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ДРАМАТИЧЕСКИЙ ИСХОД ПОЗДНЕЙ ДИАГНОСТИКИ ХРОНИЧЕСКОГО АУТОИММУННОГО ТИРЕОИДИТА С ПЕРВИЧНЫМ ГИПОТИРЕОЗОМ ТЯЖЕЛОЙ СТЕПЕНИ

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The Dramatic Outcome of the Late Diagnosis of the Chronic Autoimmune Thyroiditis with the Severe Primary Hypothyroidism

Резюме

Статья посвящена разбору клинического случая поздней диагностики тяжелого гипотиреоза. Приведен обзор так называемых «клинических масок» гипотиреоза, затрудняющих диагностику. Акцентируется внимание на необходимости своевременного включения в план комплексного обследования коморбидных пациентов анализов уровня тиреотропного гормона гипофиза и гормонов щитовидной железы. Показано, что несвоевременное начало заместительной терапии гипотиреоза ассоциировано с плохим прогнозом.

Ключевые слова: *гипотиреоз, хронический аутоиммунный тиреоидит, тиреотропный гормон, полисерозит, кишечная непроходимость*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

The article is devoted to the analysis of a clinical case of the severe hypothyroidism. A review of the "clinical masks" of the hypothyroidism is presented. The examination of the polymorbid patients should include the level of thyroid-stimulating hormone and thyroid hormones. The untimely initiation of substitution therapy is associated with a poor prognosis, and the early start of the treatment is a guarantee of saving the life of a patient with severe hypothyroidism.

Key words: *hypothyroidism, chronic autoimmune thyroiditis, thyroid-stimulating hormone, polyserositis, intestinal obstruction*

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NYHA: New York Heart Association: SpO_2: blood oxygen; BP: blood pressure; HT: Hashimoto's thyroiditis; TPO-AB: thyroid peroxidase antibody; posterior LV wall: left ventricle posterior wall; IHD: ischemic heart disease; APV: artificial pulmonary ventilation; LV: left ventricle; MSCT: multispiral computed tomography; ACS: acute coronary syndrome; ACE: acute cerebrovascular event; GFR: glomerular filtration rate; T3: triiodothyronine; T4: thyroxine; TTH: thyrotropic hormone; TRH: thyrotropin-releasing hormone; US examination: ultrasound examination; EF: ejection fraction; CKD: chronic kidney disease; CHF: chronic heart failure; RR: respiratory rate; HR: heart rate; ECG: electrocardiogram; CEA: cardiac electrical axis

Hypothyroidism is a clinical syndrome caused by persistent thyroid hormone depression, resulting in various disorders in all body organs and systems [1].

A majority of scientific papers dedicated to this topic in the 20th century start with a historical perspective that the term was introduced by William Withey Gull, an English Surgeon in Ordinary to the King, who in 1873 described myxedema in thyroid gland atrophy; he proposed the term "myxedema" in 1878. William Miller Ord [2].

According to W. Gull, hypothyroidism was the lack of substance secretion from thyroid gland [3]. These substances were not yet called hormones. The chemical formula of thyroxine (T4) was discovered approximately 50 years later, and that of triiodothyronine (T3) — approximately 80 years later. Accurate determination of thyroid hormones in patients' blood was possible only 100 years later [2].

In 1882–1883, surgeons E.T. Kocher and J.L. Reverdin found the relationship between thyroidectomy and a set of symptoms of hypothyroidism. Later, attempts were made to treat post-surgery myxedema with thyroid tissue transplantation (M. Schiff, 1884) and ovine thyroid tissue extract (G.R. Murray, 1891). Thus, hypothyroidism can be seen as the first endocrine disorder, where replacement therapy was used.

Taking into account that hypothyroidism has been studied for over one and a half centuries, the publications and studies dedicated to this topic are abundant. Medicinal products to treat this condition have improved: starting from the use of bovine thyroid extract and up to available lactose-free and encapsulated synthetic levothyroxine gels. Thyroid associations publish recommendations on the management of various types of hypothyroidism almost annually [4].

Globally, over 665 million people have hypothyroidism and other thyroid gland disorders; 1.5 billion people are at risk of developing iodine deficiency. The annual increase in the number of thyroid disorders makes 5 % [1].

According to the World Health Organisation (WHO), hypothyroidism takes the second place in terms of the incidence among endocrine disorders (after diabetes mellitus). According to various data, in Russia, 58.8 % of patients with thyroid gland pathologies have hyperthyroidism and 35.3 % have hypothyroidism [5]. When comparing these data with foreign statistics, it becomes clear that the incidence of manifest hypothyroidism in the United States of America (USA) varies from 0–3 % to 3–7 %, in Europe — from 0–2 % to 3–5 %, depending on the method used [6].

According to metaanalyses conducted in ten European countries, the incidence of undiagnosed hypothyroidism, including both manifest and mild cases, is approximately 5 %. The differences in iodine status affect the incidence of hypothyroidism. Hypothyroidism is more frequent in women, patients of over 65 years old, in patients with autoimmune disorders (for instance, type 1 diabetes mellitus, autoimmune atrophic gastritis and gluten-sensitive enteropathy, and can be accompany numerous autoimmune diseases. People with Down's syndrome or Turner syndrome are at a higher risk of hypothyroidism.

In terms of pathogenesis, hypothyroidism can be primary, secondary, and tertiary. Secondary and tertiary hypothyroidism is often called "central (pituitary-hypothalamic) hypothyroidism"; they are a result of thyrotropic hormone (TTH) and thyrotropin-releasing hormone (TRH) deficiency. In a majority of cases, central hypothyroidism is associated with deficiency of other tropic hormones of the anterior pituitary gland; it develops in inflammatory, traumatic or destructive disorders affecting the pituitary-hypothalamic area (necrosis, tumour, cysts, hemorrhage, surgeries, radiation exposure) [1]. Central hypothyroidism is rare, accounting for no more than 1 % of all hypothyroidism cases. This condition equally affects men and women; the incidence in the population varies from 1:16,000 to 1:100,000 people depending on age and ethiology [7].

Primary hypothyroidism has high clinical significance and incidence; the most common causes are Hashimoto's thyroiditis, thyroid gland surgeries, treatment

with radioactive iodine (I-131) or radiation therapy of neck tumours [5]. Usually these conditions cause persistent irreversible deficit of thyroid hormones. For some decades now, wide use of some drugs, specifically of phenytoin, glucocorticosteroids, antibiotics, barbituates, diuretics, amiodarone, led to a significant increase in the incidence of drug hypothyroidism which sometimes requires therapy discontinuation [8].

Primary hypothyroidism is one of the most frequent endocrine disorders. According to a large population study, The Third National Health and Nutrition Examination Survey (NHANES-III), the incidence of primary hypothyroidism was 4.6 % of the population. The thyroid peroxidase antibody (TPO-AB) carrier status is observed in 10 % of women and depends on the ethnic composition of the population [7].

Usually hypothyroidism is permanent; however, in a number of thyroid gland diseases it can be transient [9]. In some disorders (subacute, postpartum, cytokine-induced thyroiditis) or in case of exposure to some drugs (excessive doses of iodine, thyrostatics), transient hypothyroidism can develop which resolves along with the natural course of the disease, or once the exposure from the trigger stops (e.g., after thyrostatic drug discontinuation) [10].

There is also peripheral hypothyroidism which is caused by tissue and organ resistance to thyroid hormones or thyroid hormone antibodies. In real life, this condition is extremely rare [1].

In terms of severity, hypothyroidism can be

- Asymptomatic (or latent) — clinical symptoms can be absent or can be very mild; blood TTH levels are high against the background of normal thyroid hormone levels. This conditions is diagnosed in 10–20 % of the population. Approximately 5 % of asymptomatic hypothyroidism cases are known to progress to manifest hypothyroidism annually, and within 4–8 years this conditions affects 20–50 % of patients.
- Manifest hypothyroidism — this condition is associated with clinical manifestations, high TTH levels and low blood thyroid hormone levels.
- Severe (long-lasting) hypothyroidism progressing to hypothyreoid (myxedema) coma [1].

Myxedema coma is caused by the absence of any hypothyroidism therapy or an inadequate replacement therapy doses. Hypothyreoid coma is characterised by progressing brachycardia and arterial hypotension, hypothermia, urinary retention, bowel obstruction. Cerebral blood flow slows down, and hypercapnia develops, resulting in impaired consciousness, catatonia, and coma. Even with timely treatment, hypothyreoid coma is associated with high mortality rates (50–80 %) [1].

In a prospective study conducted by Cesar Milstein Clinic (Buenos Aires, Argentina), it was demonstrated that manifest hypothyroidism during hospitalisation is reliable associated with high mortality rates [11].

Hormone tests (TTH and free T4 levels) are enough to diagnose hypothyroidism and identify an adequate replacement therapy. Other examination methods (thyroid gland ultrasound, elastography, isotopic scintigraphy, thyroid tissue antibodies, etc.) help in identifying the cause of hypothyroidism [1].

On the one hand, hypothyroidism diagnostics can seem very simple and readily available, but on the other hand, very often hypothyroidism is concealed by numerous somatic, gynaecologic and other endocrine disorders. This is why early diagnostics of this multifaced disease is difficult [5].

Clinical manifestations of hypothyroidism are individual for each and every patient. One patient may have no hypothyroidism manifestations at all, while another person with just a slight increase in TTH level will have numerous complaints [12]. It is also worth mentioning that there is no strict correlation between clinical manifestations of hypothyroidism and TTH and thyroxine levels; thus, diagnostic search becomes even longer.

The variety of signs and symptoms of manifest hypothyroidism is due to a wide spectrum of thyroid hormone impact on cell metabolism. In addition to energy metabolism, they regulate carbohydrate, fat and protein metabolism, thus affecting all organs and systems. Very often the lack of specific clinical manifestations of hypothyroidism delays diagnosis. For a long time patients may be followed up by various medical professionals for a syndrome that has manifestations and is diagnosed earlier than any other syndromes. As a rule, therapy of such cases is inefficient, since the management is aimed towards covering conditions and not hypothyroidism itself [1].

Early symptoms of thyroid insufficiency are nonspecific, in a number of cases the disease is asymptomatic (it is true specifically for subclinic hypothyroidism). Early signs of this condition include chills, fatigue, atony, clonus, constipations, excessive menstrual bleeding [1].

Currently, there are 11 known groups of covering conditions of hypothyroidism:

- Therapeutic: main symptoms are arterial hypertension or hypotension (less frequent); cardiac insufficiency events due to impaired miocardial contractility; dyslipidemia; arthropathy; polyserositis; myocarditis; pyelonephritis; hepatitis; biliary dyskinesia, and bowel hypomobility.
- Haematological: anemias (iron deficiency, normochromal and hypochromic anemia).
- Surgical: increased lithogenicity of bile with cholelithiasis; bowel obstruction.

- Gynaecologic: opsomenorrhea; excessive menstrual bleeding; metrorrhagia; amenorrhea.
- Endocrine: obesity; erectile dysfunction; decreased interest; delayed puberty.
- Neurological: myopathy; polyneuropathy; encephalopathy.
- Dermatological: alopecia; pilosis.
- Psychiatric: depression; myxoedema delirium; drowsiness; agrypnia.
- Otorhinolaryngologic: hardness of hearing; sinusitis; laryngitis.
- Gastroenterological: anorexia; kolitis; cholecystitis.
- Nephrological: pyelonephritis.

Diagnostics of hypothyroidism in patients of over 60 years old can be quite challenging, and the incidence of hypothyroidism in this group is 6–12 %. This is primarily due to a large number and severity of comorbidities in this group of patients, the need to adjust such conditions, and the overall psychosomatic status of patients [5].

The clinical features of hypothyroidism in elderly patients include:

- Slow and gradual development of symptoms unnoted by the patient and persons around him/her.
- Various manifestations of hypothyroidism involving almost any organ and system that prolong diagnostic search and delay drug management initiation play a role in development of complications.

Elderly people with gradual hypothyroidism progression are followed up by various medical professionals who have to deal with numerous symptoms: hoarseness, loss of hearing, stiff muscles, hand numbness and weakness, unsteady gait, dry skin, anemia, constipation. These common and non-specific symptoms are frequently seen as signs of ageing [5].

Let's discuss a case study of hypothyroidism that was diagnosed at a late stage and was associated with bowel obstruction, cardiac failure, pyelonephritis, anemia, hypothyreoid coma, and, eventually, death.

Case study

Patient Yu., 60 years old, was admitted to the therapeutics department of a multi-profile clinical hospital in September 2020 and was complaining of stabbing abdominal pain with unknown localisation, diarrhea for 4 days before hospitalisation, nausea, lack of appetite, pin sensation in her chest, and marked general weakness.

History taking was hardly possible due to cognitive deterioration. According to the patient, her highest blood pressure (BP) was 140/100 mm Hg. From 2010 the patient suffered from perceptive hearing loss, chronic pyelonephritis. From September 2018 — chronic hypochromic anemia (Hb: 96 g/L), diagnostic cancer search was undertaken. In 2019, the patient was hospitalised with tetraparesis, suspected acute cerebrovascular event (ACE);

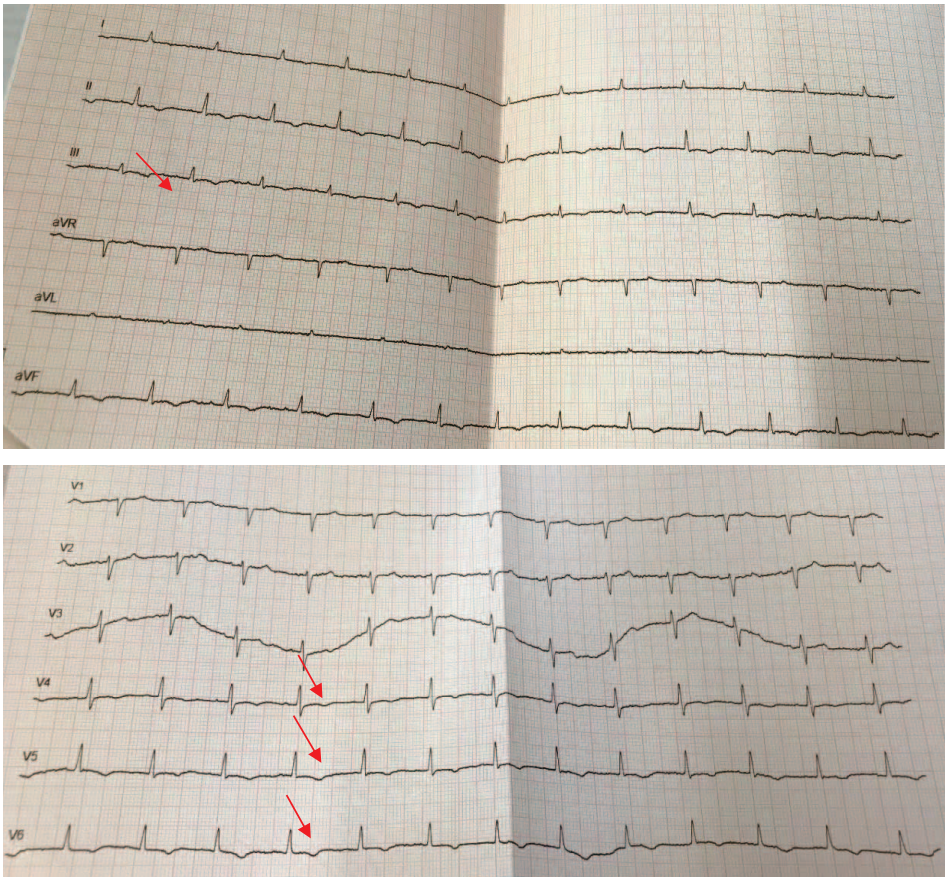


Figure. *1. Electrocardiogram of the patient with hypothyroidism: sinus rhythm, heart rate 80 per minute, normal heart axis, negative T waves in the apical, lateral and inferior walls of the left ventricle. The arrows indicate negative T waves in the respective leads*

Table 1. Hystory of symptoms of hypothyroidism, hiding behind various "masks"

Anamnesis of the disease of the patient Y.

2010	September 2018	September-November 2019	December 2019 February 2020	March 2020	September 2020
Bilateral sensorineural hearing loss, Chronic pyelonephritis	Severe general weakness, increased fatigue, hypochromic anemia (hemoglobin — 96 g/L)	Clinic of tetraparesis, acute dynamic intestinal obstruction (surgical treatment), anemia (hemoglobin 93 g/L)	The increase in edema of the lower extremities, an increase in the abdomen in size	Clinic of adhesive intestinal obstruction (conservative treatment), anemia (hemoglobin 80 g/L)	***Dynamic intestinal obstruction, stool retention, anasarca***

the diagnosis was not confirmed. During hospitalisation, the patient developed symptoms of acute dynamic bowel obstruction; laparotomy was required. The post-surgery period was complicated with staphylomycosis. After discharge from the hospital, the patient had gradually progressing lower limb edema, and her abdomen increased in size. In March 2020, the patient was re-admitted to the surgery department for the symptoms of adhesive bowel obstruction. After conservative treatment, the patient was discharged with improvements. According to the patient, she's feeling unwell due to a psychological stress, following wich she noticed stool retention for 5 days. The patient took laxatives and had loose stool for 4 days; her weakness progressed, and stabbing pain appeared in her abdomen and left chest. The electrocardiogram (Fig. 1) recorded by the ambulance team showed negative T waves in leads II, III, aVF, V4-V6. The patient was hospitalised to the cardiac intensive care unit with suspected acute coronary syndrome (ACS). Upon admission, the patient did not have any anginal pain; two troponin tests were negative; ECG did not show any negative dynamics. An abdomen and retroperitoneal space ultrasound (US) showed diffusive changes in liver and pancreas, free fluid in all sections of abdomen; in morison's pouch, the layer was up to 8 mm; kidneys: right kidney — 86*45 mm, left kidney — 99*44 mm; normal parenchymal echogenicity; the renal collecting system is indurated, not dilated; parenchymatous tissue is 15 mm thick. For diagnostic search and further management, the patient was transferred to the therapeutics department (Table 1).

Gynecologic history: two uncomplicated pregnancies and two deliveries. The patient denies smoking, alcohol consumption, narcotic and psychotropic substances.

Physical examination upon admission to the therapeutics department

Acute patient. Clear consciousness. Active position. Meningeal signs are negative. No focal neurologic symptoms. Slow speech. The patient is drowsy.

The skin has icteric discoloration, warm, not dry. Alopecia. Generalized edema of subcutaneous fat, including anterior abdominal wall, face, eyelids. Body temperature: 36.4^{0}C. The midline of anterior abdominal wall with a laparotomy scar, which healed with secondary adhesion.

Mixed shortness of breath was observed. The chest is evenly engaged in respiration. Percussion sound is clear and comes from lungs. Respiration is harsh, weak in inferolateral sections. No stridor. Respiratory rate (RR): 20/minute.

Region of the heart: unremarkable. Cardiac borders: unremarkable. The pulse is rhythmic, 66 bpm, not tense. The cardiac rhythm is regular. Muffled heart tones. No heart murmurs. Blood pressure: 90/60 mm Hg on both arms. Saturation (Sp O_2) — 94 %.

The tongue is pink, moist, with white coat. The abdomen is symmetric, enlarged due to non-tense ascites, moderately inflated, soft, sensitive to palpation in all sections. On palpation, liver is within the costal arch. Spleen is not palpable. Gall bladder is not palpable. Peristalsis is weak. Peritoneal signs are negative.

Kidney punch is negative on both sides. Urination is normal.

Clinical blood analysis: hyperskeocytosis up to 23.59 × 10^9/L, myelocytes: 3 %, stabs: 17 %, segmented cells: 71 %; lymphocyte depletion: 4 %.

Blood biochemistry shows hyperglycemia up to 7.1 mmol/L; hypercholesterolemia up to 6.0 mmol/L;

urea up to 9.7 mmol/L: ALT 23 U/L; AST 38 U/L; LDH 446 U/L; hyperbilirubinemia: total bilirubin up to 33.6 μmol/L, direct bilirubin 10 μmol/L; creatine phosphokinase increase up to 736 U/L; MB fraction 53.8 U/L, brain natriuretic peptide (BNP) 5 pg/mL, ALP 63 EU/L, total protein 67 g/L, albumin 36 g/L, potassium 4.37 mmol/L, hyponatremia up to 117 mmol/L; hypochloremia up to 93 mmol/L, C-reactive protein 5.86 mg/L, procalcitonin 1.8 ng/mL with dynamic reduction to 0.48 ng/mL, Fe reduction to 5.4 mmol/L.

Urinalysis: proteinuria 1 g/L, leukocyturia 92 per HPF, bacteriuria 18,623 (CFU/mL). Nechiporenko's test demonstrated an increase in WBC 13,500/mL, casts 9000/mL.

Echocardiography revealed enduration of aortic walls, aortal and mitral cusps. Cardiac chambers are not enlarged. Left ventricle (LV) myocardial hypertrophy. No regional contractility abnormalities were found. LV ejection fraction (Simpson's EF) is 56 %. Stage 1 mitral regurgitation, stage 1 tricuspid regurgitation. Mild cardiac dropsy — pericardial layer separation is up to 4 mm behind posterior LV wall (Fig. 2).

Chest CT native-phase images do not show any focal or infiltrative changes. Signs of dropsy of chest, abdominal dropsy.

Abdominal contrast CT: signs of colitis, abdominal dropsy, bilateral dropsy of chest (right: up to 500 cm^3; left: up to 250 cm^3), signs of lung parenchyma compression in the right lower lobe. Comparison with CT scans taken seven months ago shows negative dynamics: generalized edema, progressing colon edema. Significant diffusive colon wall edema is marked with arrows (Figure 3).

Preliminary diagnosis:

Tubulointerstitial bacterial inflammatory kidney disease. Toxic syndrome. Systemic inflammatory response syndrome. Chronic kidney disease C3a (CKD-EPI e-GFR: 51.46 mL/min/1.73 m^2), A2. Chronic moderate hypochromic anemia. Stage 3 arterial hypertension, uncontrolled AH. Edematic-ascitic syndrome: bilateral dropsy of chest, cardiac dropsy, abdominal dropsy. Fluid and electrolyte disorder syndrome/ Dyslipidemia. Extremely high cardiovascular risk. Chronic cerebral ischemia. Perceptive hearing loss. NAFLD: non-alcoholic fatty liver disease with moderate laboratory activity. Peritoneal commissures. Chronic colitis, acute stage.

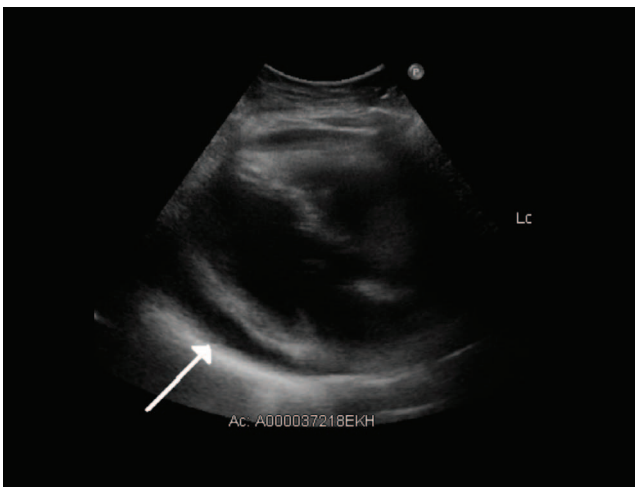


Figure 2. *Echocardiogramm of the patient with hypothyroidism. Fluid (indicated by an arrow) in the pericardial cavity, divergence of the pericardial sheets along the posterior wall up to 4 mm*

Taking into account alopecia, edema syndrome with normal systolic LV fraction and normal BNP, slow speech and movements, thyroid gland pathology with deficiency was suspected. Hypothyroidism was confirmed with laboratory tests: TTH 32.6 μU/mL; free T4 < 1 pmol/L; total T3 < 40 nmol/L; anti-TPO < 10 U/mL. Thyroid gland ultrasound revealed significantly reduced gland size which was 1.6 cm^3 (normal values for women: 4.0–18.0 cm^3). Gland echogenicity and structure, blood supply, regional lymph nodes are normal.

During hospitalisation, the patient underwent the following complex treatment:

- T. Levothyroxini 100 μg once daily per os as hormone replacement therapy, taking into account hypothyroidism severity established by laboratory tests and instrumental assessments.
- S. Cefoperazoni + Sulbactami 1 g + 1 g twice daily by intravenous infusion for an acute episode of chronic pyelonephritis.
- S. Furosemidi 40 mg 2 tablets once daily, and T. Spironolactoni 50 mg daily per os for edematic-ascitic syndrome.
- T. Omeprazoli 20 mg 1 capsule twice daily per os for gastric protection.
- S. Natrii chloridi 0.9 % 500 mL; S. Trisoli 400.0 mL once daily by intravenous infusion for water-electrolyte disorder correction.
- S. Metoclopramidi 10 mg 2 ml IM as as pro-kinetic.
- S. Platiphyllini 4 mg 2 mL IM as an antispastic drug.

Despite the therapy, on hospitalisation day 12 the patient experienced circulatory arrest. ECG monitor readings: electromechanical dissociation with HR 8–10/minute with subsequent asystole; resuscitation procedure was ineffective, and the patient was pronounced dead.

Postmortem: underlying disease — primary hypothyroidism, probably caused by Hashimoto's thyroiditis (antibody-free variant), newly diagnosed.

Complications: internal organs dystrophia. Generalized edema: cardiac dropsy (100 mL), bilateral dropsy of chest (right: 1500 mL, left: 800 mL); abdominal dropsy (2000 mL); edema of extremities, face, trunk, lungs, brain. Focal bronchial pneumonia in lower lobe of the left lung.

Anemia (Hb: 109 g/L). Proteinuria (urine protein: 1.0 g/L). Chronic fibrinous colitis, acute phase.

Comborbidities: arterial hypertension (heart mass: 320 g, LV myocardium thickness: 1.7 cm). Atherosclerosis of aorta (stage 4, 2nd degree). Atherosclerotic cardiosclerosis, atherosclerosis of aorta and coronary arteries (stage 3, 2nd degree, stenosis up to 25 %). Sequellae of acute cerebrovascular event: a brown cyst in left basal nuclei, cerebral atherosclerotic vascular disease (stage 1, 2nd degree). Dense abdominal fibrous adhesions. Laparotomy for acute dynamic bowel obstruction in 2019.

It is interesting that during postmortem examination, when the organs were removed from the body, thyroid gland was not found either by visual inspection

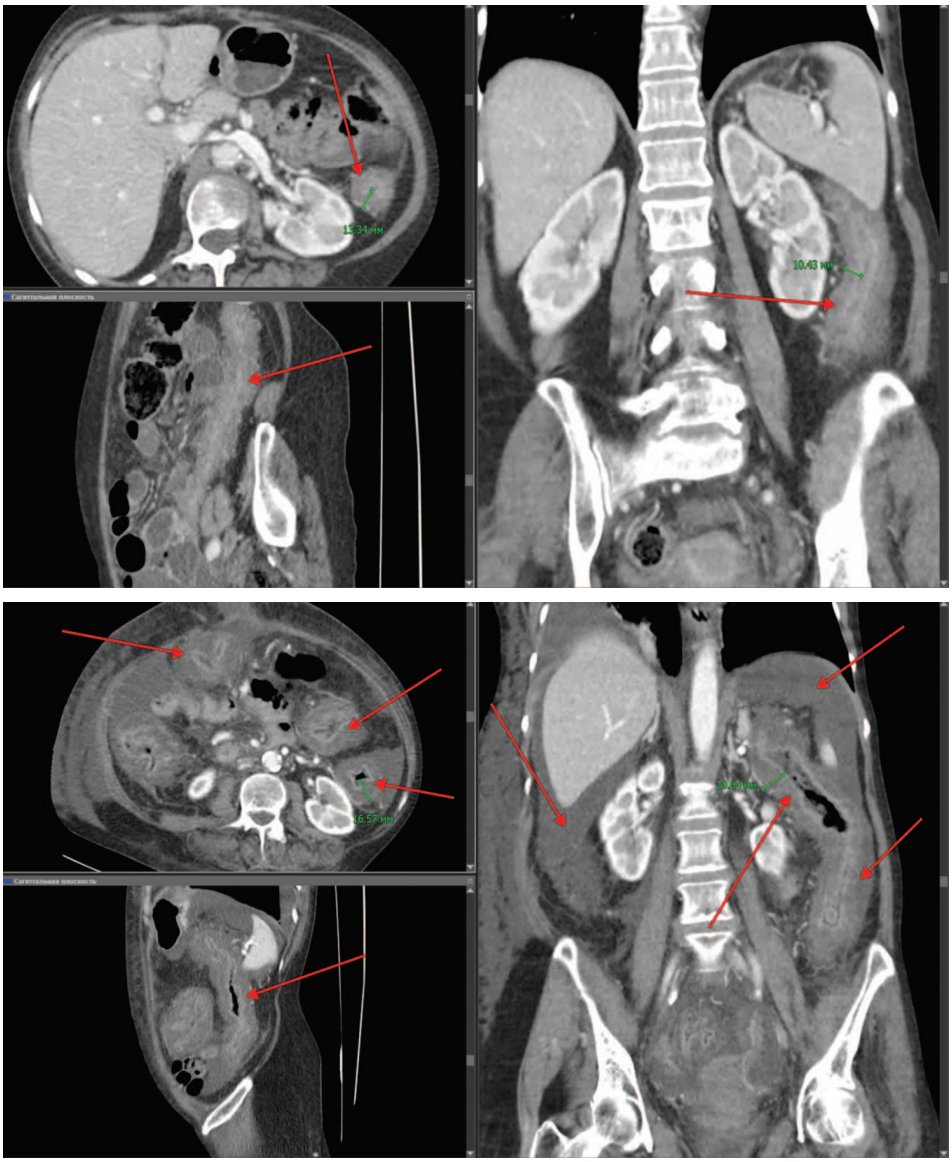
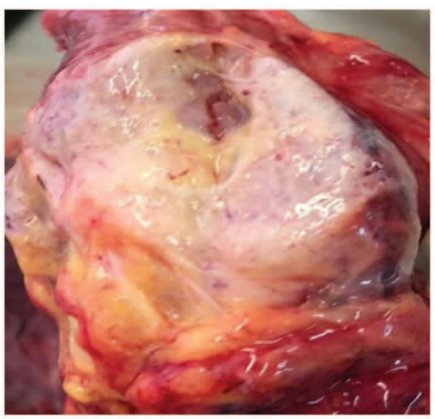
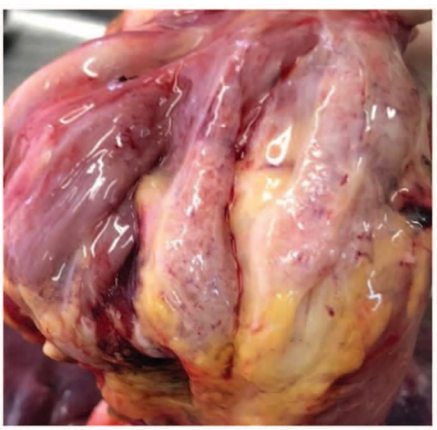


Figure 3. *Multislice computed tomography (MSCT): edema of the colon wall throughout (indicated by arrows)*



а) Правая доля щитовидной железы



б) Левая доля щитовидной железы

Figure 4. *Atrophy of the right and left lobe of the thyroid gland. macropreparation. Magnification 1×1000*

or on palpation. A series of sections in the anatomic localisation area of the right lobe showed a pale pink band (3.2×1.0×0.7 cm) (Figure 4a); a similar band was observed in the anatomic localisation area of the left lobe (3.9×0.7×0.9 cm) (Figure 4b); a macroscopic examination did not visualise the isthmus of gland.

Histologic examination of the right lobe demonstrated fibrous hyalinized connective tissue with marked edema, focal lymphocytic infiltration and single plasma cells; isolated follicles from large Hurthle cells with oxyphilic cytoplasm and central basophilic nucleus, numerous thin-wall full-blooded vessels (Figure 5).

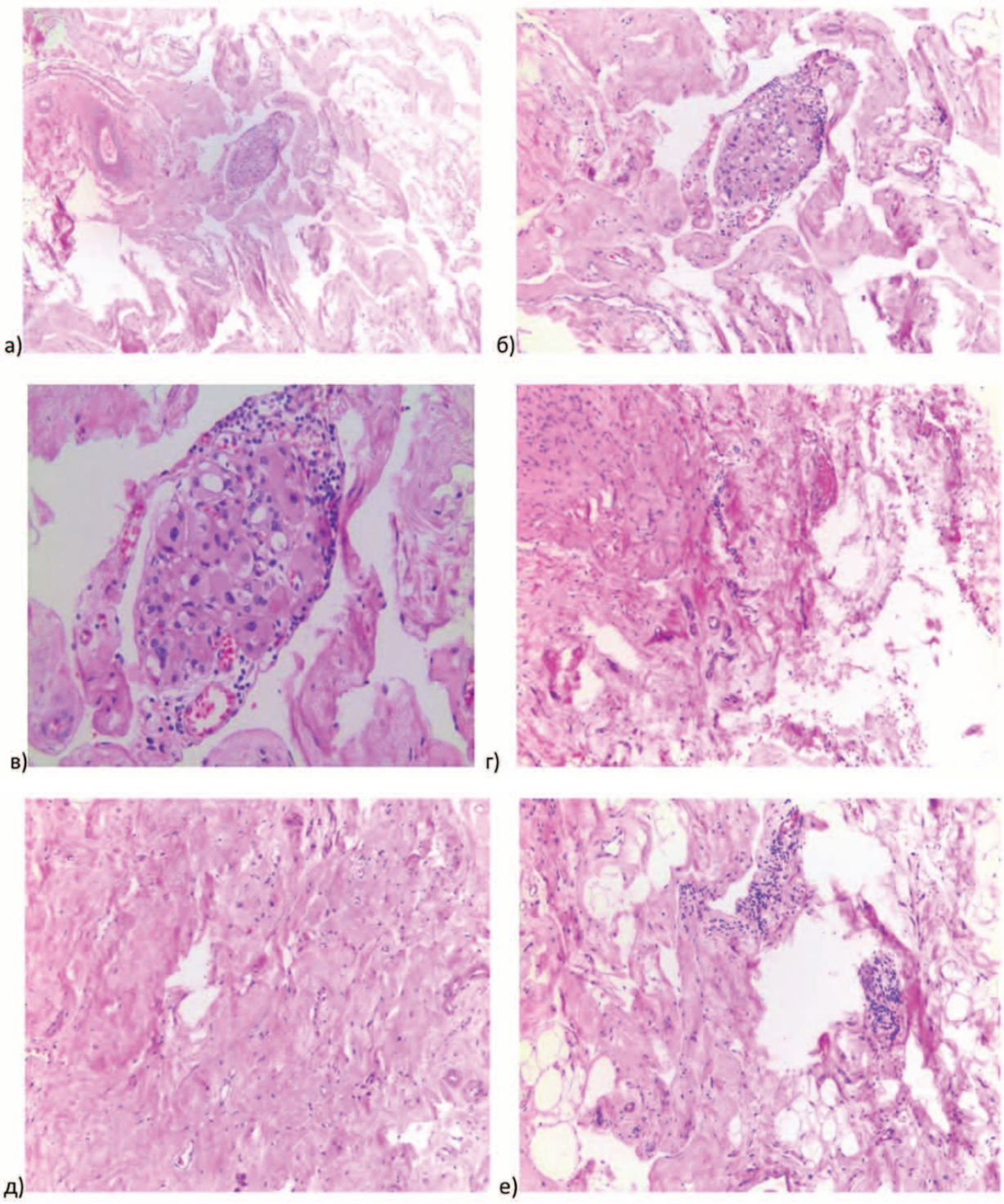


Figure 5. *Tissue of the right lobe of the thyroid gland: fields of fibrous hyalinized connective tissue with severe edema, focal lymphocytic infiltration and single plasma cells (а, б, г, д, е), single follicles of large Ashkinazi-Gurtl cells with oxyphilic cytoplasm and a centrally located basophilic nucleus (в), many thin-walled full-blooded vessels (б, в, д, е)*
Staining with hematoxylin and eosin, а) magnification ×50, б) magnification ×100, в) magnification × 200, г) magnification ×100, д) magnification ×100, е) magnification ×100

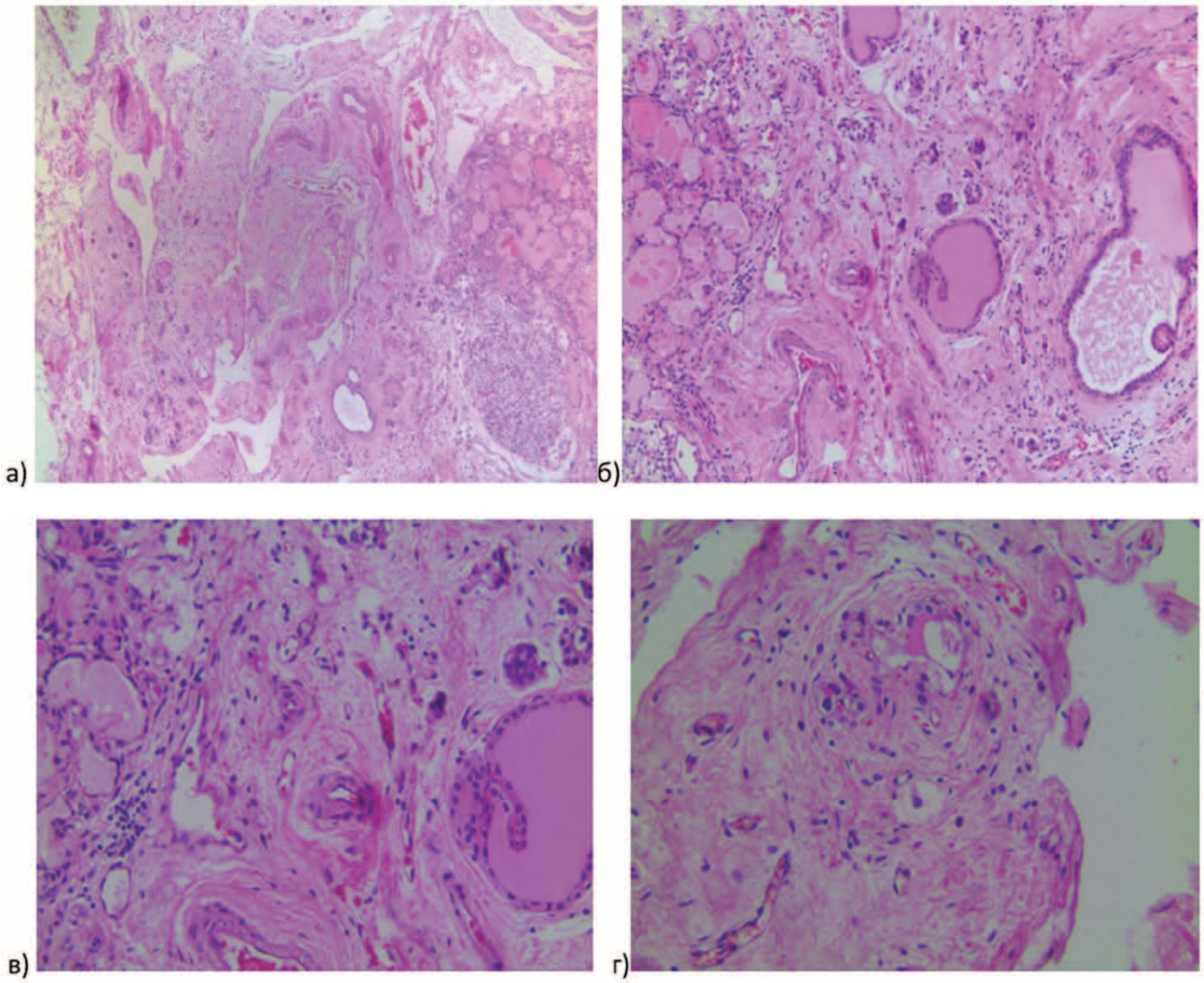


Figure 6. *Fields of fibrous connective tissue with pronounced edema, focal lymphocytic infiltration and single plasma cells, in one of the preparations, lymphocytic infiltration is represented by a lymphoid follicle (а); among the fibrous stroma, there are islands of gland tissue represented by follicles of various sizes, partially filled with colloid (а, б, в, г), in single follicles papillary growths (б, в) of the tissue of the left lobe of the thyroid gland: Staining with hematoxylin and eosin, а) ×50 magnification , б) magnification ×100, в) magnification ×200, г) magnification ×200*

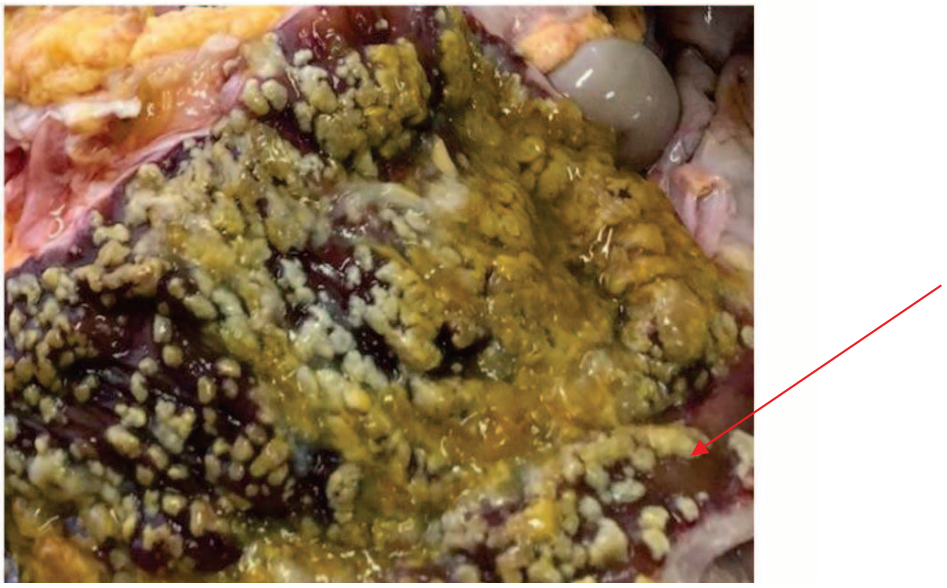


Figure 7. *Macropreparation of the large intestine. The arrow indicates the imposition of fibrin*

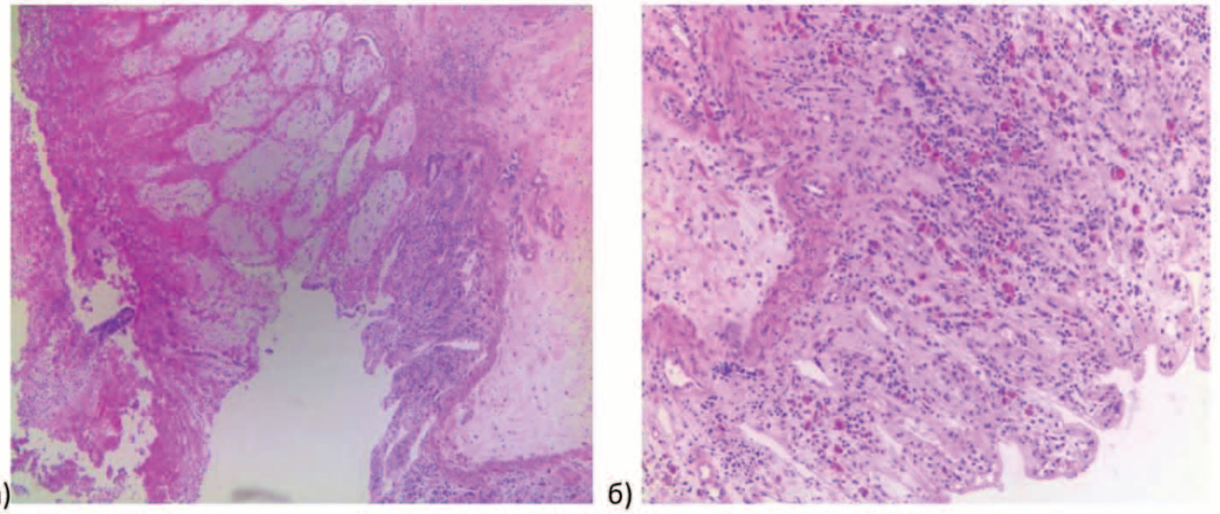


Figure 8. *Shortening and atrophy of the crypts of the mucous wall of the colon. In some areas, necrosis of the superficial sections of the crypts covered with fibrin (a). Mucosa and submucosa with severe edema and severe infiltration of lymphocytes and plasmocytes, single eosinophils and macrophages loaded with hemosiderin (б). Sclerosis of the lamina propria. In the submucosa there are full-blooded dilated vessels, the muscular membrane with moderate edema. Hematoxylin and eosin staining, a) ×50 magnification, б) ×100 magnification*

Histologic examination of the left lobe (Figure 6) revealed fibrous connective tissue with marked edema, focal lymphocytic infiltration, and isolated plasma cells; in one sample, lymphocytic infiltration is represented by a lymphoid follicle; fibrous stroma has gland tissue inlets represented by follicles of various sizes, partially filled with colloidal matter; follicles contain papillary projections.

Macroscopic examination: colon serosa is greyish-pink, smooth, glossy. The wall is edematic, indurated. Mucosa is cherry red with numerous fibrin overlaps and oval mucous defects (0.2×0.1×0.1 cm to 0.3×0.2×0.1 cm); the bed of the defects is red (Figure 7).

Pathomorphological study: the intestine wall shows shorter atrophic crypts. Necrosis of cryps surface areas covered with fibrin. Mucosa and submucosa are markedly edematic, with significant lymphocytic and plasmocytic infiltration, isolated eosinophils and hemosiderin-laden macrophages. Sclerosis of lamina propria. Submucosa contains full-blooded enlarged vessels; the muscular layer is moderately edematic (Figure 8).

Discussion and conclusion

The authors present a case study of a 60-year-old patient with severe hypothyroidism associated with chronic Hashimoto's thyroiditis. Hypothyroidism was not diagnosed until two years after manifestation of symptoms of a severe disease with almost all typical signs and symptoms of the disease. By the time when the diagnosis was made, the patient had symptoms of severe hypothyroidism, such as atony, adynamia, drowsiness, alopecia, depression, intellectual deterioration, hypotony, generalized edema with abdominal dropsy, dropsy of chest, cardiac dropsy, history of transient tetraplegia, dynamic bowel obstruction, and marked water-electrolyte disorders (hyponatremia, hypochloremia), dyslipidemia. Unfortunately, despite hormone replacement therapy, the patient's condition could not be compensated, and the patient died.

This case study is a good example of challenges with assessment of the seemingly typical symptoms of primary hypothyroidism and their interpretation as the signs of completely different somatic and psychoneurological disorders.

Though seemingly straightforward, hypothyroidism diagnosis has its own issues. First, by the time of the last hospitalisation the patient had a number of complications and conditions associated with hypothyroidism, that were concealing the clinical manifestations. Second, postmortem examination verified disease sequellae in the form of ACE, that might also have contributed to the development of intellectual and mnestic disorders. Third, the patient did not present with increased anti-TPO titer at the late stages of chronic Hashimoto's thyroiditis.

Therefore, when facing symptoms resembling hypothyroidism in the real clinical practice, including edematic-ascitic syndrome, anemia, bowel obstruction of unknown etiology, any medical professional should include hypothyroidism into differential diagnosis, in order to timely test serum TTH levels and start replacement therapy before severe complications develop.

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Список литературы/ References:

1. Новиков В.И., Новиков К.Ю. Междисциплинарные аспекты синдрома гипотиреоза: диагностика и лечение. Эффективная фармакотерапия. 2014; 46: 50-55.
   Novikov V.I., Novikov K.YU. Interdisciplinary aspects of hypothyroidism syndrome: diagnosis and treatment. Effektivnaya farmakoterapiya. 2014; 46: 50-55. [In Russian]
2. Ушаков А.В. Гипотиреоз: искажение сущности. М.: Клиника доктора А.В. Ушакова, 2020; 96 с.
   Ushakov A.V. Gipotireoz: iskazhenie sushhnosti. M.: Klinika doktora A.V. Ushakova, 2020; 96 p. [In Russian].
3. Балаболкин М.И. Эндокринология. Москва, Универсум паблишинг. 1998; 580 с.
   Balabolkin M.I. Endocrinology. Moscow, Universum Publishing. 1998; 580 p. [In Russian].
4. Кручинин Е.В., Лебедев И.А., Козлов М.В. и др. «Типичный пациент» с гипотиреозом (клинический случай). Уральский медицинский журнал. 2019; 13 (181): 97-100. DOI: 10.25694/URMJ.2019.13.26
   Kruchinin E.V., Lebedev I.A., Kozlov M.V. et al. "Typical patient" with hypothyroidism (clinical case). Ural'skij medicinskij zhurnal. 2019;13 (181): 97-100. DOI: 10.25694/URMJ.2019.13.26 [In Russian]
5. Вернигородский В.С., Власенко М.В., Паламарчук А.В. и др. Терапевтические маски гипотиреоза. Международный эндокринологический журнал. 2018; 14 (5):503-507. DOI: 10.22141/2224-0721.14.5.2018.142688
   Vernigorodskij V.S., Vlasenko M.V., Palamarchuk A.V. et al. Therapeutic masks for hypothyroidism. International Journal of Endocrinology. 2018; 14 (5):503-507. DOI: 10.22141/2224-0721.14.5.2018.142688 [In Russian]
6. Chaker L., Bianco A.C., Jonklaas J. et al. Hypothyroidism. Lancet. 2017; 390 (10101):1550-1562. DOI: 10.1016/S0140-6736(17)30703-1
7. Дедова И.И., Мельниченко Г.А. Гипотиреоз. Клинические рекомендации. Российская ассоциация эндокринологов. 2021; 34 с.
   Dedova I.I., Melnichenko G.A. Hypothyreosis. Clinical Recommendations. Russian Association of Endocrinologists. 2021; 34 p. [In Russian].
8. Бирюкова Е.В., Шинкин М.В. Гипотиреоз: клиника, диагностика, подходы к терапии. Терапия. 2017; 7 (17); 110-115.
9. Biryukova E.V., Shinkin M.V. Hypothyroidism: clinic, diagnosis, approaches to therapy. Therapy. 2017; 7 (17); 110-115. [In Russian].
10. Свириденко Н.Ю. Вопросы терапии гипотиреоза. РМЖ. 2012; 13: 633.
    Sviridenko N.Yu. Issues in the treatment of hypothyroidism. RMJ. 2012; 13: 633. [In Russian].
11. Моргунова Т.Б., Фадеев В.В. Гипотиреоз: современные принципы диагностики и Лечения. Медицинский совет. 2016; 3: 79-81. DOI:10.21518/2079-701X-2016-3-79-81
    Morgunova T.B., Fadeev V.V. Hypothyroidism: modern principles of diagnosis and treatment. Medicinskij sovet. 2016; 3: 79-81. DOI:10.21518/2079-701X-2016-3-79-81. [In Russian].
12. Jonklaas J., Bianco A.C., Bauer A.J. 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: 10.1089/thy.2013.0171
13. Петунина Н.А., Трухина Л.В. Гипотиреоз. РМЖ. 2007; 2: 89.
    Petunina N.A., Trukhina L.V. Hypothyroidism. RMJ. 2007; 2: 89. [In Russian].