CASE REPORT

AUTOIMMUNE HASHIMOTO THYROIDITIS WITH CONCOMITANT AUTOIMMUNE HEPATITIS

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Abstract

So far, the literature data have presented a combination of several autoimmune triggered disease in patients, but the research is scarce and very limited. In this context we present a rare case of autoimmune thyroiditis with a concomitant autoimmune hepatitis. Hashimoto thyroiditis is an autoimmune disorder in which immune cells lead to impairment, destruction of the thyroid hormone producing cells and tissue fibrosis with consecutive primary hypothyroidism. Autoimmune hepatitis is a chronic liver disease with unknown etiology, which is assumed to be T cell mediated condition where immune cells produce autoantibodies responsible for inflammation, destruction and fibrosis of the hepatic parenchyma. In this case report, we discuss the possible correlation in the spectrum of autoimmune diseases concerning Hashimoto thyroiditis and autoimmune hepatitis.

ПРИКАЗ НА СЛУЧАЈ

АВТОИМУН ХАШИМОТО ТИРОИДИТИС АСОЦИРАН СО АВТОИМУН ХЕПАТИТИС

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Клучни зборови: автоимун тироидитис, автоимун хепатитис, антинуклеарни антитела, антитироидни антител

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Извадок

До сега, во литературата се среќаваат податоци за комбинација од неколку автоимуни болести кај различни пациенти, но студиите од ова поле на истражување се оскудни и ограничени. Во овој приказ на случај, претставуваме редок случај на автоимун тироидитис со истовремен авотимун хепатитис. Хашимото тироидитис е автоимуно заболување во кое клетките на имуниот систем доведуваат до оштетување и уништување на клетките коишто го произведуваат хормонот на тироидната жлезда и ткивна фиброза со последователен примарен хипотироидизам. Автоимуниот хепатитис е хронично заболување на црниот дроб со непозната етиологија, за кое се претпоставува дека е состојба посредувана од Т-клетките каде што имуните клетки произведуваат автоантитела одговорни за воспаление, уништување и фиброза на хепаталниот паренхим. Во овој приказ на случај ја дискутираме можната корелација во спектарот на автоимуни болести кои се однесуваат на Хашимото тироидитисот и автоимуниот хепатитис.

Introduction

Autoimmune thyroid diseases (AITD) are organ specific autoimmune disorders, where both genetic and environmental factors are included into the etiological spectrum[1]. Patients with AITD are predisposed to develop other autoimmune disorders. Autoimmune hepatitis (AIH) is a disease of unknown etiology in which destruction of the liver tissue occurs, resulting in a permanent liver tissue damage that eventually leads to liver failure. AIH occurs in children and adults of all ages; has a female predominance and affects different ethnic groups[2].

In this paper we report a rare case of AIH in a patient with preexisting Hashimoto thyroiditis (HT).

Case report

We present a 58-year-old female referred to our Institute of Pathophysiology and Nuclear Medicine in June 2013 with symptoms of difficulties in swallowing and tachycardia, for assessment of possible thyroiditis. Initial examination excluded subacute thyroiditis. The laboratory findings revealed normal sedimentation rate and TSH and FT4 levels. However, levels of aTPO were increased 195 μIU/mL (reference values <10 μIU/mL), which was an indicator of AITD – Hashimoto thyroiditis, in the euthyroid phase. The ultrasound (US) of the thyroid gland presented hypoechoic gland structure with hyper-echoic reflections which additionally pointed to the AITD. Since the US detected also a thyroid nodule, a fine needle aspiration biopsy (FNAB) was performed. The results of the FNAB showed a combination of benign thyrocytes and lymphocyte infiltration.

The patient was scheduled for annual follow check-ups and treatment with Selenium (50 μg per day) was initiated. In 2016, TSH levels increased above the reference range and hypothyreosis was diagnosed. Anti-thyroglobulin antibodies (aTG) were also highly elevated (>3000 μIU/mL). Treatment with 25 μg of levothyroxine was initiated.

In 2017, the patient gave data that she was more prone to tiredness in the last year and she felt a constant pain under the right rib arch. She was referred to the University Clinic for Gastroenterohepatology for further examination. The results from the blood analysis showed increased levels of the liver enzymes AST 100 (normal ranges 7-52 U/L) and ALT 86 (normal ranges 13-39 U/L). Ultrasound of the abdomen was performed presenting liver inhomogeneous structure with fibrotic changes. Additional analysis suggested and confirmed the diagnosis behind the liver changes, such as serum auto-antibodies level and liver biopsy. Serum levels of the antinuclear antibodies (ANA) were elevated seven times above

reference value. ANA screen was 7.08 IE/mL (reference value < 1 negative).

The enzyme status profile is presented in Table 1.

Table 1. Enzyme status profile

Enzymes	U/L	Reference value
Alkaline phosphatase	136	36-126 U/L
Aspartate aminotransferase	26	10-34 U/L
Alpha amylase	76	30-110 U/L
Lactate dehydrogenase	142	< 248 U/L
Gamma-glutamyl transferase	136	9-64 U/L
Alanine aminotransferase	33	10-45 U/L

Liver biopsy was additionally performed and confirmed the diagnosis of autoimmune chronic active hepatitis. The patient was also put on a hepatoprotective treatment and scheduled for regular check-ups at the Gastoentorohepatology Clinic, in addition to regular examinations at the Institute of Pathophyisology and Nuclear Medicine.

Discussion

The increased liver biomarkers in patients with autoimmune thyroiditis can indicate an underlying autoimmune hepatitis, as was the case we herein presented. Our patient had elevated liver biomarkers (AST and ALT) five years after the initial diagnosis of AITD. Autoimmune serology also confirmed presence of antinuclear antibodies, which were seven times above the reference range. The levels of anti-cytoplasmatic and other analyzed autoantibodies of the IgG class were within the reference range. The seronegativity for the already mentioned auto- antibodies did not rule out the AIH. The seropositivity for ANA was a diagnostic factor that led to the necessity of performing a liver biopsy. The biopsy results were in favour of autoimmune chronic active hepatitis.

Hashimoto thyroiditis is the most frequent autoimmune disease that affects the thyroid cells by developing antibody mediated processes, lymphocytic infiltrations, formations of antithyroid antibodies and consecutive fibrosis of the tissue[3, 4].

Clinical evidence that highlights the coexistence of two or more autoimmune diseases in one patient is abundant. Since Hashimoto thyroiditis is the most common thyroid autoimmune disease (AD), it is frequently associated with another organ specific or organ nonspecific AD[5, 6].

In several studies, patients who have been suffering from rheumatoid arthritis (RA) are known to have multiple autoimmune disorders including HT. The prevalence of AITD and RA varies between regions and countries such as 37% in Columbia (America), 30% in Egypt (North Africa), 24.4% Scotland (Europe), 15.9% in Turkey (Asia). A subject of controversy for some authors is the increased prevalence of AITD in patients with systemic lupus erythematosus (SLE). The prevalence of HT in SLE, mixed connective tissue diseases, Sjögren's syndrome and polymyositis/dermatomyositis were much higher than in the general population[7, 8, 9].

Autoimmune hepatitis is an inflammatory condition of the liver with

chronic progressive characteristics. It is presented with elevated amino transferases, persisting antinuclear antibody, high levels of IgG and infiltration with plasma cells and lymphocytes. There is no specific evidence about its etiology up to date. There are two types of autoimmune hepatitis described in the literature. The first one is known as type 1, which is characterized with the presence of anti-smooth muscle antibodies in which antinuclear antibodies could be but it is not obligatory to be present. The other type is type 2, associated with anti-liver microsomal type 1 antibodies or anti-liver cytosol type 1 antibodies[10, 11].

Antinuclear antibodies are the first autoantibodies to be related with AIH, but they are not disease specific. Scientific studies showed that 50-75% of AIH patients are ANA-positive. ANA can sometimes also be found in healthy persons or patients with other liver diseases including fatty liver disease, drug produced liver lesions or viral hepatitis. Antinuclear antibodies in autoimmune hepatitis attack the nuclear chromatin, histones, centromere, double-(ds) and single-(ss) stranded deoxyribonucleic acid (DNA) and other constituents of the cell nucleus.

However, testing for ANA antibodies is necessary for AIH diagnosis[12].

In some studies, the authors confirm that patients with AH are more likely to develop concomitant autoimmune disease of the thyroid gland. Patients who had AITD and AILD showed higher levels of IgG, since IgG was positively correlated with thyroid antibodies and thyroperoxidase antibodies[13, 14].

Since AIH is a progressive disease, a missed diagnosis can have serious consequences. If untreated, AIH can have a fatal outcome due to changes of the liver tissue that might lead to cirrhosis and consecutive liver failure. Elevated levels of liver enzymes, alanine transaminase (ALT) and aspartate transaminase (AST) are common findings in asymptomatic patients. Even though history and physical examination of the patient might not suggest an underlying condition, a stepwise analysis should begin based on the prevalence of diseases that cause elevations of transaminase levels. Most common causes that can lead to liver enzymes elevations are excessive alcohol consumption, family history of hemohromatosis, hepatitis B and C and medications. Various medications are known to cause liver damage. Many of these are often included in daily practice such as NSAID, antibiotics, anti-seizure drugs, anti- tuberculosis drugs, antidepressants. The absence of specific signs and lack of symptoms and specific criteria makes the diagnosis of drug-induced liver damage (DILI) difficult. DILI occurs via several known mechanisms. Among these mechanisms are impairment of the structural and functional integrity of the liver, production of a metabolite that affects the liver structure, beginning with a systemic hypersensitivity response, production of a reactive drug metabolite that binds to liver proteins to produce new antigenic drug-protein adducts, which are subsequently targeted by hosts' defenses. Liver biopsy is used and might be quite a helpful diagnostic tool when there is an undefined liver disease or possible autoimmune hepatitis[15].

The marking of injury and typical characteristics of AIH are imprecise, thus the differential diagnosis is very comprehensive. In AIH cases with an acute hepatitis presentation of tissue deterioration, the differential diagnosis predominantly

includes acute viral hepatitis and drug- induced liver injury (DILI). In cases with a chronic hepatitis pattern, chronic viral hepatitis, other autoimmune diseases and/or Wilson disease should be appraised. Idiosyncratic DILI can mimic the clinical, biochemical and serological constitution of AIH. In non-acute AIH, non-alcoholic steatotic hepatitis (NASH) is a foremost clinical differential diagnosis. Positive autoantibody serology, usually with low levels, is present in 20-48% of NASH patients. It is necessary to exclude infection with hepatotropic viruses before the diagnosis of definite or potential AIH. Serological testing is recommended in all patients with this differential diagnosis, especially for hepatitis virus A and hepatitis virus E (HEV) infection[16].

Conclusion

Patients with HT who report symptoms of liver involvement and have high levels of aTG and aTPO autoantibodies should be referred for further investigation for possible concomitant AIH, since there could be a possible correlation and overlap in the spectrum of autoimmune diseases.

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