DOI: 10.20514/2226-6704-2025-15-2-151-160
УДК 616.45-008.64-07-085
EDN: ZBHOGQ

П.С. Саможенова[1], Е.Е. Губернаторова[1], Т.В. Адашева[1], Е.И. Горулева[2,3], Е.Г. Лобанова[4]

[1] — ФГБОУ ВО «Российский университет медицины» Минздрава России, кафедра терапии и профилактической медицины, Москва, Россия
[2] — Больница Центросоюза Российской Федерации, Москва, Россия
[3] — Медицинский институт «Реавиз», кафедра внутренних болезней, Москва, Россия
[4] — ФГБОУ ВО «Российский университет медицины» Минздрава России, кафедра фармакологии, Москва, Россия

КЛИНИЧЕСКИЙ СЛУЧАЙ ПЕРВИЧНОЙ НАДПОЧЕЧНИКОВОЙ НЕДОСТАТОЧНОСТИ: ТРУДНОСТИ ДИАГНОСТИКИ, ТЕРАПЕВТИЧЕСКАЯ ТАКТИКА

P.S. Samozhenova[1], E.E. Gubernatorova[1], T.V. Adasheva[1], E.I. Goruleva[2,3], E.G. Lobanova[4]

[1] — Federal State Budgetary Educational Institution of Higher Education "Russian University of Medicine" of the Ministry of Health of the Russian Federation, department of Therapy and Preventive Medicine, Moscow, Russia
[2] — Hospital of the Centrosoyuz of the Russian Federation, Moscow, Russia
[3] — Reaviz Medical Institute, department of Internal Medicine, Moscow, Russia
[4] — Federal State Budgetary Educational Institution of Higher Education "Russian University of Medicine" of the Ministry of Health of the Russian Federation, department of pharmacology, Moscow, Russia

Clinical Case of Primary Adrenal Insufficiency: Diagnostic Difficulties, Therapeutic Tactics

Резюме

Туберкулезное поражение надпочечников — редкая причина первичной надпочечниковой недостаточности (ПНН), характеризующаяся недостаточной выработкой глюкокортикоидов, минералокортикоидов и андрогенов. Неспецифическая симптоматика ПНН затрудняет своевременную диагностику и лечение, что нередко приводит к жизнеугрожающему состоянию — аддисоническому кризу. В данной статье представлено клиническое наблюдение пациентки 67 лет. В течение 8 месяцев пациентка отмечала постепенное нарастание общей слабости, снижение аппетита. При обращении в клинику по месту жительства в июне 2022 г. был установлен диагноз «синдром раздраженного кишечника». Состояние при госпитализации в терапевтическом отделении в октябре 2022 г: выраженная общая слабость, появление боли в животе, мышечные боли, тошнота, рвота. Учитывая вышеперечисленные симптомы, был заподозрен аддисонический криз. Не дожидаясь результатов диагностического поиска, пациентке было назначено введение гидрокортизона 100 мг внутривенно струйно 4 раза за сутки. По результатам исследований, у пациентки была подтверждена первичная надпочечниковая недостаточность, вызванная туберкулезным процессом. Пациентке была назначена заместительная гормональная терапия, проведена беседа о принципах самостоятельной коррекции гормональной терапии и рекомендована консультация врачом-фтизиатром для решения вопроса об инициировании противотуберкулезной терапии. На фоне терапии (межлекарственного взаимодействия) и диагностических процедур (бронхоскопия) и при отсутствии коррекции заместительной гормональной терапии у пациентки развился аддисонический криз. После купирования острого состояния, пациентка повторно консультирована врачом-эндокринологом: принято решение увеличить дозировку заместительной гормональной терапии на фоне лечения противотуберкулезными препаратами. Представленный клинический случай демонстрирует не только особенности диагностики и подбора заместительной терапии при лечении ПНН, но и необходимость повышения осведомленности врачей различных специальностей об алгоритме и тактике ведения пациентов с признаками аддисонического криза.

Ключевые слова: *туберкулез надпочечников, первичная надпочечниковая недостаточность, аддисонический криз, болезнь Аддисона*

Конфликт интересов

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

Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Соответствие принципам этики
Информированное согласие не требуется в силу невозможности идентифицировать пациента

Статья получена 12.11.2024 г.
Одобрена рецензентом 28.11.2024 г.
Принята к публикации 10.02.2025 г.

Для цитирования: Саможенова П.С., Губернаторова Е.Е., Адашева Т.В. и др. КЛИНИЧЕСКИЙ СЛУЧАЙ ПЕРВИЧНОЙ НАДПОЧЕЧНИКОВОЙ НЕДОСТАТОЧНОСТИ: ТРУДНОСТИ ДИАГНОСТИКИ, ТЕРАПЕВТИЧЕСКАЯ ТАКТИКА. Архивъ внутренней медицины. 2025; 15(2): 151-160. DOI: 10.20514/2226-6704-2025-15-2-151-160. EDN: ZBHOGQ

Abstract
Tuberculous adrenal insufficiency is a rare cause of primary adrenal insufficiency (PAI), characterized by insufficient production of glucocorticoids, mineralocorticoids, and androgens. Nonspecific symptoms of PAI complicate timely diagnosis and treatment, which often leads to a life-threatening condition, Addisonian crisis. This article presents a clinical observation of a 67-year-old female patient. For 8 months, the patient noted a gradual increase in general weakness, and decreased appetite. When visiting a local clinic in June 2022, she was diagnosed with irritable bowel syndrome. Condition on admission in the medical ward in October 2022 was manifested as severe general weakness, abdominal pain, muscle pain, nausea, vomiting. Given the above symptoms, Addisonian crisis was suspected. Before the results of diagnostic tests were obtained, the patient was given hydrocortisone 100 mg intravenously by jet stream 4 times per day. Based on the test results, the patient was diagnosed with primary adrenal insufficiency caused by a tuberculosis process. The patient was prescribed hormone replacement therapy, she was advised on the principles of independently adjusting the hormone therapy; a consultation with a TB specialist was also recommended to decide on initiating anti-tuberculosis therapy. The patient developed an Addisonian crisis due to a combination of factors: the treatment (the drug interaction), the impact of diagnostic procedures (bronchoscopy) and due to no correction of the prescribed hormone replacement therapy. After the acute condition was relieved, the patient was re-consulted by the endocrinologist who decided to increase the dosage of hormone replacement therapy and continue the treatment with antitubercular agents. This clinical case has demonstrated the specifics of diagnostics and selection of replacement therapy in the treatment of PNI. It has also shown that doctors of various specialties have to be better informed about the algorithm and tactics of managing patients with symptoms of Addisonian crisis.

Key words: *adrenal tuberculosis, primary adrenal insufficiency, Addison crisis, Addison's disease*

Conflict of interests
The authors declare no conflict of interests

Conformity with the principles of ethics
Informed consent is not required due to the impossibility of identifying the patient

Sources of funding
The authors declare no funding for this study

Article received on 12.11.2024
Reviewer approved 28.11.2024
Accepted for publication on 10.02.2025

For citation: Samozhenova P.S., Gubernatorova E.E., Adasheva T.V. et al. Clinical Case of Primary Adrenal Insufficiency: Diagnostic Difficulties, Therapeutic Tactics. The Russian Archives of Internal Medicine. 2025; 15(2): 151-160. DOI: 10.20514/2226-6704-2025-15-2-151-160. EDN: ZBHOGQ

PAI — primary adrenal insufficiency, ACTH — adrenocorticotropic hormone, CRH — corticotrophin-releasing hormone, DHA-S — dehydroepiandrosterone sulfate, BP — blood pressure, Ab — antibodies, CT — computer tomography, IBS — irritable bowel syndrome

Introduction

Primary adrenal insufficiency (PAI) is a rare endocrine conditions affecting 100–140 people per million. Currently, autoimmune adrenal cortex deficiencies are more common in clinical practice, whereas tuberculous damages are observed maximum in 10 % of confirmed cases [1]. Although replacement therapy considerably improves prognosis, 50 % of patients are at residual risk of a dangerous, life-threatening condition — addisonian crisis, which is a result of therapeutic errors [2]. Therefore, early diagnosis and therapeutic strategy are relevant for various healthcare professionals, because non-specific symptoms hinder early diagnosis, and errors in patient management can cost the patients their lives.

Aetiology and pathogenesis

Deficient production of adrenal cortex hormones is caused by impaired functions at various levels of the hypothalmic-pituitary-adrenal axis (Figure 1).

Adrenal insufficiency resulting from adrenal cortex damages is called primary. If a pathologic process develops in the pituitary gland, then this clinical condition is called secondary adrenal insufficiency. There is also tertiary adrenal insufficiency, meaning changes in hypothalamus functions. Secondary and tertiary adrenal insufficiency often have common clinical presentation. Adrenal insufficiency can be innate or acquired **(Table 1)**.

Acquired primary adrenal insufficiency is often caused by an autoimmune process; the second most common cause of acquired PAI is an infection, mostly TB [1, 2].

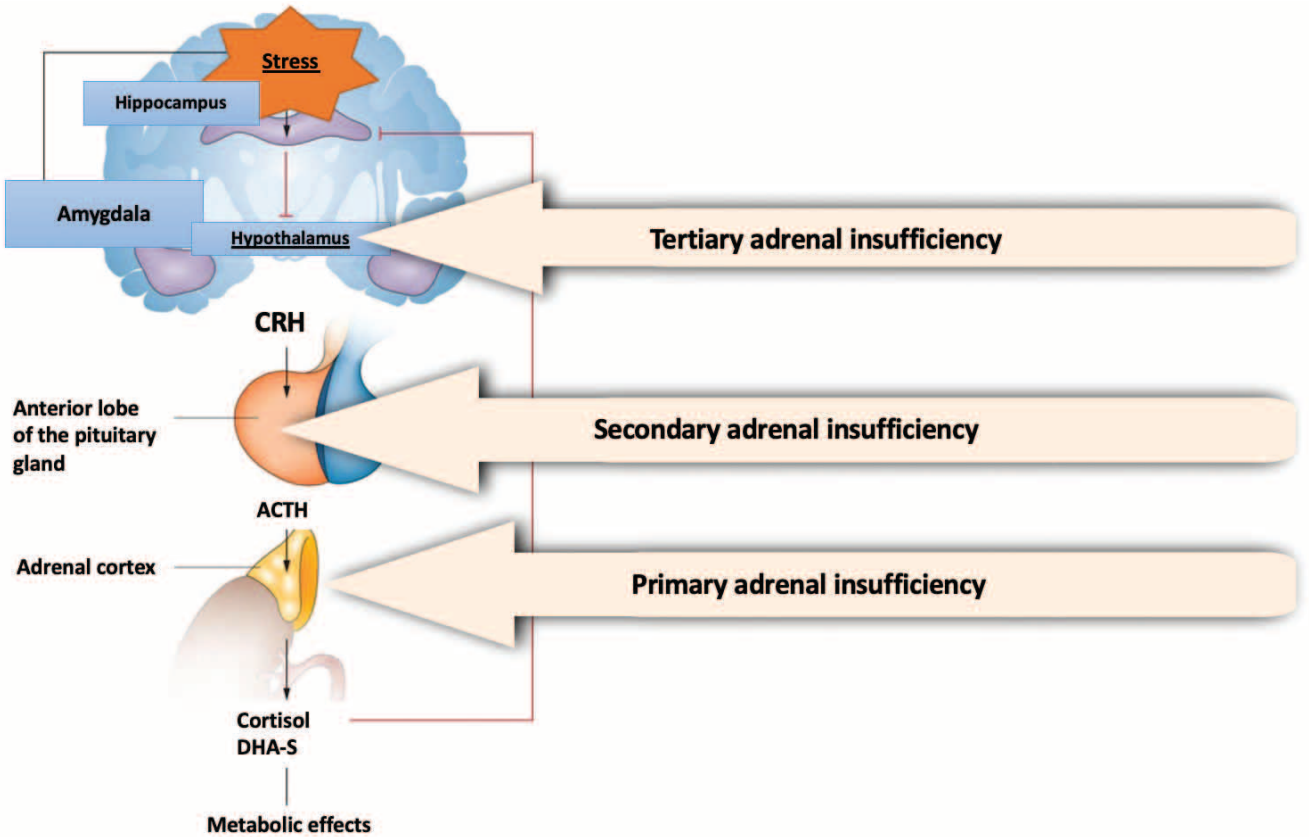

Figure 1. *Hypothalamic-pituitary-adrenal axis and types of adrenal insufficiency according to the level of lesion*

Note: ACTH — adrenocorticotropic hormone, CRH — corticotropin-releasing hormone, DHA-S — dehydroepiandrosterone sulfate (Adapted from Papadopoulos, A. S., & Cleare, A. J. (2011). Hypothalamic–pituitary–adrenal axis dysfunction in chronic fatigue syndrome. Nature Reviews Endocrinology, 8(1), 22–32.doi: 10.1038/nrendo.2011.153) [3]

Table 1. *Causes of primary adrenal insufficiency*

Causes of primary adrenal insufficiency	
Congenital causes	**Acquired causes**

• Congenital adrenal cortex dysfunction (the most common cause of primary adrenal insufficiency in children, 80%)
• Congenital insensitivity to adrenocorticotropic hormone (isolated glucocorticoid deficiency)
• Congenital adrenal hypoplasia
• Adrenoleukodystrophy
• Mitochondrial diseases
• Vollmann's disease
	• Autoimmune damage to the adrenal glands
	• Damage to adrenal tissue:
	  Infections
	  Metastasis
	  Hemorrhage
	• Medical causes (rifampicin, ketoconazole, anticancer drugs, certain aromatase inhibitors, protein kinase inhibitors, diagnostic drugs, general anesthesia drugs)
	• Total adrenalectomy
	• Unilateral adrenalectomy with contralateral adrenal atrophy
	• Infiltrative diseases (hemochromatosis, amyloidosis, sarcoidosis)

Notes: PAI — primary adrenal insufficiency. Adapted from the clinical guidelines of the endocrinology association "Primary adrenal insufficiency" 2021 [1].

Clinical presentation

Clinical presentation of primary adrenal insufficiency is a result of reduced glucocorticoid and mineralocorticoid levels. At the beginning of the pathologic process, the clinical manifestations are unclear, which can delay timely diagnosis. *Non-specific* symptoms are: loss of body weight, developing general weakness, musculoskeletal pain, abdominal discomfort, anxiety, depression. *Specific* and pathognomonic symptoms of PAI are skin and mucosa hyperpigmentation due to an elevated production of proopiomelanocortin, a biological precursor of chromatophorotropic hormones. Hyperpigmentation is clearly visible in natural skin folds, point of contact with clothes, and near post-surgery scarring. Proopiomelanocortin is also a precursor of lipotrophic hormones, facilitating subcutaneous tissue lipolysis, which is an additional factor of body weight loss [1].

Clinical presentations of *addisonian crisis* are marked general weakness, hypotonia, nausea, vomiting, abdominal and muscle pain.

Diagnostic algorithm

The PAI diagnostic algorithm is presented in Figure 2.

Management

Addisonian crisis management. Adrenal insufficiency is a life-threatening condition. **When addisonian crisis is suspected, replacement therapy should be initiated immediately, and there is no need to wait for laboratory test results** [1]. According to clinical guidelines, patients demonstrating signs of addisonian crisis should have hydrocortisone or prednisolone injections at equivalent doses. If hydrocortisone or prednisolone therapy is impossible, dexamethasone should be considered. (Dosage regimens are presented in 2021 Clinical Recommendations: Primary Adrenal Insufficiency) [1].

Replacement therapy. Once the acute condition has been relieved, the patient requires long-term therapy selected.

Replacement therapy in PAI patients is based on several principles:

1. Characteristics of replacement therapy. The dose regiment of replacement therapy mirrors the characteristic expression of adrenal cortex hormones in a healthy individual. The most active production of cortisol is known to be taking place in the morning, while aldosterone has a pulsating cycle of production, and this is taken into account when selecting a dose. Therefore, in order to compensate for the glucocorticoid component, hydrocortisone is administered in the morning, a half to two thirds of the daily dose; and one third is administered in the afternoon, thus mimicking the physiological production of this hormone. As for the compensation of the mineralocorticoid component, its purpose is to prevent

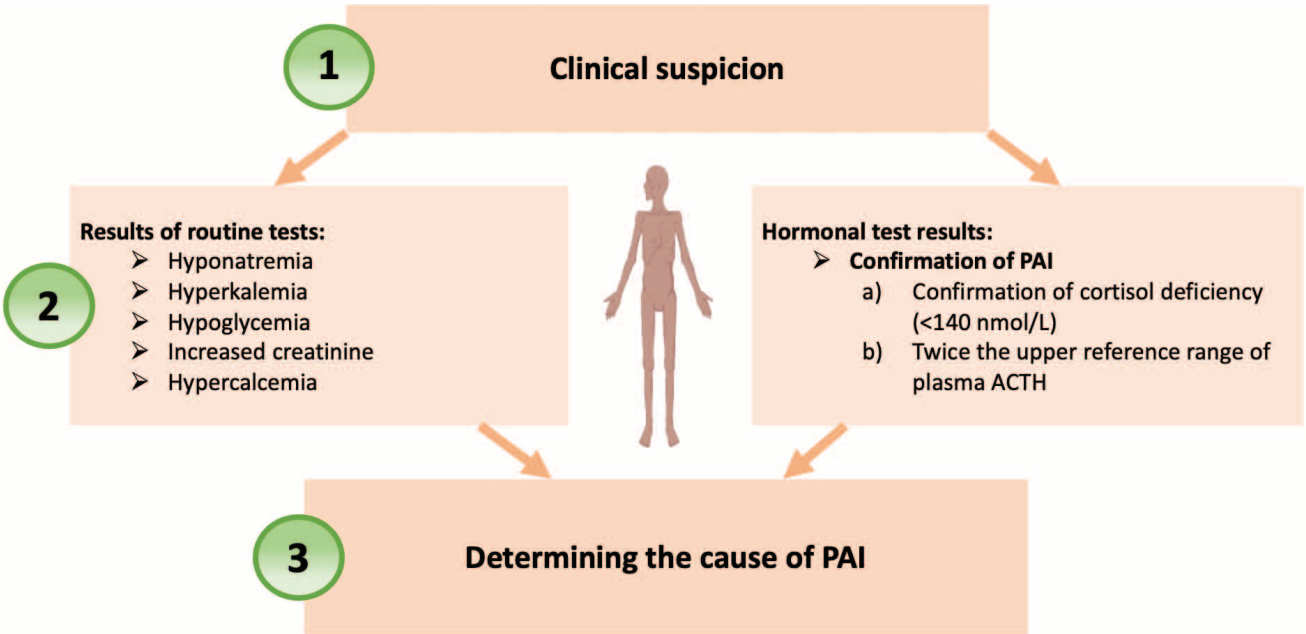

Figure 2. *Algorithm for diagnosing PAI. Adapted from the clinical guidelines of the endocrinology association "Primary adrenal insufficiency" 2021 [1].*

Note: PAI — primary adrenal insufficiency, ACTH — adrenocorticotropic hormone

hyponatraemia and dehydration. Fludrocortisone is used in this case, and the dose is selected depending on the blood pressure values.

2. Assessment of replacement therapy efficacy. Since there are no objective parameters to assess the adequate replacement therapy, internal medicine specialists have to rely on clinical presentation. The efficacy criteria of the replacement therapy are:

- Normalised blood pressure
- Improved general condition and emotions
- Appetite, improved skin colour.

The following are the signs of possible overdose:

- Uneven colour
- Rapid gain of weight
- Osteopenia.

3. Training the patients in the principles of replacement therapy dose correction. Another important aspect in the therapy is training both the patient and their close ones during the initial and follow-up visits. Diagnosed PAI requires understanding that the replacement therapy is life-long, and in some cases the patient will need dose adjustments. Any event associated with release of stress hormones must be medicated. Patients are recommended to carry hydrocortisone injections with them in order to arrest an addisonian crisis, a pendant, a memo and any other available attributes, which can facilitate timely medical assistance [1]. Dose should be adjusted in the following situations: fever, gastroenteritis or trauma, surgery (a manor or a major intervention), addisonian crisis. (Dosage regimens are presented in 2021 Clinical Recommendations: Primary Adrenal Insufficiency) [1].

Case study

A female patient, 67 y.o., was admitted to the medical ward of the hospital of the Central Union of Consumer Cooperatives of the Russian Federation (Moscow) on October 4, 2022. She was complaining ofgeneral weakness, nausea, loss of 35 kg of body weight over seven months, iliac pain, insomnia.

Past medical history: the patient first complained of weakness in March 2022. Blood pressure (BP): 150/90 mm Hg, weight: 86 kg. Antihypertensive therapy was not administered. In June 2022, general weakness progressed; blood pressure dropped to 100/60 mm Hg; and body weight reduced to 71 kg with no changes in the lifestyle. She started complaining of nausea and vomiting and called for medical assistance at the hospital at the place of residence, where she was diagnosed with *irritable bowel syndrome*. Since 2022, here general condition deteriorated; BP: 80/40 mm Hg; the patient started complaining of iliac pain, insomnia, no appetite, nausea, and was admitted to the medical ward of the hospital of the Central Union of Consumer Cooperatives of the Russian Federation for further diagnostics and therapy (Fig. 3).

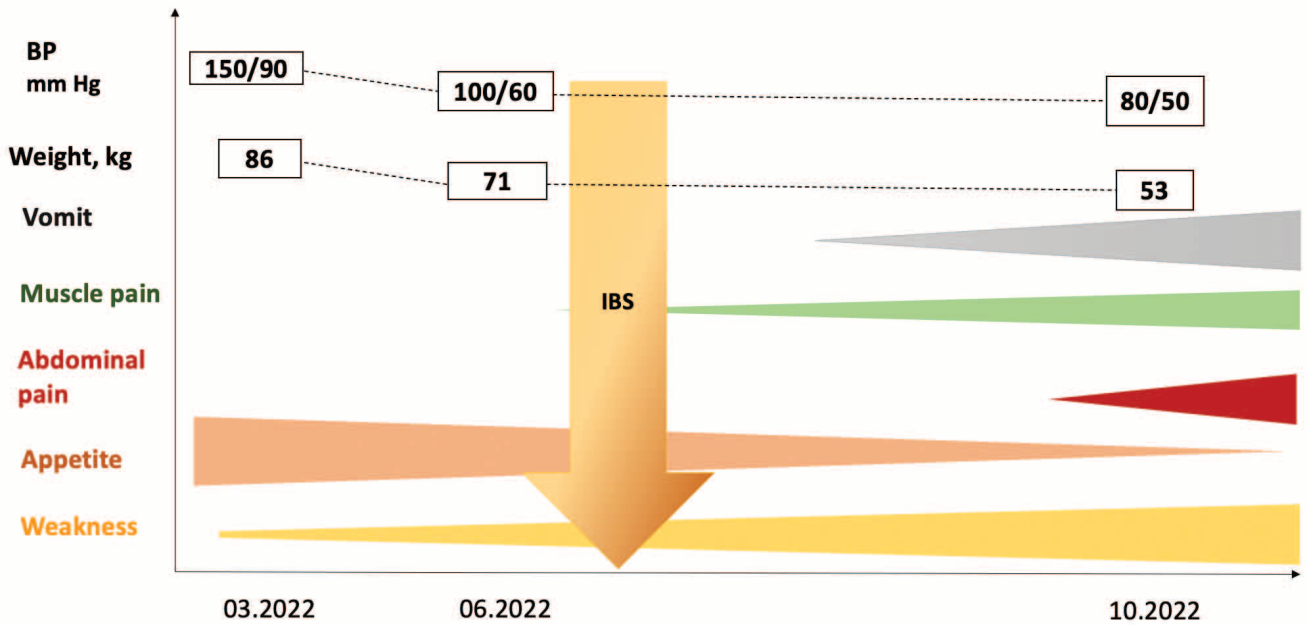

Figure 3. *Patient's medical history*
Note: BP — blood pressure, IBS — irritable bowel syndrome

Life history: a citizen of Turkmenistan, high education, widow. Allergies: denies. Family history: her brother died of lung TB in 2014. It is known that until 2014 she was a tutor for deaf and mute children and came for regular medical check-ups; chest X-ray did not show any abnormalities.

Initial examination: moderately severe general condition, lucid. Body temperature: 36.7 °C. She can move unattended only near the bed. Skin examination shows regions of hyperpigmentation in natural folds of the body (Fig. 4a); skin tightness is extremely low. Visible mucosa: point hyperpigmentations on the tongue (Fig. 4b). No body hair in axillary creases and on the pubis. Subcutaneous fat is feebly marked (height: 165 cm, weight: 53 kg, BMI: 19.5). Respiratory rate: 18 respirations per minute. By percussion: clear pulmonary sounds in the projection of the lung tissue; by auscultation: vesicular breathing with individual dry rales in the interscapular space.

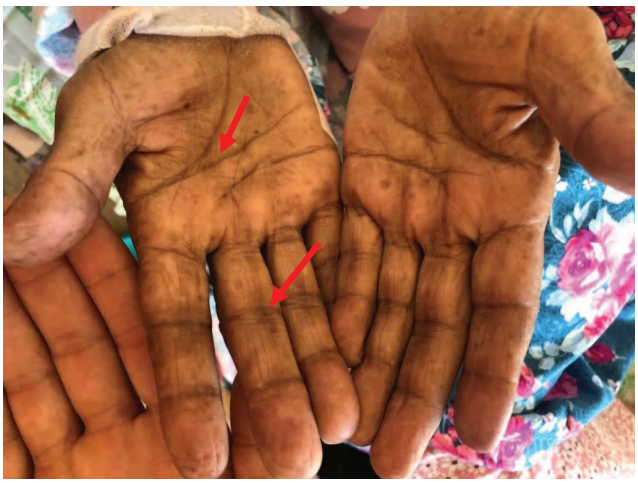

Figure 4a. *Hyperpigmentation zones in natural body folds*

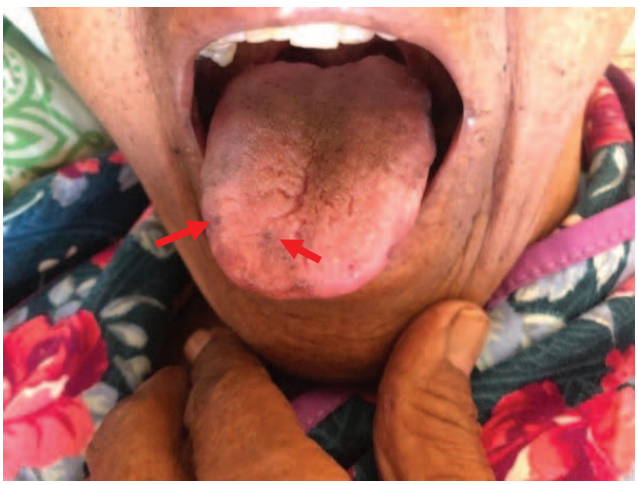

Figure 4b. *Hyperpigmentation zones on the tongue*

Regular cardiac rhythm, muffled heart tones, no heart murmurs. A. radialis, a. dorsalis pedis pulse is symmetrical, with satisfactory volume. Pulse: 100 bpm, rhythic; BP: 80/50 mm Hg (D=S). When palpated, the abdomen is soft, sensitive in iliac region. The liver is within the costal arch. Bowel movements: tendency to constipations. Region of the kidneys: visually unremarkable. When palpated, the bladder is painless. Kidney punch is negative on both sides. Neurological status: speech and memory are normal, the patient is oriented to place and time, adequate, communicative.

Examination results

ECG dd 05/10/2022: Sinus, regular rhythm; heart rate: 69 bpm; electrical axis of the heart: vertical.

Complete blood count dd 05/10/2022: HCT — 36.6 % (35–47), Hb — 12.9 g/dL (11.7–16.1), RBC — 4.60 mln/μL (3.8–5.2), platelets — 309 ths/μL (150–400), WBC — 4.5 ths/μL (4.5–11), ESR — 14 mm/h (< 30), K — 4.7 mmol/L (3.5–5.1), creatinine — 48 mmol/L (49–50), glucose — 3.7 mmol/L (4.1–6.0), albumin — 36.8 g/L (37.5–50.1).

Urinalysis dd 05/10/2022: colour — light-yellow; clarity — not completely clear; specific density — 1.020, pH — 5.0, protein — 0.0, KET — 0.0, WBC — 0.0, salt — 0.0, bacteria — 0.0, mucous — +.

Blood biochemistry dd 05/10/2013: AST — 35 U/L (< 31), **glucose — 3.7 mmol/L** (4.1-6.0), **Na — 120 mmol/L** (136–145), **Cl — 88 mmol/L** (101–110), **creatine kinase — 1211 U/L** (<167).

First, the critically low sodium levels stand out, which is a life-threatening condition. Considering that the patient had pronounced asthenic syndrome, abdominal syndrome, skin and mucosa hyperpigmentation, hypoglycaemia, hyponatraemia, chloropenia, hypotonia, *addisonian crisis was suspected*. High creatine kinase levels show active myolysis in the patient, hence her complaints of muscle pain.

According to the clinical guidelines [1], the patient was prescribed hydrocortisone 100 mg as intravenous push four times daily, not waiting for laboratory test results for cortisol and adrenocorticotropic hormone (ACTH).

Hormone test results dd 05/10/2022: dehydroepiandrosterone sulfate (DHA-SO4) < 0.08 μmol/L (0.8–4.9), cortisol < 27.6 nmol/L (blood drawn before 10 am, reference range: 101.2–535.7), ACTH — 769.0 pg/mL (< 46), renin (plasma) — 121.1 μIU/mL (4.4–46.1), aldosterone — 15.0 pg/mL (25.2–392).

Plasma ACTH levels is more than 16-fold (!) higher than the upper limit of normal, while cortisol level is

below 140 nmol/L, which is a criterion to diagnose primary adrenal insufficiency. Also, elevated renin is a compensatory response to low aldosterone levels, according to the mechanisms of renin-angiotensin-aldosterone system (RAAS) functioning.

Once the acute condition was resolved, the following replacement therapy was initiated: hydrocortisone 10 mg in the morning, 5 mg at lunchtime, 5 mg in the evening; fludrocortisone 25–50 mg in the morning, with dose adjustment depending on well-being.

If a patient is diagnosed with PAI, diagnostic search should continue in order to identify the cause of adrenal damage [1]. According to the diagnostic algorithm of PAI, the autoimmune origin of adrenal insufficiency should be ruled out in the first instance. For this purpose, a test for anti-steroid-producing adrenal cell antibodies (AB) was performed.

Test for anti-21-hydroxylase AB: < 1:10 (reference range: <1:10). Therefore, anti-21-hydroxylase AB test came back negative.

Once the autoimmune origin of adrenal insufficiency was ruled out, adrenal computer tomography (CT) was performed (Fig. 5a).

Adrenal computer tomography. Adrenals: regular position; both adrenals are diffusely thickened up to 14 mm, with uneven structure due to numerous calcifications. Surrounding fat tissue: unremarkable. Kidneys: regular position and shape, not enlarged. Contours are clear, uneven. Parenchyma structure is even. The renal collecting system is not dilated. No stones. Paranephric fat tissue: unremarkable. Inferior vena cava is distinguished and normal. Aorta: calcified walls. Retroperitoneal lymph nodes are not enlarged. Destructive bone changes in the lumbar spine, visible pelvic and hip bone sections are not detected.

Conclusion. CT signs of adrenal calcifications.

Given the CT pattern of adrenal calcifications and the family history of the patient, the decision was made to continue the diagnostic search for TB. According to the scientific references, enlarged adrenals are often a sign of an active infectious process, whereas minor atrophic changes and visible calcifications in adrenal cortex evidence a chronic process, which is most likely inactive [4].

Chest computer tomography (Fig. 5b).

Chest CT: S2 of the right lung shows focal cord-like thickening adjacent to the costal pleura; the surrounding pulmonary tissue is unchanged. S1 of the right lung has a single focus with unclear even margins. Apical adhesions on both sides. The lung pattern is trackable and is not deformed. The lumen of the trachea, main and segmental bronchi is trackable and is not deformed. Pleural spaces do not hold any effusion or free gas. Mediastinal organs and soft tissue: clinically unremarkable.

Conclusion. CT signs of focal changes in the upper lobes of both lungs; differentiation should be made between focal TB and post-infection changes.

To rule out TB, the patient underwent Mantoux test, DST and sputum analysis for M. tuberculosis.

Mantoux test and DST results: papules of up to 30x30 mm with subcutaneous haemorrhage and marked swelling.

Sputum analysis for M. tuberculosis: negative.

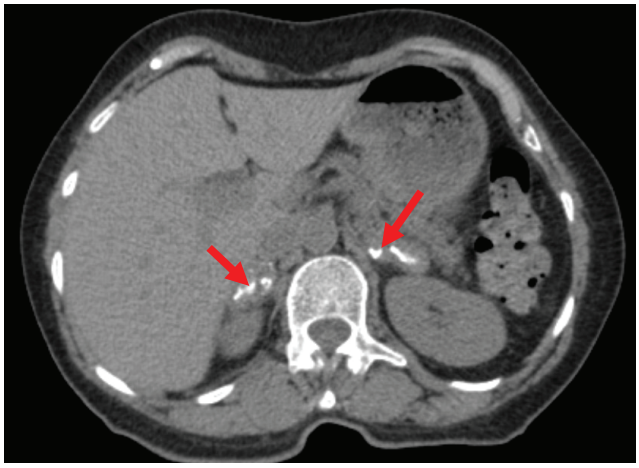

Figure 5a. *Computed tomography (CT) of the adrenal glands*
Arrows indicate multiple adrenal calcifications

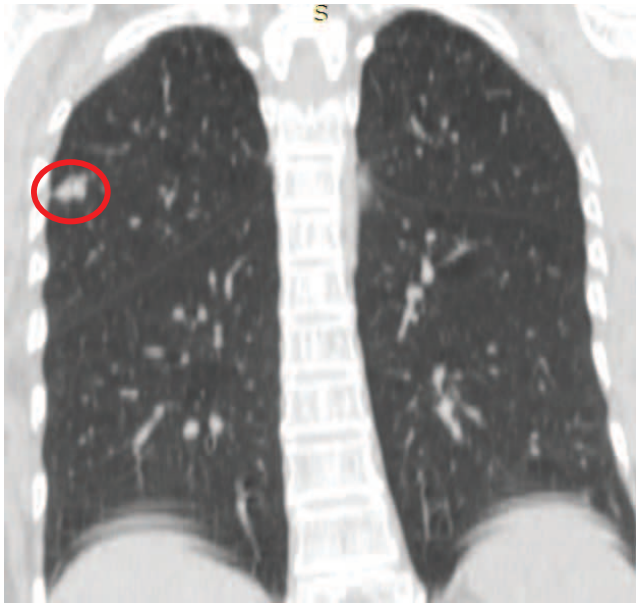

Figure 5b. *Computed tomography of the chest organs*
A single focus with blurred smooth contours of the apical segment of the left lung is highlighted in color

Once M. tuberculosis infection was confirmed, the patient was referred to a TB specialist. Diagnosis: *Focal TB of the right lung, M. tuberculosis infiltration phase. M. tuberculosis (–). Adrenal tuberculosis. Primary adrenal insufficiency, medically compensated.*

Upon discharge, the patient was prescribed replacement therapy with hydrocortisone: hydrocortisone 10 mg in the morning, 5 mg at lunchtime, 5 mg in the evening; fludrocortisone 25 mg in the morning; she was also provided with recommendations on dose adjustment depending on various real-life situations and possible scheduled therapy according to clinical guidelines (in case of addisonian crisis, fever, severe emotional stress, minimally invasive surgeries, etc.). Besides, scheduled hospitalisation to TB hospital was recommended.

On July 24, 2023, the patient was hospitalised to the National Medical Research Centre for Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation for antituberculosis therapy (rifampicin 450 mg in the morning before meal; isoniaside 300 mg in the morning after meal; pyrazinamide 1,500 mg in the morning after meal; ethambutol 1,200 mg after lunch). After bronchoscopy on August 2, 2023, the patient started complaining of nausea, vomiting, general weakness again. In inpatient settings, the patient was prescribed prednisolone tablets; since no significant therapeutic effects were observed, the patient visited the hospital of the Central Union of Consumer Cooperatives of the Russian Federation for replacement therapy adjustment regarding PAI and dose selection for antituberculosis therapy initiation.

Rifampicin is a potent cytochrome P-450 inducer, engaged in adrenocorticosteroid metabolism, resulting in accelerated glucocorticoid metabolism and reduced glucocorticoid effects [5, 6]. Therefore, the dose was increased for the duration of antituberculosis therapy.

The patient was discharged in satisfactory condition, with stable haemodynamics. The following replacement therapy with hydrocortisone was selected: 15 mg in the morning, 7.5 mg at lunchtime, 7.5 mg in the evening; fludrocortisone: 50 mg in the morning. The patient underwent a repeated training in self-correction of the hormone therapy. The antituberculosis therapy recommended for six months: isoniaside 300 mg in the morning; pyrazinamide 1,500 mg in the morning; ethambutol 1,200 mg at lunch.

The patient completed the antituberculosis therapy and is followed-up by a TB specialist (visits at least two times a year) and thyroid specialist (consultations twice a year).

Discussion

Primary adrenal insufficiency and addisonian crisis are often ignored by medical professionals due to their non-specific symptoms. Clinical presentation, i.e. body weight loss, general weakness, abdominal discomfort can mislead clinicians, and patients are referred to a wrong ward with clinical signs of acute abdomen, irritable bowel syndrome, etc. In this case study, the patient was followed up for irritable bowel syndrome at the place of her residence, and only after her condition deteriorated, and the patient was hospitalised with symptoms of addisonian crisis, the correct diagnostic hypothesis was made. PAI was finally diagnosed eight months after the onset of clinical symptoms.

Despite rare cases of tuberculosis as a cause of PAI, clinicians should take into account the patient's epidemiological anamnesis and include TB verification methods (DST, Mantoux test, chest CT, Quantiferon test, etc.) to the diagnostic algorithm.

In their clinical observation, Van Haren Noman S, Visser H et al. (2018) described adrenal tuberculosis. Upon hospitalisation, the patient was complaining of abdominal discomfort and weigh loss. The final diagnosis was made two months later after CT, the results of which showed enlarged adrenals. A hormone test, which confirmed adrenal insufficiency, was preformed after X-ray imaging. The authors also discuss challenges with PAI diagnosis due to non-specific symptoms and characteristics of simultaneous therapy of adrenal insufficiency and adrenal tuberculosis. In this case study, once antituberculosis therapy was initiated, hydrocortisone and fludrocortisone doses were increased three- and two-fold, respectively [6]. Besides, antituberculosis therapy initiation caused adrenal insufficiency decompensation, requiring repeated hospitalisation for addisonian crisis and subsequent correction of replacement therapy.

In selecting a dose of hormone replacement therapy, it is essential to take into account any comorbidities. Antituberculosis drugs accelerate glucocorticosteroid metabolism, reducing their blood levels, and clinicians have to adjust the dose empirically, based on the patient's well-being and blood pressure values [1].

Zhao N, Gao Y et al. (2021) described autopsy results of a patient, who died of addisonian crisis. A 45-year-old male patient was hospitalised with finger trauma and bleeding. On day 13 of hospitalisation, the patient's condition suddenly deteriorated: vomiting, blood pressure 104/70 mm Hg, hypoglycaemia, hyponatraemia (108.2 mmol/L (!)). Brain CT confirmed

brain swelling caused by hyponatraemia. Hormone test results: ACTH — 855.00 pg/mL, cortisol — < 1.00 mg/dL. A microscopic examination of the lung tissue sample showed caseous necrosis with calcifications and granulomas in the lower lobe of the right lung. The microscopic examination also showed caseous necrosis with calcifications in the left adrenal. The patient did not have typical skin hyperpigmentation and symptoms of PAI. This case study illustrates that the patient developed addisonian crisis amidst an acute clinical situation, which requires higher glucocorticosteroid production (trauma, bleeding). Most likely, symptoms of adrenal insufficiency before the incident were non-specific and did not raise red flags in the patients and his doctors. Adrenal insufficiency was not diagnosed before hospitalisation. In our case study, addisonian crisis was most likely caused not only by drug-drug interaction, but also by diagnostic procedures (bronchoscopy), which can also lead to decompensation.

After replacement therapy selection, the patient should be trained in the principles of hormone replacement therapy selection depending on various situations, which are physiologically associated with higher blood glucocorticoid levels (stress, fever, minor invasive interventions, diagnostic procedures, etc.) [1]. In this case study, drug-drug interactions between hormone replacement therapy and antituberculosis drugs were not taken into account, and doses were not adjusted, causing addisonian crisis [7].

Conclusion

This case study illustrates challenges with timely diagnostics of adrenal insufficiency. Currently, there are up-to-date methods to reliably verify the diagnosis; and drug therapy regimens have been developed. However, referrals of patients with addisonian crisis to wrong wards show low level of awareness among medical professionals. A speedy diagnosis is still an issue among various doctors.

Вклад авторов:

Все авторы внесли существенный вклад в подготовку работы, прочли и одобрили финальную версию статьи перед публикацией

Саможенова П.С.: ведение пациента, разработка дизайна публикации, написание текста рукописи, обзор публикаций по теме статьи, утверждение окончательного варианта, принятие ответственности за все аспекты работы, целостность всех частей статьи и ее окончательный вариант, взаимодействие с редакцией в процессе подготовки публикации и печати

Губернаторова Е.Е.: ведение пациента, доработка текста, обзор публикаций по теме статьи, утверждение окончательного варианта, предоставление иллюстративного материала

Адашева Т.В.: научное руководство, разработка концепции, сбор данных и обработка материала, подготовка и редактирование текста, утверждение окончательного варианта

Горулева Е.И.: ведение пациента, обзор публикаций по теме статьи, доработка текста, сбор данных и обработка материала

Лобанова Е.Г.: обзор публикаций по теме статьи, доработка текста, сбор данных и обработка материала

Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Samozhenova P.S.: patient management, development of the publication design, writing the manuscript text, review of publications on the topic of the article, approval of the final version, taking responsibility for all aspects of the work, the integrity of all parts of the article and its final version, interaction with the editorial board during the preparation of publication and printing

Gubernatorova E.E.: patient management, revision of the text, review of publications on the topic of the article, approval of the final version, provision of illustrative material

Adasheva T.V.: scientific guidance, concept development, data collection and material processing, text preparation and editing, approval of the final version

Goruleva E.I.: patient management, review of publications on the topic of the article, revision of the text, data collection and processing of the material

Lobanova E.G.: review of publications on the topic of the article, revision of the text, data collection and processing of the material

Список литературы / References:

1. Российская Ассоциация Эндокринологов. Клинические рекомендации: Первичная надпочечниковая недостаточность. 2021
   Russian Associacion of Endocrinologist. Clinical practice guidelines: Primary adrenal insufflciency. 2021 [In Russian]
2. Eystein S Husebye, Simon H Pearce, Nils P Krone, et al. Adrenal insufficiency. Lancet. 2021; 397: 613–629: DOI: 10.1016/S0140-6736(21)00136-7
3. Papadopoulos AS, Cleare AJ. Hypothalamic-pituitary-adrenal axis dysfunction in chronic fatigue syndrome. Nat Rev Endocrinol. 2011 Sep 27;8(1):22-32. doi: 10.1038/nrendo.2011.153.
4. Gupta S, Ansari MAM, Gupta AK, et al. Current Approach for Diagnosis and Treatment of Adrenal Tuberculosis-Our Experience and Review of Literature. International Surgery Journal. 2022. 8(1): e92-e97. DOI: 10.1055/s-0042-1743523
5. Справочник Видаль «Лекарственные препараты в России». Рифампицин (RIFAMPICIN) описание. URL: https://www.vidal.ru/drugs/molecule/925 (дата обращения: 20.07.24).
   Vidal Directory 'Medicines in Russia'. Rifampicin (RIFAMPICIN) description. URL: https://www.vidal.ru/drugs/molecule/925 (date of the application: 20.07.24). [In Russian]
6. van Haren Noman S, Visser H, Muller AF,et al. Addison's Disease Caused by Tuberculosis: Diagnostic and Therapeutic Difficulties. European Journal of Case Reports in Internal Medicine. 2018. 5(8):000911. doi: 10.12890/2018_000911.
7. Zhao N, Gao Y, Ni C, Zhang D, et al. An autopsy case of unexpected death due to Addison's disease caused by adrenal tuberculosis. European Journal of Medical Research. 2021 Dec 4;26(1):137. doi: 10.1186/s40001-021-00611-w.

Информация об авторах:

Саможенова Полина Сергеевна — аспирант кафедры терапии и профилактической медицины ФГБОУ ВО «Российский университет медицины» Минздрава России, Москва, e-mail: samozhenowapolina@gmail.com, ORCID ID: https://orcid.org/0000-0002-8170-0863

Губернаторова Екатерина Евгеньевна — к.м.н., ассистент кафедры терапии и профилактической медицины ФГБОУ ВО «Российский университет медицины» Минздрава России, Москва, e-mail: creativeone@list.ru ORCID ID: https://orcid.org/0009-0009-4149-9497

Адашева Татьяна Владимировна — д.м.н., профессор, профессор кафедры терапии и профилактической медицины ФГБОУ ВО «Российский университет медицины» Минздрава России, Москва, e-mail: adashtv@mail.ru, ORCID ID: https://orcid.org/0000-0002-3763-8994

Горулева Екатерина Игоревна — к.м.н., доцент кафедры внутренних болезней Медицинского университета «Реавиз», заведующая отделением терапии Больницы Центросоюза РФ, Москва, e-mail: ekaterina.gorulyova@gmail.com, ORCID ID: https://orcid.org/0000-0002-7536-7937

Лобанова Елена Георгиевна — д.м.н., профессор кафедры фармакологии ФГБОУ ВО «Российский университет медицины» Минздрава России, Москва, e-mail: e.g.lobanova@mail.ru, ORCID ID: https://orcid.org/0000-0002-3426-1853

Authors Information

Polina S. Samozhenova — Postgraduate student of the Department of Therapy and Preventive Medicine Federal State Budgetary Educational Institution of Higher Education "Russian University of Medicine" of the Ministry of Health of the Russian Federation. e-mail: samozhenowapolina@gmail.com ORCID ID: https://orcid.org/0000-0002-8170-0863

Ekaterina E. Gubernatorova — Candidate of Medical Sciences, Assistant of the Department of Therapy and Preventive Medicine Federal State Budgetary Educational Institution of Higher Education "Russian University of Medicine" of the Ministry of Health of the Russian Federation, e-mail: creativeone@list.ru, ORCID ID: https:// orcid.org/0009-0009-4149-9497

Tatyana V. Adasheva — Doctor of Medical Sciences, Professor of the Department of Therapy and Preventive Medicine Federal State Budgetary Educational Institution of Higher Education "Russian University of Medicine" of the Ministry of Health of the Russian Federation, e-mail: adashtv@mail.ru, ORCID ID: https:// orcid.org/0000-0002-3763-8994

Ekaterina I. Goruleva — Candidate of Medical Sciences, Associate Professor of the Department of Internal Medicine at the Reaviz Medical University, Head of the Therapy Department at the Centrosoyuz Hospital of the Russian Federation, Moscow, e-mail: ekaterina.gorulyova@gmail.com, ORCID ID: https://orcid.org/0000-0002-7536-7937

Elena G. Lobanova — Doctor of Medical Sciences, Professor of the Department of Pharmacology Federal State Budgetary Educational Institution of Higher Education "Russian University of Medicine" of the Ministry of Health of the Russian Federation, Moscow, e-mail: e.g.lobanova@mail.ru, ORCID ID: https://orcid.org/0000-0002-3426-1853

Автор, ответственный за переписку / Corresponding author