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Exceptional Evolution of Autoimmune Hypothyroidism to Graves' Disease

Otoimmun Hipotiroidinin Graves' Hastalığına Sıradışı Değişimi

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Abstract

The occurrence of Graves' disease after an autoimmune hypothyroidism is particularly outstanding and raises questions about the mechanisms involved. Here, we report an 18-year-old patient who has been followed up for autoimmune hypothyroidism since 2009. Hormonal biological monitoring has led to gradually reduce the dose of substitution therapy and to stop it in September 2011 due to the occurrence of hyperthyroidism. The diagnosis of Graves' disease was confirmed by the positivity of TSH-receptor antibodies. Carbimazole treatment is then undertaken. This new observation shows that this seemingly paradoxical combination is not impossible and encourages regular surveillance of these patients. *Turk Jem 2014; 18: 95-96*

Key words: Autoimmune thyroid diseases

Özet

Otoimmun hipotiroidi sonrası gelişen Graves Hastalığı oldukça sıradışıdır ve altta yatan mekanizmalar konusunda soru işaretleri barındırır. Burada 2009 yılından bu yana otoimmun hipotiroidi nedeni ile takip edilen 18 yaşındaki bir hasta sunulmaktadır. Hormon izlemine göre yerine koyma tedavisindeki dozlar kademeli olarak azaltılmış ve hipertiroidi nedeni ile Eylül 2011 de tedavi kesilmiştir. Graves Hastalığı tanısı TSH-reseptör antikoru pozitifliği ile doğrulanmıştır. Karbimazol tedavisi başlanmıştır. Bu gözlem paradoksal kombinasyonların imkansız olmadığını göstermekte ve düzenli kontrollerin yapılmasını desteklemektedir. *Turk Jem 2014; 18: 95-96*

Anahtar kelimeler: Otoimmün tiroid hastalıkları

Introduction

Graves' disease and autoimmune thyroiditis are part of autoimmune thyroid disease (AITD). Although they seem to coexist (1), the occurrence of Graves' disease after an autoimmune hypothyroidism is particularly outstanding and raises questions about the mechanisms involved. Only a few cases have been reported in the literature (2,3).

Case Report

An 18-year-old patient presented to our clinic in 2009 without a history of significant pathology. The diagnosis of autoimmune hypothyroidism was established based on the usual symptoms and a TSH level of 258.20 mIU/l (n=0.27-4.20 mIU/L) and anti-thyroid peroxidase antibody level of 132.5 IU/ml (n=<30 IU/l). Unexpectedly, the hormone replacement therapy that he received should be reduced in February 2011 due to overdose, and then, gradually stopped in September 2011. While not receiving L-thyroxine, during follow-up, the patient was found to have hyperthyroidism with the following values: TSH: 0.005 mIU/l (n=0.27-4.20 mIU/l), FT3:20.48 pmol/l (n=3.10-6.80 pmol/l) and FT4:44.85 pmol/l (n=12-22 pmol/l). Ultrasonography revealed increased thyroid volume size and echogenicity that was generally hypoechoic. Scintigraphy showed that the contours of the thyroid gland were generally regular and there was no nodule clearly visualized. Ocular examination showed the appearance of exophtalmos. Hertel ophthalmometry confirmed the presence of bilateral exophthalmos. The orbitofrontal cortex was not investigated. Carbimazole treatment was started for Graves' disease based on the presence of anti-TSH receptor antibodies. A year later, while treatment with carbimazole and levothyroxine was continued, biological control showed negativity of antithyroid peroxidase antibodies and a decrease in anti-TSH receptor antibodies.

Discussion

AITD results in infiltration of the thyroid by T and B cells that react with thyroid antigens inducing the production of antibodies and

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clinical manifestations of hypo-or hyper-thyroidism, this variability of clinical expression is poorly explained (4).

Autoimmune hypothyroidism has two different mechanisms: cell destruction by humoral and cellular mechanisms or cell functional blocking particularly in the forms of thyroiditis with goiter (4). While in Graves' disease, mechanism is linked to stimulating antibodies that activate all cellular functions (metabolic and secretory).

Autoimmune hypothyroidism and Graves' disease are both defined by the presence of circulating antithyroid antibodies. Thyroglobulin antibodies are the oldest described but their responsibility in the occurrence of thyroid disease is not engaged and their dosing is not recommended by the National Agency for Accreditation and Evaluation in Health (NAAEH) and the National Academy of Clinical Biochemistry (NACB) (5). Anti-thyroid peroxidase, the main antigen of the thyroid microsomal fraction, plays an important role in inducing cellular cytotoxicity (4).

In Graves' disease, anti-thyroid peroxidase and anti-thyroglobulin antibodies are serological markers and not modulators of clinical expression; their positivity reflects the importance of the autoimmune process (6,7). Anti TSH receptor antibodies have a direct pathogenic role; they are present in 90% of cases and are specific to the disease. They belong to several families and their nomenclature is complex: TSH-binding inhibiting antibody (TBIAb) and TSH-binding inhibitor immunoglobulin (TBII) inhibit the binding of TSH to its receptor, thyroid stimulating antibody (TSAb) and thyroid-blocking antibody (TBab) act through the cyclic AMP pathway.

Therefore, in this observation, the onset of Graves' disease after autoimmune hypothyroidism can only be explained by the persistence of a strong contingent of functional thyroid cells that may be stimulated by anti TSH receptor antibodies. The joint presence of blocking antibodies and stimulating antibodies reflects the initial silence of Graves' disease. The time to onset of hyperthyroidism is highly variable and ranges from a few months to several years. This type of fluctuation of thyroid function has been reported in a few cases in the literature (2,8). Some specific situations such as iatrogenic induction during immunotherapy or allograft, changes in terrain during pregnancy, in genetic diseases or dysimmune disorders and cancers may well be the cause. The clinically overt orbitopathy in this observation is found in about 40% of cases during the diagnosis of Graves' disease (4). Its pathophysiology is still unknown (9). Anti-TSH receptor antibodies appear to be a determining element based on the notion of a common antigen in the thyroid tissue and orbital tissue: the TSH receptor (10). Factors contributing to its occurrence may be genetic or environmental, such as smoking, stress, etc.

Conclusion

The finding of an autoimmune hypothyroidism usually leads to the final prescription of hormone replacement therapy. The occurrence of Graves' disease during evolution as illustrated in this case is not impossible and justifies regular monitoring.

Conflicts of Interest

There are no conflicts of interest.

References

1. Kraiem Z, Baron E, Kahana L, Sadeh O, Sheinfeld M. Changes in stimulating and blocking TSH receptor antibodies in a patient undergoing three cycles of transition from hypo- to hyperthyroidism and back to hypothyroidism. Clin Endocrinol. 1992;36:211-214.
2. Le Berre JP, Rousseau C, Dupuy O, Bordier L, Mayaudon H, Bauduceau B. [Unusual evolution of autoimmune hypothyroidism: occurrence of Grave's disease]. Rev Med Interne. 2004;25:841-843.
3. Takasu N, Yamada T, Sato A, Nakagawa M, Komiya I, Nagasawa Y, Asawa T. Graves' disease following hypothyroidism due to Hashimoto's disease: studies of eight cases. Clin Endocrinol (Oxf). 1990;33:687-698.
4. Mayer A et Orgiazzi J. Auto-immunité et thyroïde. Encycl Méd Chir , Endocrinologie-Nutrition, 2000. 10-002-G-10.
5. Kratzsch J, Fiedler GM, Leichtle A, Brügel M, Buchbinder S, Otto, Sabri O, Matthes G, Thiery J. New reference intervals for thyrotropin and thyroid hormones based on national academy of clinical biochemistry criteria and regular ultrasonography of the thyroid. Clin Chem. 2005;51:1480-1486.
6. Ducornet B, Moisson-Meer A, Duprey J[Hypothyroidism and blocking antibodies]. Ann Med Interne (Paris). 1995;146:559-574.
7. Osorio-Salazar C, Lecomte P, Madec AM, Baulieu JL. [Basedow disease following autoimmune primary hypothyroidism. Apropos of 7 cases]. Ann Endocrinol (Paris). 1994;55:185-189.
8. Kasagi K, Takeda K, Goshi K, Takamatsu J, Hidaka A, Hatabu H, Misaki T, Iida Y, Kuma K, Konishi J. Presence of both stimulating and blocking types of TSH-receptor antibodies in sera from three patients with primary hypothyroidism. Clin Endocrinol (Oxf). 1990;32:253-260.
9. Teissier MP, Lopez S. [Thyroid-associated ophthalmopathy: physiopathology, endocrine status]. J Fr Ophtalmol. 2004;27:806-809.
10. Spitzweg C, Joba W, Hunt N, Heufelder AE. Analysis of human thyrotropin receptor gene expression and immunoreactivity in human orbital tissue. Europ J Endocrinol. 1997;136:599-607.