

Case report:

Clinical case of Carpenter syndrome (autoimmune-polyglandular syndrome 2) in the practice of an endocrinologist

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Absrtact:

Presentation of case: patient 36 years old, appealed to complaints about changing the color of the skin, reducing body weight by 10 kg in 2 months, expressed general weakness, lowering blood pressure, reducing sexual desire. **Discussion:** prescribed treatment: insulin therapy (aspart, degludec) day dose 42 OD, levothyroxine 100 mcgr/day, vitamin E, selenium 100 mcgr, chorionic gonadotrophin 1500 OD intramuscularly once per week, monthly courses with the same break. After the therapy, the patient's condition improved. Repeatedly the patient appeared on the review 6 months after treatment. Hyperpigmentation of the skin and natural areas of pigmentation are reduced, there is a stabilization of blood pressure at a level of 120 / 70-110 / 70 mm Hg, reduction of clinical symptoms, achieved target level of glycemia and hormonal blood parameters the target glycemia level was reached (4.6-5.1 mmol / L), glycosylated hemoglobin (8.1%) and hormonal blood parameters (TTG 3.4 mmol / L) cortisol serum 1.7 µg / dl (norm 6.2-19.4 µg / dl), testosterone free 3.4 pg / ml (N 1.7-8.2), total testosterone - 12.28 (N 8.64 - 29 nmol / l), sex steroid binding globulin (CHD) (67 nmol / l, at the rate of 13-71 nmol / l,), testosterone free 8.9 pg / ml (N 8.8 - 42.5 pg / ml). **Conclusions:** Decomposition of adrenal insufficiency (decrease in glucocorticoids as contrinsular hormone) can lead to untypical cours of diabetes with steaolyhipoglicemia in autumn-summer period and normalizabionglycemia glycemia in winter-autumne period. Presents of 2-3 decompensate, endocrine diseases in the same moment suppresses pronounced typical symptomatics each of them precedes with erased or disguised picture.

Keyword: Carpenter syndrome; autoimmune poluglandular syndrome; diabetes mellitus type 1; primary hypogonadism.

*Bangladesh Journal of Medical Science Vol. 18 No. 03 July'19. Page : 646-650
DOI: <https://doi.org/10.3329/bjms.v18i3.41642>*

Presentation of case:

Today, in the practice of endocrinologists, ever more common is the combined endocrine pathology. The most common endocrinopathies include autoimmune polyglandular syndromes (APGS) that are characterized by primary damage to the endocrine glands. Then in most cases, glands' functional deficiency is formed, which is often combined with autoimmune genesis diseases of other organs and

systems¹⁻².

Today the most common is APGS-2, characterized by endocrine glands defeat with the development of primary hypocorticism, autoimmune thyroiditis (AIT), diabetes mellitus type 1 (DM1), and primary hypogonadism. Commonly this endocrine disorder is often accompanied by such manifestations as vitiligo, alopecia, pernicious anemia, scleroderma, myasthenia, celiac disease, atrophy of the optic

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nerves, etc.³.

The variants of the APGS of type 2 include the so-called Carpenter syndrome, which is characterized by autoimmune disease of adrenal (hypocorticism), thyroid gland (lymphocytic thyroiditis) and type 1 diabetes mellitus (DM) in any combination of these symptoms with hypoparathyroidism and hypogonadism.

This syndrome occurs quite rarely - with a frequency of 1.4-4.5 cases per 100 thousand populations and affects mostly women. Carpenter syndrome is believed to be a genetic disorder that is inherited by the autosomal recessive mechanism, which is indicated by the presence of pathology in several generations in one family.

The development mechanism of Carpenter syndrome is associated with autoimmune destructive processes: the immune system produces antibodies and killer cells that destroy healthy body tissues. Polyglandular insufficiency develops as a result of an immunity attack on abnormal HLA antigens, which are present on the membranes of the endocrine glands cells. Another aspect is the lack of suppressor T-lymphocytes that inadequately suppress antibodies synthesized by the body's protective system.

Typically, APGS type 2 manifests itself after 30 years and mostly the first time of onset is the development of primary adrenal insufficiency, which is subsequently joined by AIT and DM type 1 (on average in 7-10 years). In the presence of chronic adrenal insufficiency (CAI) of autoimmune genesis, about half of the patients suffer from other autoimmune diseases.

Below is a case of self-observed Schmidt's syndrome. Patient K., 36 years.

Complaints 20.12. 2016y. - patient 36 years old, appealed to complaints about changing the color of the skin, reducing body weight by 10 kg in 2 months, expressed general weakness, lowering blood pressure, reducing sexual desire.

From the history of the patient it is known that the first visit to the endocrinologist was 8 years ago (2009 y.) (at the time the patient was 28 years old) about complaints of weight gain (BMI 32 kg / m²), memory impairment, sleep disturbances, decrease in physical and mental capacity, swelling on the face

(especially in the morning), fluctuations in blood pressure. The diagnosis was established 8 years ago (2009y.): Autoimmune thyroiditis, hypotrophic form with hypofunction of the thyroid gland. Alimentary-constitutional obesity Ist. Treatment was prescribed: levothyroxine 75 µg / day and metformin 1000 µg 2 times a day.

Since then, the patient did not visit the endocrinologist regularly, dose correction or adjustment levothyroxine was not performed, the level of TSG was not controlled, metformin was received irregularly.

When the patient was 32 years old (2013y.), he re-married (first marriage - no children's). Two years after marriage (6 years after the first visit to the endocrinologist), he began to notice weight loss, general weakness and rapid tiredness, polyuria and polydipsia, decreased sexual desire and erection, decreased testicle size.

The second marriage - no children. At an endocrinologist's examination (15.02.2013), glycemia - 11.2 mmol / l, total cholesterol - 5.0 mmol / L, glued hemoglobin 9.7%, Anti-Islet Cell antibodies (ICA) 1/126 (positive result > 1 / 10), GAD-autoantibodies, IgG 1/68 (positive result > 1/10), C-peptide - not detected, luteinizing hormone (LH) 4.5 mU / ml (N 4-18), follicle stimulating hormone (FSH) 7.54 mU / ml (N 4-25), total testosterone - 6.23 (N 8,64 - 29 nmol/l (15.02.2013)), sex steroid binding globulin (SSBG) (132 нмоль/л, N 13-71 nmol / l, (15.02.2013)), free testosterone 4.1 pg/ml (N 8.8 - 42.5 pg/ml), antibodies to thyroperoxidase 687 IU / ml (N to 32 IU / ml), TSG 15.6 µM / ml (N 0.4-4.2), prolactin 9.7 ng / ml (N 2.6-17.2). Cariotype: 46 XY. Study of ejaculate: V 1.5 ml (N 2-5 ml), morphologically normal sperm 20% (N > 30%), live - 35% (N > 50%), progressive movement 30% (N > 50%).

Radiography of the sellaturcica: (19.02.2013).

Dimensions of the sellaturcica 9mm and 11 mm. (possibly in more detail).

Conclusion: osteoporosis not found.

21.02.2013. Diagnosis: Primary (autoimmune) hypothyroidism, moderate severity, state of decompensation. Secondary hypogonadism. Diabetes mellitus type 1, detected for the first time, state of decompensation.

Prescribed treatment: insulin therapy (aspart,

degludec) day dose 42 OD, levothyroxine 100 mcgr / day, vitamin E, selenium 100 mcgr, chorionic gonadotrophin 1500 OD intramuscularly once per week, monthly courses with the same break.

In 4 months (21.06.2013)), the indicators of spermograms has improved (Investigation of ejaculate: V 1,5 мЛ (N 2-5 мЛ), Morphologically normal sperm 32% (N> 30%), live - 51% (N> 50%), with progressive movement of 50% (N> 50%)., TTG 4.2 μM / ml. Glycated hemoglobin level 8.9%, TSG 4.2 μM / ml. Glycemic level (biforbekfast 4.6-5.3 mmol / l.

It is known from a family history that a year later (2014y.) a child was born.

It is known from anamnesis that in recent years (from 2014 to 2016) he was treated irregularly, the last 3 months did not use levothyroxine, often did not administer short-acting insulin before dinner, due to frequently hypoglycemia. The worst patient feeling in the winter-spring period.

At the moment, the patient is 36 years old (8 years after the first treatment), and is complaining about a change of the skin color, a decrease in body weight for 10 kg in 2 months, a marked general weakness, a decrease in blood pressure and sexual desire.

Data of objective examination: (20.06. 2016 рік) height 180 cm, body weight 69 kg, pubis and face hairy is scanty. BMI 21.29 kg / m². Skin and visible mucous membranes are pure, pale pink, hyperpigmentation of skin and mucous membranes open to the sun, natural folds are hyperpigmented. Pulse 60 per minute, BP 80/50 mm Hg. The activity of the heart is rhythmic, the tones are muffled, pure. Breathing is vesicular. Tongue is wet. Abdomen is soft, painless. The liver protrudes from the edge arc by 1 cm. The edges are rounded, non-pleural while palpation. The spleen is not palpable. No edema.

Data of laboratory and instrumental surveys (20.06-27.06 2016). Indicators of general urine and blood tests are normal. Glycemic profile 3, 2-4, 1-15, 7 ммоль/л, часті гіпоглікемії натще. At the biochemical examination of blood – there is an increase in glycemia to 11.8 mmol, HbA1c - 10.6%. Antibodies to thyroperoxidase level - 334 IU / ml (N to 32 IU / ml), TSG 9.2 (N 0.4-4.2) on the background of receiving 100 μg levothyroxine, serum cortisol 1.7

μg / dl (norm 6.2 -19.4 μg / dl), free testosterone 5,9 pg / ml (N 8,8-42pg/ml,5), total testosterone 7,28 (N 8,64-29 nmol/l), SSBG97 nmol/k (N 13-71 nmol/l). ECG: sinus rhythm, wrong, bradycardia, normal position of the electric axis of the heart, single ventricular extrasystoles.

Consultation of an ophthalmologist: diabetic nonproliferative retinopathy of both eyes.

Consultation of the cardiologist: metabolic cardiomyopathy, sinus bradycardia, single ventricular extrasystole, CI I st.

Consultation of a neurologist: Mixed encephalopathy 1st.

Taking in to account the presence of the following diseases in the patient: Autoimmune thyroiditis, primary hypothyroidism, moderate severity, state of decompensation. Secondary hypogonadism. Primary chronic adrenal insufficiency, moderate severity, state of decompensation. Diabetes mellitus type 1, moderate severity, state of decompensation, diabetic nonproliferative retinopathy of both eyes. Metabolic cardiomyopathy, sinus bradycardia, CI 1 st. Mixed encephalopathy of 1 degree, diagnosis was established: Schmidt's syndrome.

Prescribed treatment: hypoglycemic food with restriction of easily digestible carbohydrates, hydrocortisone 20 mg / day, cortinef 0.5 mg per day, insulin therapy: trisiba (deglyudec) 22:00 - 22 units per pc; Novarapid (aspart) before breakfast 6 OD, before dinner 6 OD, before supper 6 OD, tiocetam 10.0 U intravenously 1 time a day, levothyroxine 125 mg / day, cefazel 100 mg twice daily, testosterone -proviron (mesterolol) 75 mg/d.

After the therapy, the patient's condition improved. Repeatedly the patient appeared on the review 6 months after treatment (20.12.2016)

The patient's condition has improved on the background of the therapy. Hyperpigmentation of the skin and natural areas of pigmentation are reduced, there is a stabilization of blood pressure at a level of 120 / 70-110 / 70 mm Hg, reduction of clinical symptoms, achieved target level of glycemia and hormonal blood parameters

the target glycemia level was reached (4.6-5.1 mmol / L), glycosylated hemoglobin (8.1%) and hormonal blood parameters (TTG 3.4 mmol / L) cortisol serum 1.7 μg / dl (norm 6.2-19.4 μg

/ dl), testosterone free 3.4 pg / ml (N 1.7-8.2), total testosterone - 12.28 (N 8.64 - 29 nmol / l), sex steroid binding globulin (SHBG) (67 nmol / l, at the rate of 13-71 nmol / l,), testosterone free 8.9 pg / ml (N 8.8 - 42.5 pg / ml)

Discussion

Specific parameters of testosterone levels physiological lowering in the blood vary considerably, depending on age, ethnicity, and other factors. Usually it starts at the age of 45-50 years (rarely less than 30 years) and is quite slow, namely 1-1.5% per year⁴. As for the free fraction of testosterone, that is, the physiologically active fraction, it is reduced twice as fast, ahead of an increase in the level of SHBG, which is 1.3% per year.

The medical and social significance of hypogonadism is determined by the fact that it not only negatively affects the standard of living, but is also a recognized risk factor for death, primarily of cardiovascular disease³. The development and progression of hypogonadism is influenced by various concomitant diseases, among which the leading role belongs to obesity. Literary sources indicate that a healthy lifestyle, prevention, and treatment of concomitant diseases can slow down the decreasing of testosterone levels². The direct relation to the disruption of metabolism with hypogonadism, especially the increase in fatty matter up to obesity, has an increased conversion of testosterone into estradiol, and androstenediol - in estrone. Estrogens stimulate the synthesis of SHBG in the liver, increasing its content in systemic circulation and binding of testosterone. Hence - a decrease in the active fraction of free testosterone is observed, and as a consequence - an increase in androgen deficiency.

According to European studies, obesity in men may be due not only to the lowering of testosterone but also to its cause. That is, obesity provokes testosterone deficiency, and testosterone deficiency leads to obesity, forming a closed circle that can only be discontinued by substituting testosterone. There is evidence that pathospermia develops in patients with hypofunction of the thyroid gland on the background of testicular insufficiency. In this case, in the majority of patients, the hypoandrogenic status is formed by the type of normal anadotropic hypogonadism, when

the levels of LH and FSH are within the normal range. Most likely, the violation of the fertile ability of sperm is due to the development of oxidative stress in the testicles⁴. It is the factor that explains the reason for the appointment of antioxidants.

It is known that hypothyroidism decreases the activity of enzymes, which are responsible for the synthesis of testosterone in the testicles³. Probably the elimination of thyroid hormones deficiency restores the biosynthesis of testosterone in the testicles. Consequently, the main factor contributing to the growth of testosterone in infertile men with hypofunction of the thyroid gland is primarily the normalization of the thyroid status. Erectile dysfunction is a result of reducing the activating effect of testosterone on all levels of its regulation - the cerebral cortex, the middle brain, penis smooth muscle, vascular endothelium. Sexual disorders are deepened by depression, sleep disturbance, memory loss, cognitive impairment, irritability. These psycho-physiological disorders are accompanied by increased fatigue, reduced physical and mental performance, a number of vegetative-vascular disorders, fluctuations of blood pressure, hands tremor, and increased sweating.

The presence of vitiligo in patients may serve as an additional marker for the presence of concomitant diseases of the autoimmune genes.

In the case of diagnosing one of the autoimmune diseases, the clinician should be careful about the spread of autoimmune damage to other endocrine glands, which may develop not simultaneously, but for a long time.

In case of APGS suspicion, it is necessary to determine immediately in patients levels of antibodies to thyroperoxidase, antibodies to thyroglobulin, antibodies to beta-cells of the pancreas and conduct screening tests for the detection of allergies. In the treatment of APGS (in particular Schmidt's syndrome), it is necessary to carry out a complex continuous treatment of hypothyroidism, chronic adrenal insufficiency, and type 1 diabetes until complete compensation is obtained.

Conclusions

1. In course diagnostic one of autoimmune diseases doctor must have alertness about distribute

autoimmune damage endocrine glands, which can develop not at the moment but during long time.

2. Decompensation of adrenal insufficiency (decrease in glucocorticoids as contrinsular hormone) Can lead to untypical course of diabetes with steaolyhipoglicemia in autumnne-summer period and normalizabionglycemia in winter-autumne period.

3. Predisposition to hypoglicemia at high level glycosylated hemoglobin must setting doctor in diagnostic search about adrenal insufficiency.

4. Presents of 2-3 decompensatee, endocrine diseases in the same moment suppresses pronounced typical symptomatics each of them proceeds with erased or disguised picture.

Ethical approval: This research proposal was accepted by the commission from bioethics Ternopil

State Medical University. There are no violations of moral and ethical norms during preparing this research.

Ukraine.

Conflict of interest: none declared.

Acknowledgment: weacknowledgeandthankallpeoplewhodicatedtheirtimeandparticipatedinthisrese arch.

Author's contribution:

Data gathering and idea owner of this study – Pasiechko N.

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References:

1. Neuteld M. Polyglandular autoimmune diseases Pinchera A. Doniach D . ,Fenzi G.F. , Baschieri L. Symposium on Autoimmune Aspects of Endocrine Disorders.-New York.Academic press , 1980- p357-365
2. Bensing S. Hulting A. Husebye E. Kampe O. Lovas K. Management of endocrine disease: epidemiology, quality of life and complications of primarri adrenal insufficiency a review

Europen journal of Endocrinology- 2016 – Vol 175 (3) .- P. 107-116

3. Prylutska A.S ,Prylutska O.A. , Strelchenko E.S. , Autoimmune poliendocrine syndrome International magazine -2014 - №4(60).- p.13-20
4. Cernikova V. , Soloviuk o. , Soloviuk o. Autoimmune polyglandral syndrome type 2 (clincal case of Carpenter syndrome) International endocrine magazine 2017 №(13) – P 124-126