Check for updates

Манифестация диффузного токсического зоба у женщины с пангипопитуитаризмом, развившимся в результате радиохирургического лечения акромегалии

© Л.И. Астафьева[1]*, П.Л. Калинин[1], Т.А. Киеня[2], В.В. Фадеев[2]

[1]ФГАУ «Национальный медицинский исследовательский центр нейрохирургии им. акад. Н.Н. Бурденко» Минздрава России, Москва, Россия;
[2]ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова (Сеченовский университет)» Минздрава России, Москва, Россия

Случаи манифестации тиреотоксикоза на фоне предшествующего вторичного гипотиреоза крайне редки. В статье представлено клиническое наблюдение манифестации диффузного токсического зоба у пациентки с вторичным гипотиреозом, развившимся после радиохирургического лечения акромегалии.
Пациентке 38 лет с акромегалией и эндо-супра-латероселлярной аденомой гипофиза после нерадикального удаления было проведено радиохирургическое лечение остаточной ткани опухоли гипофиза в области кавернозного синуса. Через 14 мес достигнута ремиссия акромегалии, через 24 мес после лучевого лечения развился пангипопитуитаризм (вторичный гипотиреоз, гипокортицизм, гипогонадизм, СТГ-дефицит). Однако через 1,5 года после диагностики пангипопитуитаризма была отмечена манифестация диффузного токсического зоба, что потребовало тиреостатической терапии и радиойодтерапии. Диагностическими критериями вторичного гипотиреоза является низкое содержание тиреоидных гормонов (св. T_4 и св. T_3) при сниженной, нормальной или слегка повышенной концентрации ТТГ. Критерием развития тиреотоксикоза на фоне вторичного гипотиреоза было стойкое повышение концентрации св. T_4 на фоне адекватной терапии левотироксином. Выявление высокой концентрации антител к рецептору ТТГ в описанном случае подтвердило манифестацию диффузного токсического зоба.

Ключевые слова: вторичный гипотиреоз, тиреотоксикоз, акромегалия, диффузный токсический зоб, пангипопитуитаризм, радиохирургическое лечение, клинический случай.

Manifestation of Graves' disease, resulting from radiosurgical treatment of acromegaly, in a patient with panhypopituitarism

© Ludmila I. Astafyeva[1]*, Pavel L. Kalinin[1], Tatyana A. Kienia[2], Valentin V. Fadeyev[2]

[1]N.N. Burdenko national medical research center of neurosurgery, Moscow, Russia;
[2]I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia

Cases of thyrotoxicosis associated with a previous case of secondary hypothyroidism are extremely rare. This article presents a rare clinical case of Graves' disease manifestation in a patient with secondary hypothyroidism after radiosurgical treatment of acromegaly. A 38-year old woman presented with acromegaly and endo-supra-laterosellar pituitary adenoma. After non-radical removal of the pituitary adenoma, radiosurgical treatment of the of the residual tissue of the pituitary tumor in the cavernous sinus area was performed. After 14 months of radiation therapy, the acromegaly was in remission; after 24 months of radiation therapy, panhypopituitarism developed (secondary hypothyroidism, adrenal insufficiency, hypogonadism, and growth hormone deficiency). Furthermore, 1.5 years after the panhypopituitarism was diagnosed, the manifestation of Graves' disease was also noted, requiring thyrostatic and radioactive iodine treatments.
Diagnostic criteria for secondary hypothyroidism are low levels of the thyroid hormones free T_4 and free T_3, with a reduced, normal or slightly elevated level of thyroid stimulating hormone (TSH). The criterion for the development of thyrotoxicosis in the context of the secondary hypothyroidism was the persistent increase in the level of free T_4 despite adequate drug therapy with levothyroxine. In the case report, the patient's diagnosis of Graves' disease was confirmed by the presence of a high level of antibodies to the TSH receptor.

Keywords: secondary hypothyroidism, thyrotoxicosis, acromegaly, Graves' disease, panhypopituitarism, radiosurgical treatment, case report

Background

Thyrotoxicosis and hypothyroidism are two polar types of thyroid dysfunction. It is known that thyrotoxicosis can be naturally replaced by hypothyroidism as a result of the destructive process in the thyroid gland. Cases of thyrotoxicosis manifestation under previous hypothyroidism are much less common; for this to occur, the gland must retain the potential for functional activity, that is, the nature of hypothyroidism must be secondary.

Secondary hypothyroidism is a pathological condition that develops as a result of insufficient production of thyroid-stimulating hormone accompanied by an unchanged thyroid gland. Unlike primary hypothyroidism, its prevalence is same in men and women. According to various sources, its prevalence in the population varies

Copyright © 2019 by the MediaSphere
Licensee: CC BY-NC-ND
doi: 10.14341/probl10026

 DOI: https://doi.org/10.14341/probl10026

from 1:16,000 to 1:100,000 people, depending on age and aetiology [1, 2].

Congenital and acquired forms of secondary hypothyroidism exist. Congenital secondary hypothyroidism, as a rule, is caused by a genetic disorder. Acquired secondary hypothyroidism in paediatric patients is most often associated with surgical and radiation treatment of craniopharyngioma [3, 4]. In the adult population, acquired secondary hypothyroidism is caused by hormonally active and inactive pituitary macroadenomas in >50% of cases. Following radiotherapy of brain tumours, secondary hypothyroidism develops in 65% of cases, and it may occur years after the treatment [5-7].

Thyrotoxicosis syndrome is one of the most common endocrinological disorders. In 80%–90% of cases, this condition is caused by diffuse toxic goitre (DTG). The incidence rate of new DTG cases in different regions across the world varies from 5–7 to 200 per 100,000 of the population per year. The second most common cause of thyrotoxicosis is multinodular toxic goitre, followed by more rare causes, such as solitary toxic adenoma, thyroiditis and thyrotropinoma [8].

We describe a rare clinical case of DTG manifestation in a patient with secondary hypothyroidism that developed after radiosurgical (RS) treatment of acromegaly.

Case description

Patient *B.*, aged 38 years, visited the N.N. Burdenko National Medical Research Center of Neurosurgery (NMRCN) in March 2010 with complaints of headaches, swelling and menstrual irregularities. She began to notice the emergence of headaches, coarsening of facial features, swelling, an increase in shoe volume and irregular menstruation 2 years ago and had considered herself to be ill since then.

Physical, laboratory and instrumental studies

The patient presented with rough facial features, macroglossia and large hands and feet; her BP was 130/85 mmHg. Hormone examination revealed an increase in somatotrophic hormone (STH) levels to 28.2 ng/mL (reference value: <10 ng/mL) and insulin-like growth factor-1 (ILGF-1) levels to 730 ng/mL (97.5–259 ng/mL); the other findings were as follows: prolactin (PRL) level, 494.0 mU/L (40–530 mU/L); TSH level, 1.02 mU/L (0.4–4.0 mU/L) and free T4 level, 16.1 pmol/L (11.5–22.7 pmol/L). Magnetic resonance imaging (MRI) of the pituitary gland revealed a volumetric formation of 2.1×2.3×1.6 mm, which had supra-latero(D)sellar distribution with chiasm compression. On the basis of clinical data and examination results, the patient was diagnosed with the active phase of acromegaly. On 10th March 2010, endoscopic endonasal transsphenoidal removal of the pituitary adenoma was performed. On postoperative day 3, a decrease in the basal STH levels to 1.64 ng/mL, as well as regression of headaches and a decrease in oedema, was noted. During the 3-month follow-up examination at a primary care facility, STH levels were found to be 2.08 ng/mL, but ILGF-1 levels were not determined. Following ultrasound of the thyroid gland, the total thyroid volume was determined to be 15.7 cm^3, with the gland exhibiting a heterogeneous structure, reduced echogenicity and absence of focal pathology. Over the next 2 years, the patient's well-being remained satisfactory, and she did not seek medical help.

In March 2012, the patient visited NMRCN again due to the recurrence of headaches and menstrual irregularities. Upon examination, an increase in ILGF-1 levels to 380 ng/mL (112–295 ng/mL) and the absence of STH level suppression (STH level, 3.1 ng/mL) were observed during oral glucose tolerance test (OGTT). A follow-up MRI of the brain revealed residual tumour tissue in the right cavernous sinus. Due to the lack of acromegaly remission, treatment with long-acting somatostatin analogues was prescribed to the patient; after 3 months of the treatment, ILGF-1 levels were normalised and a regular menstrual cycle was restored.

However, subsequently, when attempting to discontinue the drug, an increase in ILGF-1 levels to 362 ng/mL and the absence of STH level suppression during OGTT (STH level, 2.8 ng/mL) were recorded again. Due to the inability to regularly administer somatostatin analogues, radiation therapy was recommended to the patient. In March 2013, RS treatment was performed using a Cyberknife linear accelerator; the average dose to the target region (PTV = 1.5 cm^3) was 22 Gy using the multiple beam technique (n=94).

According to the follow-up examination performed in May 2014, acromegaly remission was achieved, with the STH level being 0.15 ng/mL and ILGF-1 level being 151 ng/mL (112–295 ng/mL); thyroid hormone and cortisol levels were within the reference range.

Six months later, in November 2014, the patient noted ischomenia. In January 2015, she complained of weight loss, lack of appetite, nausea and joint pain.

A follow-up examination at NMRCN in March 2015 (24 months after the initial RS treatment) revealed a decrease in the levels of free T4 levels to 5.1 pmol/L, cortisol to 30 nmol/L; LH, FSH and estradiol and ILGF-1 to 64 ng/mL (112–259 ng/mL); TSH level was 1.06 mU/L. Panhypopituitarism was diagnosed in the form of secondary hypocorticism, secondary hypothyroidism, secondary hypogonadism and STH deficiency. Treatment with hydrocortisone 15 mg/day and L-thyroxine 100 μg/day was prescribed. During the treatment, the patient's condition markedly improved—the joint pain stopped and weight was normalised.

Subsequently, under dynamic control in April and September 2016, free T4 levels were 10.7 and 11.7 pmol/L, respectively, and the TSH level was 0.12 mU/L (while taking L-thyroxine 100 μg per day). Ultrasound of the thyroid gland performed in February 2016 revealed a gland volume of 7.5 mm^3, as well as normal echogenicity and a

homogeneous structure. In the right lobe, a formation with clear contours and a diameter of 7.8 mm was observed, whereas in the left lobe, a formation with a diameter of 7.9 mm, with small calcifications, was observed.

In November 2016, the patient complained palpitation, sleep disturbance and weight loss amid normal appetite. An examination in a primary care facility revealed an increase in free T4 levels to to 35.2 pmol/L; subsequently, L-thyroxine was withdrawn. However, even 2 months after the discontinuation of the drug (February 2017), free T4 levels remained elevated (38.8 pmol/L).

In May 2017, due to the persistence of complaints, the patient visited NMRCN; her examination revealed an increase in free T4 levels to 54.1 pmol/L, a suppression of TSH levels to <0.01 ng/ml and a thyroid receptor antibody titre of 33.093 U/L (⩽1 U/L). Ultrasound of the thyroid gland revealed a total volume of 19.4 cm^3 (normal volume ⩽18 cm^3), diffuse structure and a nodular formation 9 mm in diameter in the right lobe with CDI; furthermore, a marked increase in blood flow in both lobes was noted. Thus, DTG was diagnosed, and tyrosol therapy (30 mg/day) was prescribed. Drug dose titration was performed with TSH and free T4 levels under control. Given the high titre of AT to the TSH receptor, radioiodine therapy was recommended for the patient; however, the patient refused the proposed treatment and continued taking the drugs. In November 2017, under tyrosol (10 mg/day) therapy, the TSH level was 14.7 mU/L and free T4 level was 2.3 pmol/L; therefore, tyrosol dose was reduced and L-thyroxine (50 μg/day) was incorporated into the therapy. Ultrasound revealed a marked increase (up to 37.4 cm^3) in the thyroid gland volume. In May 2018, under tyrosol (5 mg/day) and L-thyroxine (50 μg/day), the TSH level decreased to 1.35 mU/L and free T4 level increased to 9.35 pmol/L. Ultrasound revealed a decrease in the thyroid gland volume to 19.2 cm^3 (normal volulme ⩽18 cm^3) was registered.

Outcome and follow-up results

In July 2018, radioiodine therapy was performed. After 2 months, the free T4 level was decreased to 7.05 pmol/L and TSH to 1.11 mU/L; consequently, L-thyroxine therapy was resumed.

Discussion

The literature describes several cases of thyrotoxicosis manifestation in cases of previous secondary hypothyroidism developing in patients with tumours of the hypothalamic–pituitary region, including the cases of thyrotoxicosis manifestation after tumour removal or hypophysectomy or due to a haemorrhage in the pituitary gland (postpartum hypopituitarism) [9-12]. The duration between secondary hypothyroidism diagnosis and thyrotoxicosis manifestation varies, ranging from several months to 20 years. Moreover, thyrotoxicosis resulting from DTG develops earlier (within up to 5 years) after the occurrence of secondary hypothyroidism than that occurring in a case of functional autonomy of the thyroid gland.

In 1958, a clinical case of the development of thyrotoxicosis in a woman with Sheehan syndrome was reported. Massive postpartum haemorrhage leading to panhypopituitarism occurred when the patient was 26 years old, and thyrotoxicosis syndrome developed 20 years later. Thyrostatics were prescribed to the patient, following which the woman noted the appearance of menstrual-like secretions, which were three times the normal menstrual secretions; however, hormonal examination showed that gonadotropin levels remained reduced. Later, thyroidectomy was performed due to failure to achieve the compensation of thyrotoxicosis. According to a histological examination, changes in the gland were described as 'severe atrophy ... with small areas of hyperplasia'. Thus, it can be assumed that in this case, there was functional autonomy of the thyroid gland [9].

A year later, another case was reported about the development of thyrotoxicosis in a patient with panhypopituitarism after hypophysectomy for metastasis of breast carcinoma. In this case, the cause of the hyperproduction of hormones was autonomous formation of the thyroid gland [10].

In 1961, Taunton observed the development of DTG in a 20-year-old man. In 1958, 4 years before thyrotoxicosis manifestation, the patient underwent surgical treatment of craniopharyngioma. Even before the surgery, the patient exhibited signs of hypogonadism; postoperatively, testosterone preparations were prescribed to the patient. Additionally, due to the development of diabetes insipidus for 6 months, the patient received vasopressin (Pitressin). Corticosteroids and thyroid hormones were not prescribed. Six months postoperatively, the patient began to notice weight gain, weakness, chilliness and bradycardia. On examination, secondary hypothyroidism was diagnosed, and replacement therapy with a thyroid gland drug (extract) was prescribed. In this case, the patient's condition markedly improved, with no complaints over the next year and a half. In 1961, the patient sought medical help again with the complaints of emotional lability, rapid weight loss and palpitations (heart rate, 140 beats/min). After examination, including thyroid scintigraphy, the patient was diagnosed with DTG, and treatment with thyreostatics was prescribed [11].

Primary thyrotoxicosis manifestation after the removal of an FSH-secreting pituitary tumour has also been reported. In 1995, a 47-year-old man sought medical help due to visual impairment. His examination revealed visual field narrowing, decreased TSH and free T4 levels and increased FSH levels. On MRI, a suprasellar adenoma was visualised. Regarding the presence of secondary hypothyroidism, even before the surgery, L-thyroxine 50 μg/day was prescribed to the patient; this was continued after the removal of the transsphenoidal tumour. Three months postoperatively, the patient noted muscle weakness and tremor of the fingers. On the basis of hormonal examina-

 DOI: https://doi.org/10.14341/probl10026

tion findings, thyrotoxicosis was diagnosed, and L-thyroxine was withdrawn. Two months after the discontinuation of the drug, the patient continued to exhibit the signs of thyrotoxicosis. On thyroid scintigraphy, a diffused increase in drug uptake was detected, and treatment with thiamazole (30 mg/day) was started. After 2 months, the compensation of thyrotoxicosis could be achieved; however, due to the pronounced tendency for an increase in free T4 levels when trying to discontinue the drug, a maintenance dose of thiamazole (2.5 mg/day) was recommended [12].

Another case of thyrotoxicosis in a case of existing secondary hypothyroidism was described in 2009 in a 62-year-old patient after the RS treatment of cabergoline-resistant macroprolactinoma. Hyperproduction of thyroid hormones occurred 8 years after the treatment of the pituitary adenoma and was caused by the presence of an active node in the left lobe of the thyroid gland [13].

Thyroid gland pathology with acromegaly is detected in 43%–76% cases; most often, nodular or multinodular goitre is diagnosed in patients with acromegaly [14]. Compression of the pituitary macroadenoma or its stem can lead to hypopituitarism, including secondary hypothyroidism. In addition, the pituitary tissue may get damaged due to the neurosurgical treatment of acromegaly, resulting in the development of secondary hypothyroidism. However, the highest risk of hypopituitarism (30%–80% of cases) is registered in patients who have undergone radiation treatment for pituitary tumours [15]. The high incidence of hypopituitarism limits the use of this method, which is used only as a third-line therapy after a non-radical neurosurgical intervention and after the ineffectiveness or inaccessibility of drug therapy [16].

Although patients with acromegaly and DTG have been described in the literature, a combination of these pathologies is considered random [14]. Nevertheless, there is evidence that hypersecretion of STH and ILGF-1 can aggravate the course of Graves' disease [17].

In the present case, the patient developed panhypopituitarism (secondary hypothyroidism, hypocorticism and hypogonadism) 2 years after the radiation treatment for acromegaly, and DTG manifestation was noted 1.5 years after the diagnosis of panhypopituitarism.

Diagnostic criteria for secondary hypothyroidism include low levels of thyroid hormones (free T4 and free T3), with reduced, normal or slightly increased TSH levels [18, 19]. For the treatment of secondary hypothyroidism, levothyroxine sodium is used, dose adjustment of which does not depend on TSH levels (as in primary hypothyroidism) but on serum free T4 levels. For the treatment of secondary hypothyroidism, according to most researchers, and in accordance with the recommendations of the American Thyroid Association, free T4 levels should be in the upper half of the reference range [20]. Therefore, early diagnosis of thyrotoxicosis in patients monitored for secondary hypothyroidism is difficult because an increase in free T4 levels is usually associated with an overdose of levothyroxine. However, a persistent increase in free T4 and free T3 levels in patients who have previously received adequate therapy is a criterion for the diagnosis of thyrotoxicosis. Moreover, additional methods are required for confirming the diagnosis, namely, determining the level of antibodies to the TSH receptor and thyroid scintigraphy. The detection of a high level of antibodies to the TSH receptor in the present case confirmed DTG manifestation.

Conclusion

Thyrotoxicosis can manifest alongside secondary hypothyroidism. Considering the difficulties involved in the early diagnosis of thyrotoxicosis with the treatment of secondary hypothyroidism, some researchers have suggested evaluating the level of antibodies to the TSH receptor in patients scheduled for pituitary gland surgery and in those at risk of developing tropic hormone deficiency [12]. However, numerous questions arise, such as whether this investigation is justified, given the rarity of thyrotoxicosis in secondary hypothyroidism. Indeed, determination of the level of antibodies to the TSH receptor will not enable the prediction of thyrotoxicosis risk due to hormonally active thyroid adenoma. Thus, the search for additional markers for the compensation of secondary hypothyroidism (in addition to free T4), which would allow more accurate assessment of the adequacy of the levothyroxine dose and an earlier diagnosis of disorders, will be important in future cases.

Additional information

Foundation source: the article was prepared and published at the personal expense of the authors.

Patient consent. Medical data is published with the written permission of the patient.

Conflict of interest. The authors declare no apparent or potential conflicts of interest related to this publication.

Authors contributions: all authors made a significant contribution to the article preparation, have read and approved the final version before publication.

ЛИТЕРАТУРА | REFERENCES

1. Persani L, Bonomi M. Uncertainties in endocrine substitution therapy for central endocrine insufficiencies: hypothyroidism. *Handb Clin Neurol*. 2014;124:397-405. doi: https://doi.org/10.1016/B978-0-444-59602-4.00027-7
2. Price A. Screening for central hypothyroidism is unjustified. *BMJ*. 2001;322(7289):798-798. doi: https://doi.org/10.1136/bmj.322.7289.798
3. Feldt-Rasmussen U, Klose M. Central hypothyroidism and its role for cardiovascular risk factors in hypopituitary patients. *Endocrine*. 2016;54(1):15-23. doi: https://doi.org/10.1007/s12020-016-1047-x
4. Yamada M, Mori M. Mechanisms related to the pathophysiology and management of central hypothyroidism. *Nat Clin Pract Endocrinol Metab*. 2008;4(12):683-694. doi: https://doi.org/10.1038/ncpendmet0995
5. Grunenwald S, Caron P. Central hypothyroidism in adults: better understanding for better care. *Pituitary*. 2015;18(1):169-175. doi: https://doi.org/10.1007/s11102-014-0559-8
6. Constine LS, Woolf PD, Cann D, et al. Hypothalamic-pituitary dysfunction after radiation for brain tumors. *N Engl J Med*. 1993;328(2):87-94. doi: https://doi.org/10.1056/NEJM199301143280203
7. Snyder PJ, Fowble BF, Schatz NJ, et al. Hypopituitarism following radiation therapy of pituitary adenomas. *Am J Med*. 1986;81(3):457-462. doi: https://doi.org/10.1016/0002-9343(86)90299-8
8. Глушаков Р.И., Козырко Е.В., Соболев И.В., и др. Заболевания щитовидной железы и риск возникновения нетиреоидной патологии. // Казанский медицинский журнал. – 2017. – Т. 98. – №1. – С. 77-84. [Glushakov RI, Kozyrko EV, Sobolev IV, et al. Thyroid diseases and risk of non-thyroidal pathology. *Kazan medical journal*. 2017;98(1):77-84. (In Russ.)] doi: https://doi.org/10.17750/KMJ2017-77
9. Fajans SS. Hyperthyroidism in a patient with postpartum necrosis of the pituitary: case report and implications. *J Clin Endocrinol Metab*. 1958;18(3):271-277. doi: https://doi.org/10.1210/jcem-18-3-271
10. Gurling KJ, Baron DN, Smith EJ. Thyroid adenomas and thyrotoxicosis in patients with hypopituitarism following hypophysectomy. *J Clin Endocrinol Metab*. 1959;19(6):717-725. doi: https://doi.org/10.1210/jcem-19-6-717
11. Taunton OD, Pittman JA, Jr. Hyperthyroidism Following Secondary Hypothyroidism. *J Clin Endocrinol Metab*. 1964;24:934-938. doi: https://doi.org/10.1210/jcem-24-9-934
12. Otsuka F, Ogura T, Hayakawa N, et al. Manifestation of Primary Hyperthyroidism after Pituitary Adenomectomy: A Case Report. *Endocr J*. 1997;44(6):887-893. doi: https://doi.org/10.1507/endocrj.44.887
13. Foppiani L, Ruelle A, Cavazzani P, Del Monte P. Hyperthyroidism unmasked several years after the medical and radiosurgical treatment of an invasive macroprolactinoma inducing hypopituitarism: a case report. *Cases J*. 2009;2:6449. doi: https://doi.org/10.4076/1757-1626-2-6449
14. Wolinski K, Czarnywojtek A, Ruchala M. Risk of thyroid nodular disease and thyroid cancer in patients with acromegaly-meta-analysis and systematic review. *PLoS One*. 2014;9(2):e88787. doi: https://doi.org/10.1371/journal.pone.0088787
15. Gheorghiu ML. Updates in outcomes of stereotactic radiation therapy in acromegaly. *Pituitary*. 2017;20(1):154-168. doi: https://doi.org/10.1007/s11102-016-0783-5
16. Katznelson L, Laws ER, Jr., Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(11):3933-3951. doi: https://doi.org/10.1210/jc.2014-2700
17. Di Cerbo A, Pezzuto F, Di Cerbo A. Growth hormone and insulin-like growth factor 1 affect the severity of Graves' disease. *Endocrinol Diabetes Metab Case Rep*. 2017;2017. doi: https://doi.org/10.1530/EDM-17-0061
18. Alexopoulou O, Beguin C, De Nayer P, Maiter D. Clinical and hormonal characteristics of central hypothyroidism at diagnosis and during follow-up in adult patients. *Eur J Endocrinol*. 2004;150(1):1-8. doi: https://doi.org/10.1530/eje.0.1500001
19. Beck-Peccoz P, Persani L. Variable biological activity of thyroid-stimulating hormone. *Eur J Endocrinol*. 1994;131(4):331-340. doi: https://doi.org/10.1530/eje.0.1310331
20. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. *Thyroid*. 2014;24(12):1670-1751. doi: https://doi.org/10.1089/thy.2014.0028

Рукопись получена: 05.12.2018
Одобрена к публикации: 13.02.2019
Опубликована online: 19.02.2019

ИНФОРМАЦИЯ ОБ АВТОРАХ

*__Астафьева Людмила Игоревна__, д.м.н. [Ludmila I. Astafyeva, MD, PhD]; адрес: ул. 4-я Тверская-Ямская 16, Москва, Россия, 125047 [address: 16, 4th Tverskaya-Yamskaya street, Moscow 125047, Russia]; ORCID: http://orcid.org/0000-0003-4480-1902; eLibrary SPIN: 4209-4723; e-mail: Last@nsi.ru

Калинин Павел Львович, д.м.н. [Pavel L. Kalinin, MD, PhD]; ORCID: http://orcid.org/0000-0001-9333-9473; eLibrary SPIN: 1775-7421; e-mail: PKalinin@nsi.ru

Киеня Татьяна Александровна [Tatyana A. Kienia MD]; ORCID: http://orcid.org/0000-0001-9205-8979; eLibrary SPIN: 9309-0178; e-mail: tatyana2336@yandex.ru

Фадеев Валентин Викторович, д.м.н., профессор, член-корр. РАН [Valentin V. Fadeyev, MD, PhD, Professor]; ORCID: http://orcid.org/0000-0002-2504-7468; eLibrary SPIN: 6825-8417; e-mail: walfad@mail.ru

КАК ЦИТИРОВАТЬ:

Астафьева Л.И., Калинин П.Л., Киеня Т.А., Фадеев В.В. Манифестация диффузного токсического зоба у женщины с пангипопитуитаризмом, развившимся в результате радиохирургического лечения акромегалии. // *Проблемы эндокринологии*. – 2019. – Т. 65. – №2. – С. 101-106. doi: https://doi.org/10.14341/probl10026

TO CITE THIS ARTICLE:

Astafyeva LI, Kalinin PL, Kienia TA, Fadeyev VV. Manifestation of Graves' disease, resulting from radiosurgical treatment of acromegaly, in a patient with panhypopituitarism. *Problems of Endocrinology*. 2019;65(2): 101-106. doi: https://doi.org/10.14341/probl10026