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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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A RARE CASE OF A PATIENT WITH HYPERTHYROIDISM AFTER HYPOTHYROIDISM

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Abstract.

Primary hypothyroidism caused by an underlying autoimmune thyroiditis disease is very common in clinical practice, while one of the most commonly seen types of hyperthyroidism states is Graves' disease. In hypothyroidism, patients are thought to be lifelong treated with substitution therapy with the lacking levothyroxine hormone. Usually due to the started autoimmune process that progressively destroys the thyroid tissue, the doses of levothyroxine increase in a different period of time during the follow ups. Rarely, the doses need to be tapered down, and that is the exact moment when the physician should be suspicious of a possible conversion from a hypothyroid state to a hyperthyroid one.

We describe a case of a woman who was diagnosed with hypothyroidism and treated with suitable doses of levothyroxine, and then gradually the levothyroxine doses were tapered and eventually discontinued because of the clinical and laboratory confirmed state of hyperthyroidism- requiring a treatment with thiamazole. To our knowledge, this case is one of rarest worldwide so far published cases that illustrate the shortest time interval between the diagnosis of hypothyroidism and its switch to a hyperthyroid state.

Key words. Hyperthyroidism, hypothyroidism.

Introduction.

Hashimoto's thyroiditis and Graves' disease are the most common autoimmune thyroid conditions. They are more common in women than in men. Both conditions are characterized by symptoms and signs on the opposite spectrum of the scale and have entirely different appearances on radioactive iodine nuclear imaging studies [1]. Thyrotropin receptor (TSHR) antibodies that stimulate the thyroid (TSAb) cause Graves' hyperthyroidism and TSHR antibodies which block thyrotropin action (TBAb) are occasionally responsible for hypothyroidism. Occasionally, patients switch from TSAb to TBAb with concomitant thyroid function changes [2].

Usually there is evolution from Graves' disease (GD) to Hashimoto's thyroiditis (HT), whereas the switch from HT into GD seems to be less common. This is probably due to the lack of critical mass of functioning thyroid tissue able to react to thyrotropin (TSH) receptor autoantibodies (TRABs) in individuals with long-standing HT [3].

The exact incidence of this conversion is not known due to its presumed rarity, and we could only find a limited number of similar cases in the literature, where this process took place over a variable time course spanning from months to years [1].

Case report.

53 years old woman presented in our office in January 2021, with symptoms of tiredness, palpitations, sweating, uncontrolled movements of the extremities and neck. Her hair started to fall rapidly in the past few months.

She was diagnosed with autoimmune hypothyroidism in 2013, based on ultrasound of the thyroid gland and elevated aTP-O->600 iU/ml (<34 iU/ml), TSH-15,3mU/l (0,27-4,2mU/l), fT4-5,6Pmol/l (10,30-24 Pmol/l), fT3-2,9 (3,1-6,8 Pmol/l). After six months the patient achieved euthyroid status- following treatment with Levothyroxine 75 mcg/daily. The results were aTP-O->600 iU/ml (<34 iU/ml) , TSH- 3,2 mU/l (0,27-4,2mU/l), fT4-11,5 Pmol/l (10,30-24 Pmol/l), fT3-3,7 (3,1-6,8 Pmol/l). This almost stable status was interestingly interrupted after 8 years (January 2021) when the patient on a laboratory result showed suppressed TSH levels <0,004 mU/l (0,27-4,2mU/l) and a high fT4 35,7 Pmol/l (10,30-24 Pmol/l). Substitution therapy with levothyroxine was discontinued immediately. The ultrasound of the thyroid gland showed nonspecific changes: hypoechoic, inhomogeneous gland without any markable pathological formations (Figure 1).

Radioactive scan of the thyroid gland was done- symmetrical homogeneous accumulation of the radiopharmaceutical preparation in the projection of both lobes of the thyroid gland, without defects in the parenchyma in terms of thyroid dysfunctional nodules (Figure 2).

She was given beta blocker and acetyl salicylic acid during the first visit. Started form January until October 2021 she was not on antithyroid therapy. She was regularly followed, and the analysis revealed normal levels of fT4 with suppressed levels of TSH.

In October 2021, the new laboratory results showed TSH <0.005 mU/l (0,27-4,2mU/l), fT4 =33.36 Pmol/l (10,30-24 Pmol/l), aTPO= 22.77 iU/ml (<34 iU/ml), thyroglobulin =46,62ng/ml (0,73-84 ng/ml) , Vit. D3=27.3 ng/ml (20-40 ng/ml), TSH receptor antibodies= 15.40 IU/l (0,00- 1,76 IU/l). Antithyroid therapy was required, and she was given methimasol 40 mg daily, benzodiazepine 4 mg daily and therapy with beta blocker (propronalol 40 mg daily) because of the developed clinically and laboratory confirmed hyperthyroidism. The precipitating factors remained unclear, but according to anamnesis that she gave (divorce), severe psychological stress lead to this provoked conversion in the whole metabolism of not only the thyroid status, but also on the way the whole organism responded to the unknown trigger factor.

It is important to note that it took a while (October 2022) until the therapy reached a stable level. During that year the patient was bi-monthly controlled, and the dose of thiamazole was gradually tapered until the discontinuation which happened in October 2022. The anti-thyroid therapy was administered again after six months and the patient is so far clinically stable under regular control. The patient is feeling good with the anti-thyroid and cardiologic medications and the primary symptoms are diminished and she can function in her everyday life as in the moments before diagnosing the disease.

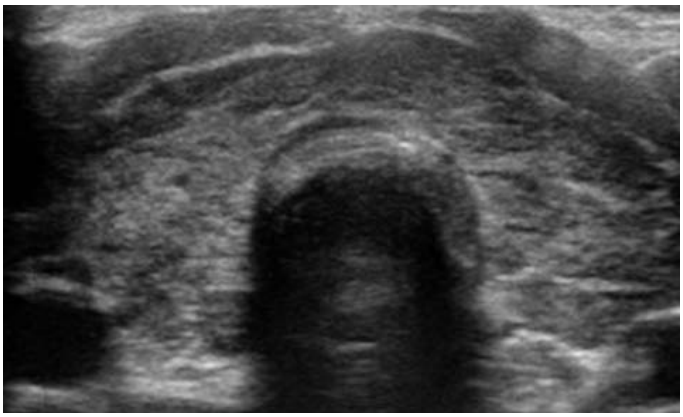

Figure 1. *Ultrasound of the thyroid gland.*

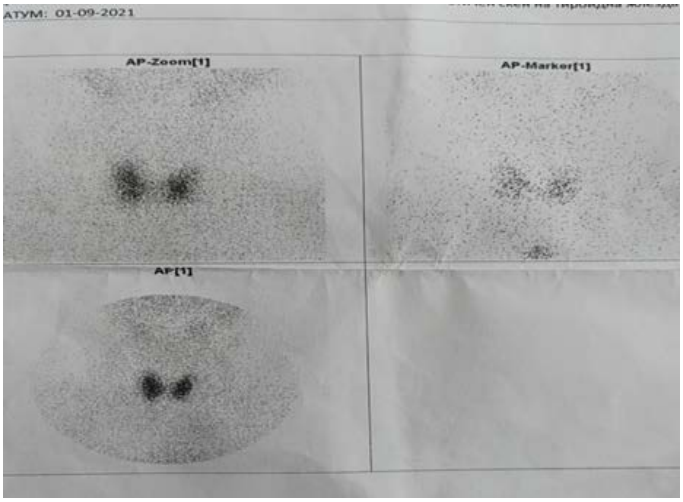

Figure 2. *Normal thyroid scan.*

Methods and laboratory tests.

Serum concentrations of TSH (normal range 0.27- 4.2mU/L), fT4 (normal range 10,30 -24.00 pmol/L), and fT3 (normal range 3,1-6,8 pmol/L) were measured by electrochemiluminescence methods. Anti-TPO (anti-thyroid peroxidase) autoantibodies (normal range <34 IU/ml) were measured using electrochemiluminescence immunoassay methods. TBAb antibodies (Thyroid Receptor Binding antibodies) were not available at our laboratory at the first moment when the patient was diagnosed with hyperthyroidism in 2021. TBAb were measured for the first time by electrochemiluminescence in October 2021, when the reagents became available for use at our clinic laboratory, therefore comparison regarding the time lapse values of TBAb for our patient is not presented.

Discussion.

The first similar case was described by Joplin and Fraser in 1959 [7] and was followed by several others in the later 60s and 70s [1]. In 1990 Takasu et al. [4] described a case series of eight cases converting to Graves' disease following Hashimoto's disease, and it was observed that those cases could be divided into three groups: a group of transiting Graves' disease following hypothyroidism, a group of persistent Graves' thyrotoxicosis following hypothyroidism and a group of persistent hypothyroidisms despite positive thyroid-stimulating immunoglobulins [1,4,5]. Moriarty et al. [6] described a case of a conversion related with thyroid eye disease, and according to their report, a variable behavior of the TRAB with the TSH receptor is responsible for the conversion from hypothyroidism to hyperthyroidism and vice versa.

An important distinguishing sign on physical examination is thyroid atrophy presenting at the onset of the disease while thyroid atrophy usually develops at advanced stages (long standing disease) in Hashimoto thyroiditis [2,8].

The potential mechanisms regarding the pendulum swinging from hypothyroidism to hyperthyroidism are suggested by Sandra M. McLaclan et al. [2] who stated that the switch may occur after treatment with levothyroxine (LT4), after anti-thyroid drug therapy (reverse switch, from TBAb to TSAb), and alterations may occur during pregnancy and are well recognized in transiting neonatal thyroid dysfunction. Factors that may impact the shift include: 1. LT4 treatment, usually associated with decreased thyroid autoantibodies, in some patients induces or enhances thyroid autoantibody levels; 2. antithyroid drug treatment decreases thyroid autoantibody levels; 3. hyperthyroidism can polarize antigen-presenting cells, leading to impaired development of regulatory T cells, thereby compromising control of autoimmunity; 4. immune-suppression/hemodilution reduces thyroid autoantibodies during pregnancy and rebounds postpartum; 5. maternally transferred IgG transiently impacts thyroid function in neonates until metabolized; 6. a Graves' disease model involving immunizing TSHR-knockout mice with mouse TSHR-adenovirus and transfer of TSHR antibody-secreting splenocytes to athymic mice demonstrates the TSAb to TBAb shift, paralleling the outcome of maternally transferred "term limited" TSHR antibodies in neonates. Finally, but not less important, as illustrated by dilution analyses of patients' sera in vitro, TSHR antibody concentrations and affinities play a critical role in switching TSAb and TBAb functional activities in vivo [2].

More extensive cohort, immunological and genetic studies are necessary to gain insight into this interesting phenomenon [5]. Despite its rarity, it is possible that patients developing this conversion could be encountered by primary care physicians as well as hospital-based doctors and may be mistaken for over-replacement with levothyroxine. Treatment is straightforward with anti-thyroid medications once the diagnosis is confirmed [1].

Conclusion.

This rare switch from a state of hypothyroidism to a state of hyperthyroidism is not very common in clinical endocrinology practice but should not be missed or misdiagnosed. Suspicion should be raised in the very first moment of tapering the levothyroxine doses in any patient with diagnosed HT during a regular follow up. Our recommendation is doing the TRABs (if available) at the moment of lowering the levothyroxine doses along with the regular laboratory tests of fT4, TSH, ATPOs. If there are any TRABs elevated, the leading way is to think and manage the possible and probable onset of hyperthyroidism.

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