyrotrpin. Some other antigenic structures of the thyroid, against which some antibodies are directed and thyroid growth initiating immunoglobulins, other than thyrotrpin receptor stimulating ones, have been mentioned and highly suspected but they couldn’t be demonstrated exactly for now[10].

In addition to the thyroidal autoantibodies, the ultrasonographic pattern can help to identify the patients with AT[11]. Fibrotic septations may produce a pseudolobulated appearance of the parenchyma. Multiple and discrete hypoechoic micronodules from 1 to 6 mm in diameter have been described as strongly suggestive of AT. Histologically, they represent lobules of thyroid parenchyma which have been infiltrated by lymphocytes and plasma cells. Micronodulation is a highly sensitive sign of AT. Besides identification of thyroid nodules[11], US is able to characterize the echostucture of thyroid tissue. The normal thyroid parenchyma has a peculiar echo density determined by the typical follicular structure. The interface between thyroid cells and colloid exhibits high acoustic impedance, causing high frequency acoustic waves to be reflected back to the probe. In AT, however, lymphocytic infiltration and dissection of tissue architecture cause a reduction in thyroid echogenicity and this hypoechogenicity is statistically higher than in normal subjects[13]. The echogenicity of the gland has been demonstrated secondary to the comparison with the surrounding hypereffective neck muscles[14]. It has been shown that the development of hypothyroidism is strictly

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<th>Table 1: Features of the patients with autoimmune thyroiditis.</th>
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<td><strong>Female</strong></td>
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<th>Table 2: Diagnostic values of the already known thyroidal autoantibodies and ultrasonography for autoimmune thyroiditis.</th>
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<td><strong>Sensitivity (%)</strong></td>
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related with the degree of the thyroidal hypoechogenicity. So clinical hypothyroidism is not developed in AT cases if at least 38% of the thyroidal parenchyma is hyperechogenous with comparison to the neck muscles and hypothyroidism is developed in cases with the hypoechogenicity of at least 68% of gland[13]. The reported prevalence of this hypoechogenicity in AT varies from 19 to 95%. In our study, US has a 80% sensitivity and 69% specificity for the diagnosis of AT (p=0.0001). The positive and negative predictive values of US have been calculated as 83 and 65%, respectively.

Furthermore, the current practice in assessing sonographic findings of chronically inflamed thyroidal tissue and the reproducibility of data are qualitative and are strictly dependent both on the physician’s experience and used ultrasonographic equipments. But although the presence of such disadvantages of US, it is still the preferred radiological tool to detect the pathologies of the thyroid gland. Radionuclear imagings are not essential in AT, US has a statistically significant role for the disease, thyroidal autoantibodies is necessary for the diagnosis of AT until demonstration of highly diagnostic parameters of AT until demonstration of highly significant[14].

As a conclusion although serum positivity of thyroidal autoantibodies is necessary for the diagnosis of AT, US has a statistically significant role for the disease, too. Therefore it should be accepted as one of the diagnostic parameters of AT until demonstration of highly suspected new thyroid autoantibodies. By this way, many unnecessary radionuclear imaging, FNAB and even operations could be prevented in a significant percentage of cases, in whom AT is highly suspected by the ultrasonographic findings, but couldn’t absolutely be diagnosed by any known thyroidal antibody for now.

REFERENCES