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ОТ СИНДРОМА ШЕГРЕНА К СИСТЕМНОЙ СКЛЕРОДЕРМИИ: КЛИНИЧЕСКИЙ СЛУЧАЙ МАНИФЕСТАЦИИ ЗАБОЛЕВАНИЯ С ТЯЖЕЛОЙ ЛЕГОЧНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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From Sjogrens' Syndrome to Systemic Scleroderma: A Clinical Case of Disease Manifestation with Severe Pulmonary Arterial Hypertension

Резюме

Своевременное распознавание и лечение такого опасного осложнения системных заболеваний соединительной ткани как легочная артериальная гипертензия имеет крайне важное значение, так как данные пациенты имеют неблагоприятный прогноз.

В данной статье врачи-кардиологи демонстрируют клинический случай развития тяжелой легочной артериальной гипертензии высокого функционального класса и перикардиального выпота у пациентки 60 лет с подозрением на синдром Шегрена. Была проведена оценка клинического состояния и аутоиммунных маркеров, выполнены эхокардиография, компьютерная и магнитно-резонансная томографии, коронароангиография и зондирование правых отделов сердца, офтальмологическое тестирование, а также биопсия, ультразвуковое исследование и сцинтиграфия слюнных желез. В последующем верифицированы синдром Рейно и склередема, а также специфические иммунологические нарушения, что позволило установить диагноз лимитированной формы системной склеродермии, назначить иммуносупрессивную терапию и установить вторичный характер синдрома Шегрена.

Результаты проведенной диагностики, подтвержденные заключениями курирующих врачей, могут быть обсуждены медицинским сообществом и носят полезный прикладной характер для врачей-кардиологов, которые редко встречаются с ревматологическими заболеваниями в рутинной практике.

Ключевые слова: *Синдром Шегрена, системная склеродермия, CREST-синдром, легочная артериальная гипертензия, диагностика, клинический случай*

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

Пациентка дала согласие на опубликование данных лабораторных и инструментальных исследований в статье «ОТ СИНДРОМА ШЕГРЕНА К СИСТЕМНОЙ СКЛЕРОДЕРМИИ: КЛИНИЧЕСКИЙ СЛУЧАЙ МАНИФЕСТАЦИИ ЗАБОЛЕВАНИЯ С ТЯЖЕЛОЙ ЛЕГОЧНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ» для журнала «Архивъ внутренней медицины», подписав информированное согласие

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Abstract

Timely recognition and treatment of pulmonary arterial hypertension, a dangerous complication of systemic connective tissue diseases, is extremely important, as these patients have a poor prognosis.

In this article, cardiologists present a clinical case of a diagnostic search for the cause of severe pulmonary arterial hypertension of high functional class and pericardial effusion in a 60-year-old female patient with suspected Sjögren's syndrome. An assessment of the clinical status and autoimmune markers was performed, echocardiography, computed tomography and magnetic resonance imaging, coronary angiography and right heart catheterization, ophthalmological testing, as well as biopsy, ultrasound examination and salivary gland scintigraphy were performed. Subsequently, Raynaud's syndrome and scleredema, as well as specific immunological disorders, were verified, which made it possible to diagnose a limited form of systemic scleroderma, prescribe immunosuppressive therapy, and establish the secondary nature of Sjögren's syndrome.

The diagnostic results, supported by the opinions of the supervising doctors, can be discussed by the medical community and are of practical use for cardiologists, who rarely encounter rheumatological diseases in their routine practice.

Key words: *Sjögren's syndrome, systemic sclerosis, CREST syndrome, pulmonary arterial hypertension, diagnostics, clinical case*

Conflict of interests

The authors declare no conflict of interests

Sources of funding

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Conformity with the principles of ethics

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BP — blood pressure, CTD — connective tissue disorder, IFN — interferon, CAG — coronary arteriography, PAH — pulmonary artery hypertension, MSCT — multispiral computed tomography, SLI — systemic lupus erythematosus, SSD — systemic scleroderma, SS — Sjögren's syndrome, PATE — pulmonary artery thromboembolia

Introduction

Sjögren's syndrome (SS) is a chronic systemic autoimmune inflammatory disease, characterised by T-cell-mediated B-cell hyperactivity and cytokine production, the clinical presentation of which includes oral and ocular dryness, caused by local lymphocyte infiltration, sometimes with joint paint and fatigue. The disease can progress from asymptomatic adenopathy to systemic manifestations or even lymphoma. More often, clinical cases (up to 80 %) present with very dry mucous membranes, especially in the mouth and eyes; however, the disease may involve skin, nose, throat, and vagina. SS may present without significant involvement of the salivary glands, instead affecting other exocrine glands or systemic organs. This condition is called extraglandular SS; it has been described in literature sources and is reported in up to 20 % of patients with primary SS [1].

Historically, SS was classified into two categories: where symptoms appear independently (primary SS); and where symptoms go together with other systemic autoimmune diseases (secondary SS). The most common SS-associated conditions are rheumatoid arthritis, systemic lupus erythematosus (SLE) and systemic scleroderma (SSD) [2]. Currently, clinical studies aim mostly at primary SS [3]. Based on the most robust evidence from large population-based studies, the prevalence of primary SS is estimated to range from 0.01 % to 0.05 %. This condition affects primarily women; the women-to-men ratio varies from 9:1 to 28:1. Disease onset typically occurs between 40 and 50 years of age; in cases where the diagnosis is established in younger patients, at around 35 years of age, the disease often presents with fever and lymphadenopathy [4]. The majority of non-HLA genetic variants related to susceptibility to primary SS are associated with interferon (IFN) pathways or IFN-stimulated genes. Recent studies show that the long non-coding RNA XIST (X-inactive specific transcript), which is specific to women, is a unique and abundant source of ligands of Toll-like receptor (TLR) 7 and IFN activator in SLE patients. This gender-related difference can be the cause of gender-based predisposition not only to SLE, but also to primary SS [5].

Pulmonary artery hypertension (PAH) is a rare manifestation of SS and is a significant cause of death in such cases. SS patients have a higher risk of PAH, which is likely to be associated with chronic inflammation, vascular dysfunction and immune-mediated endothelial damage, which can contribute to higher pressure in the pulmonary artery and right ventricular overload [6]. By the time the classical symptoms of PAH become apparent, it is often already too late, as morphological and structural changes in the pulmonary vasculature have already occurred.

Clinical Case Report

Patient N., 60 years of age, was admitted to the hospital with suspected pulmonary artery thromboembolia (PATE). The patient complained of shortness of breath at minimal physical activity and at rest, with shortness of breath getting worse when lying on her left side; edematic lower extremities; constricting, pressing retrosternal pain at minor physical activity; dry mouth.

Her medical history did not show any neurological or rheumatologic diseases, cramps or head injuries. The family history did not indicate any autoimmune diseases. Also, there were no data on the use of any anticholinergic medications. The patient denied a history of mucosal ulcers, fever, arthralgia, photosensitivity, thrombosis or thrombophlebitis, and miscarriages.

Her medical history included an adenoma of the right thyroid lobe, cardia insufficiency, cardia-fundal prolapse, a sliding hiatal hernia, and chronic antral gastritis. In 2006, she underwent cholecystectomy due to an exacerbation of calculous cholecystitis. The patient had also been diagnosed with arterial hypertension (AH), with blood pressure values reaching up to 160/100 mm Hg. She did not take antihypertensive medications regularly. Since April 2025, the patient had been having episodes of pronounced shortness of breath. Subsequently, she noted decreased exercise tolerance and shortness of breath during walking at a usual pace. On 19 August 2025, she was evaluated by a local cardiologist, and ischaemic heart disease was suspected. The patient was advised to undergo coronary arteriography (CAG), and the following medications were prescribed: Torasemide 10 mg, Lisinopril 5 mg, Ivabradine 2.5 mf twice daily, isosorbide mononitrate 40 mg twice daily. Later, amlodipine and trimetazidine were added. The patient did not notice any improvement from the therapy.

In September 2025, the patient noted progressive worsening of shortness of breath, which began to occur after walking approximately 10 steps at a slow pace, as well as a marked decline in exercise tolerance, lower extremity oedema, and pressing, constricting retrosternal pain. The patient reported improvement in her shortness of breath and chest pain when lying in the prone position or on her right side. On September 27, 2025, multispiral computed tomography (MSCT) of the chest was performed, revealing signs of moderate hydropericardium (pericardial effusion up to 15 mm). Areas of ground-glass opacification within the lung parenchyma could not be excluded, although assessment of the pulmonary parenchyma was limited. During the outpatient visit, an ambulance was called, and the patient was transported to Regional Clinical Hospital No. 1 in Tyumen.

Objective findings: the patient's consciousness was clear. The body mass index was 28 kg/m2. The body temperature was 36.4 °C. The oral mucosa was clean, pink, and dry, with no defects. The skin was clean, pale. Marked peripheral oedema involving the feet and lower legs extending up to the knees was present. Respiratory rate was 20 breaths per minute. Oxygen saturation was 94 % while receiving supplemental oxygen. Breath sounds were vesicular but diminished at the lung bases. No crackles or wheezes were auscultated. Shortness of breath was mixed at rest. The heart rate was 96 beats per minute. The pulse was rhythmical. Blood pressure measured in the left arm was 170/90 mm Hg. Heart sounds were regular and muffled, with an accentuated second heart sound over the pulmonary artery. No cardiac murmurs were auscultated. The tongue was dry and uniformly coated with a thin film. The abdomen was soft and non-tender. The liver edge was palpable at the costal margin. Bowel and bladder function were unremarkable.

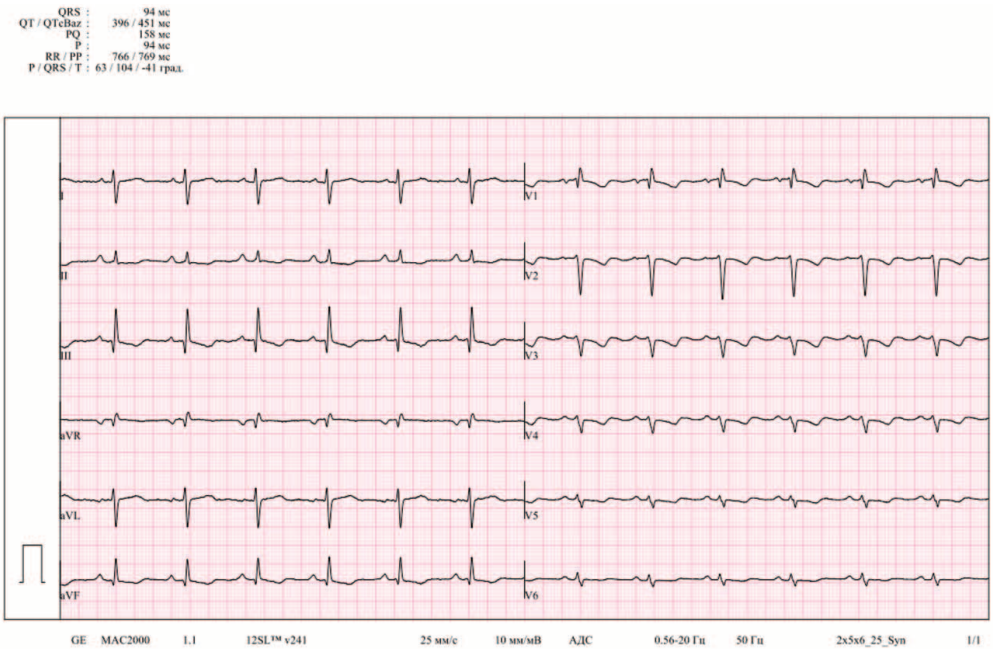


Figure 1. *Electrocardiogram from October 1, 2025.*

The patient had not undergone gynaecological examination; however, she denied vaginal dryness.

Given the elevated troponin levels (troponin I, 121 ng/L; reference range, 0.1–20.3 ng/L), a diagnostic CAG was performed to further assess the coronary anatomy. CAG dated September 30, 2025 did not reveal any visible pathology of the coronary arteries. Electrocardiography demonstrated sinus rhythm, a vertical electrical axis of the heart, incomplete right bundle branch block, low QRS voltage in the precordial leads, an S-wave pattern in the chest leads, and diffuse repolarisation abnormalities (Figure 1).

Table 1. *Patient's blood parameters from October 1, 2025.*

Test	Meaning	Reference
Sodium uretic peptide	3,298 pg/ml	0.00–464.20 pg/mL
Procalcitonin	1.1 ng/ml	0.000–2.000 ng/mL
C-reactive protein	0.657 mg/dl	< 0.5 mg/dL
Free thyroxine	12.6 pmol/l	9–22 pmol/L
Thyroid-stimulating hormone	0.455 µIU/ml	0.350–5.100 µIU/mL
CA 125	17.9 U/ml	0.0–35.0 U/mL
CA 19-9	14.11 units/ml	0.00–40.00 U/mL
Carcinoembryonic antigen	1.5 ng/ml	Non-smokers 0–5 ng/mL Smokers 0–10 ng/mL

CA 125 — cancer antigen 125, CA 19-9 — cancer antigen 19-9.

Table 2. *Immunological examination of the patient from October 9, 2025.*

Test	Meaning	Reference
Rheumatoid factor	5.9 IU/ml	0.1–14.0 IU/ml
Antinuclear antibody screening (ANA)	2.979 Positive	< 0.9 — Negative (normal)
Anti-double-stranded DNA antibodies	9.62 IU/ml	0.00–25.00 IU/ml
Anti-SS-A 52 antibodies	10 IU/ml Borderline (+)	<10 IU/ml
Anti-nucleosome antibodies	0.00 IU/ml Not detected	Absence
Anti-Scl-70 antibodies	0.00 IU/ml Not detected	Absence
Antibodies to the SS-A/Ro family	0.00 IU/ml Not detected	Absence
Antibodies to SS-B (La) antigens	147 IU/ml Strongly positive (+++)	Absence
Antibodies to RNP (ribonucleoproteins)	0.00 IU/ml Not detected	Absence
Antibodies to the Jo-1 (histidine) antigen	0.00 IU/ml Not detected	Absence
Anticentromere antibodies CENT-B	0.00 IU/ml Not detected	Absence
Anti-Sm (Smith)	0.00 IU/ml Not detected	Absence
Anti-histone antibodies (Histone)	0.00 IU/ml Not detected	Absence
Antibodies to ribosomal protein P	0.00 IU/ml Not detected	Absence

Because of her severe condition, the patient was admitted to the ICU. Complete blood count revealed mild chronic iron deficiency anaemia (haemoglobin, 99 g/L). Serological tests for HIV, viral hepatitis, and respiratory viruses were negative. The blood test results most relevant to the differential diagnosis are presented in Table 1. Thyroid and renal function tests, as well as urinalysis and stool studies, were within normal limits.

A direct Coombs test was performed and yielded a positive result. The patient was subsequently evaluated by a rheumatologist and underwent testing for additional autoimmune markers, which revealed positive antinuclear antibodies (ANA) and anti-La (SSB) antibodies. In contrast, rheumatoid factor, anti-double-stranded DNA antibodies, anti-ribosomal P protein antibodies, anticentromere antibodies, anti-Scl-70 antibodies, and anti-ribonucleoprotein antibodies were negative (Table 2).

Table 3. *Echocardiography dated from September 30, 2025.*

Parameters	Value
Mitral valve:	Thin leaflets, mitral valve annulus 2.6 cm. Regurgitation (+): Grade 1.
Ascending aorta:	Walls are thickened; Aortic base size: 1.9 cm; Ascending aorta size: 3.6 cm.
Aortic valve:	Thick leaflets, pressure gradient 4.5 mmHg.
Tricuspid valve:	Thin leaflets, PGr TR — 60 mmHg; Regurgitation (++-+++): Grade 2-3, central;
Pulmonary artery size:	3.0 cm
Pulmonary valve: Estimated PASP:	The valves are thin; 75 mmHg
Left atrium in M mode:	4.5 cm
LA volume in B mode:	65 ml
LVIDd:	3.9 cm
LVIDs:	2.6 cm
ESV:	64 ml
EDV:	26 ml
SV:	38 ml
Simpson ejection fraction:	60 %
IVS thickness in diastole:	0.9 cm
LV posterior wall thickness:	0.8 cm
Presence of pericardial effusion:	circular — up to 16-18 mm
PSV:	8 mm
RA area:	26.0 cm^2
IRAV:	55 ml/m^2
RV/LV ratio:	1.3
Shape index (eccentricity) EL:	1.9
TAPSE/e PASP:	0.15 mm/mmHg
RVOT acceleration time:	65 ms
IVC diameter:	2.3 cm, decreases less than 30 %

Note: EDV — end-diastolic volume; ESV — end-systolic volume; IRAV — indexed right atrial volum; IVC — inferior vena cava; IVS — interventricular septum; LA — left atrium; LV — left ventricle; LVIDd — left ventricular internal dimension in diastole; LVIDs — left ventricular internal dimension in systole; PASP — pulmonary artery systolic pressure; PSV — peak systolic velocity; RA — right atrium; RV — right ventricle; RVOT — right ventricular outflow tract; SV — stroke volume; TAPSE/ePASP — tricuspid annular plane systolic excursion/ estimated pulmonary artery systolic pressure.

On October 1, 2025, the patient underwent an ultrasonic Doppler examination of the lower extremity veins, which did not reveal any intravascular elements in the superficial and deep veins of the legs.Abdomen ultrasound performed on October 1, 2025 showed hepatomegaly and diffuse changes in the liver.On October 8, 2025, spirometry was conducted, which showed impaired pulmonary function (obstruction). A mild obstruction was reported. Reduced airflow was observed at the level of the distal bronchi. The bronchodilator test with salbutamol was negative, with a 1 % increase in FEV1. Echocardiographic findings obtained on 30 September 2025, are presented in Table 3.

Given the presumptive diagnosis at admission and as part of the differential diagnostic work-up, contrast-enhanced MSCT of the lungs was performed to exclude malignancy and rare conditions, including interstitial lung diseases. The findings are shown in Figures 2, 3, and 4.

Given the complaints of dry mouth, the patient was examined for diabetes mellitus, which was ruled out. A salivary gland ultrasound examination was performed on October 14, 2025, which showed diffuse changes in the salivary glands and mildly enlarged parotid glands; no hypoechogenic areas were observed. Later, right heart catheterisation (RHC) was performed, and the haemodynamic data are presented in Table 4.

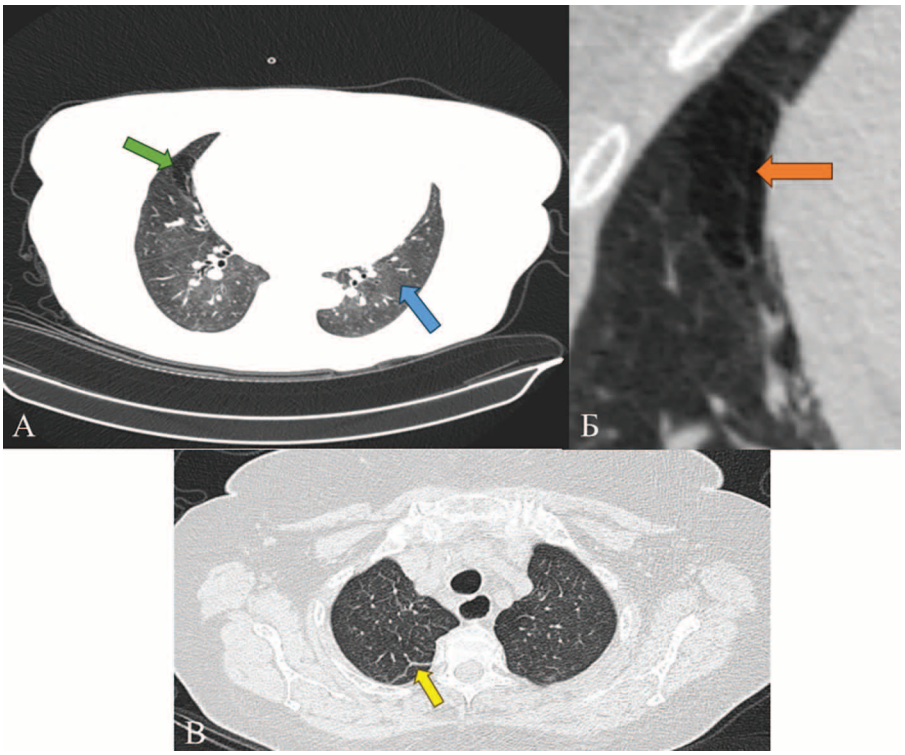


Figure 2. *MSCT pulmonary angiography, native phase scanning, pulmonary electron window, axial projection: A — mosaic density of lung tissue is determined, caused by the presence of areas of normal (blue arrow) and increased (green arrow) airiness associated with uneven blood flow. B — in the area of increased airiness, narrowing of the vessel lumen is visible (orange arrow), associated with obstruction or hypoxic vasostriction. C — at the level of the apical segments on both sides, uniform thickening of the interlobular septa is visible (yellow arrow), associated with venous congestion in the pulmonary circulation.*

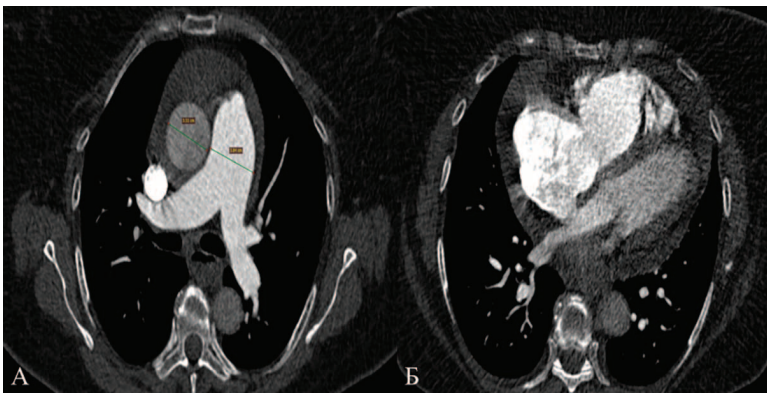


Figure 3. *MSCT pulmonary angiography, pulmonary artery contrast phase, soft tissue electron window, axial projection: A — a dilated main pulmonary artery is visible, as well as an increase in the ratio of the pulmonary artery diameter to the diameter of the ascending aorta to 1.1. B — The right ventricle and right atrium are significantly enlarged compared to the left chambers of the heart. In addition, a moderate amount of pericardial effusion is observed.*

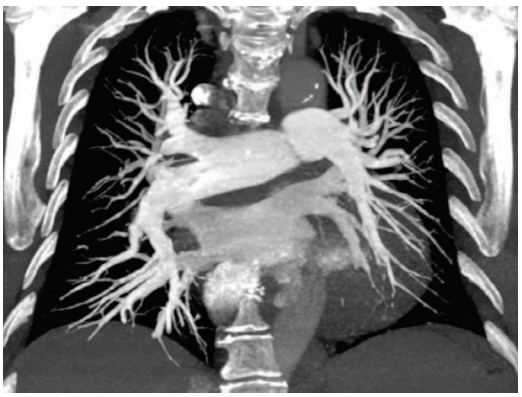


Figure 4. *MSCT pulmonary angiography, pulmonary artery contrast phase, soft tissue electron window, coronary projection with MIP reconstruction (maximum intensity projection): no signs of acute or chronic pulmonary embolism.*

Inpatient treatment consisted of Dapagliflozin 10 mg, Spironolactone 25 mg, Carvedilol 6.25 mg twice daily, Prednisolone 5 mg 2 tablets @ 07:00 am; no other cardiotropic drugs were prescribed due to predisposition to hypotonia. Given the diagnostic complexity of the case, the patient's medical data were referred for a telemedicine consultation to the E.I. Chazov National Medical Research Centre in order to determine the optimal further management strategy. The patient stayed in the hospital for one and a half months with no significant improvement in her condition; she was discharged on her own request. Later, an expert opinion was received stating absence of any solid evidence of chronic thromboembolic pulmonary hypertension. Immunological abnormalities are noteworthy, and a salivary gland biopsy together with ophthalmologic testing is required to rule out SS. According to right heart catheterisation findings, severe precapillary pulmonary hypertension was confirmed (pulmonary artery wedge pressure: 10 mm Hg); however, there was no indication that diuretic therapy had been discontinued. Taking into account test results, mixed origin pulmonary hypertension cannot be ruled out, including pulmonary veno-occlusive disease, (post/precapillary type, since there are risk factors of diastolic dysfunction). Currently, supportive therapy is recommended, while PAH-specific therapy is associated with a risk of life-threatening complications.

The patient was notified of the expert opinion and was referred for an additional examination by an eye specialist and dentist (in outpatient settings). Ophthalmologic examination revealed a positive Schirmer test result (3 mm after 5 minutes). A biopsy of the submandibular gland was performed (see Figure 5).

Salivary gland scintigraphy was also performed and demonstrated no reduction in radioactive tracer uptake in either the parotid or the submandibular glands (see ***Figure 6***).

Radiopharmaceutical retention was observed in the right lobe of thyroid gland, which is in line with the history of adenoma. The patient was referred to a MRI of her neck soft tissue for anatomical details and confirmation of the gland biopsy results, which can be false negative (see ***Figure 7***).

On December 30, 2025, the patient lost consciousness in the stairwell; loss of consciousness was not accompanied by unprompted defecation and urination. The patient gained consciousness within minutes and called for an ambulance, which transported her to the outpatient therapeutic ward. According to the patient, she had eight similar episodes of syncope last month. The patient was examined by a neurologist, who ruled out the neurogenic nature of syncope. Given the past medical history, the patient was admitted to the rheumatology ward. She underwent another immunological testing, which revealed antinuclear antibodies; immunoblot testing showed positive anti-SS-A/Ro, SS-B (La) antibodies and anticentromere antibodies CENT-B. The patient was diagnosed with systemic scleroderma, specifically the limited form (CREST syndrome), associated with secondary Sjögren's syndrome, Raynaud's phenomenon, sclerodactyly (non-pitting swelling of the fingers), and oesophageal dysmotility manifested by dysphagia. Prednisolone dose titration therapy was initiated.

Table 4. *Right heart catheter probing (Swan-Ganz catheter) from October 5, 2025.*

Parameters	Value
Systolic BP:	125/80/90 mmHg (cuff)
RA Pressure:	8/4 (mean 8) mmHg
RV Pressure:	59/10 (mean 12) mmHg
PA Pressure:	62/31 (mean 33) mmHg
PAWP:	mean 10 mmHg
Cardiac Output:	0.511 ml/min
Cardiac Index:	2.88 l/min*m^2
PA SO2:	69.0 %
Pulmonary vascular resistance:	361 dynes/s*cm^2 or 5 Wood Units
Total pulmonary resistance:	518 dynes/s*cm^2 or 6 Wood Units
After iloprost inhalation, 10 minutes Hemodynamic parameters were measured and calculated:	
Systolic BP:	125/85/91 mmHg (cuff)
AP Pressure:	3/0 (mean 2) mmHg
RV Pressure:	47/5 (mean 8) mmHg
PA Pressure:	49/24 (mean 25) mmHg
PAWP:	mean 6 mmHg
Cardiac Output:	0.65 ml/min
Cardiac Index:	3.67 l/min*m^2
PA SO2:	76.0 %
Pulmonary vascular resistance:	234 dynes/s*cm^2 or 3 Wood Units
Total pulmonary resistance:	308 dynes/s*cm^2 or 4 Wood Units

Note: BP — blood pressure; PA — pulmonary artery; PAWP — pulmonary artery wedge pressure; RA — right atrium; RV — right ventricle; SO2 — saturation.

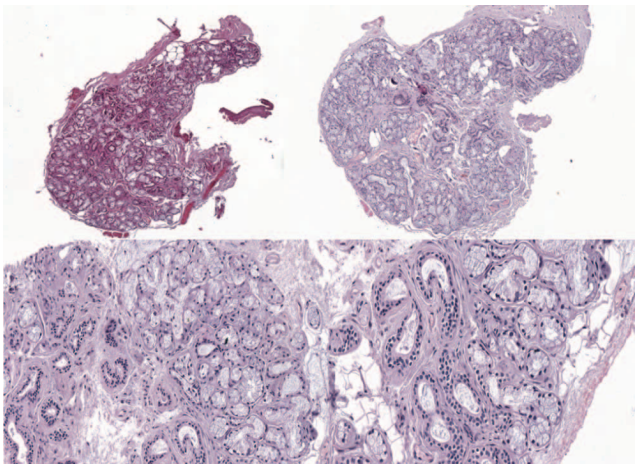
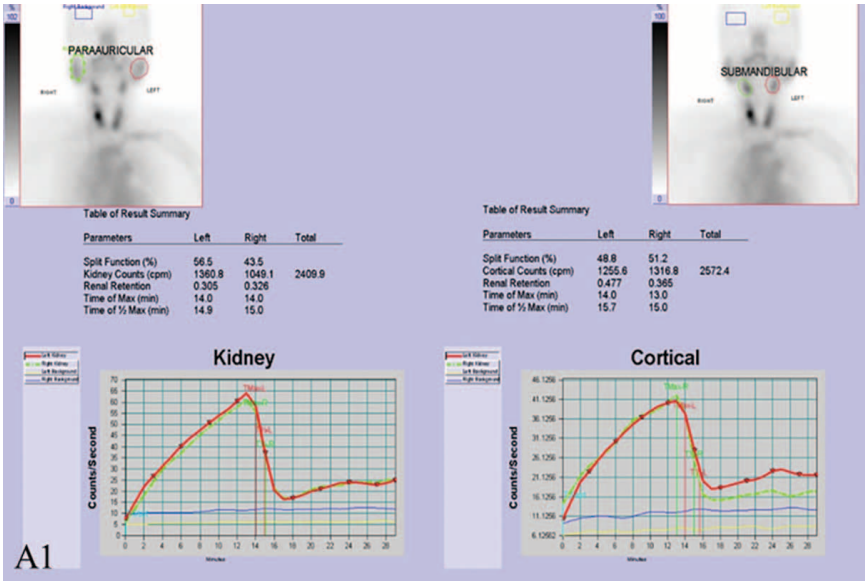
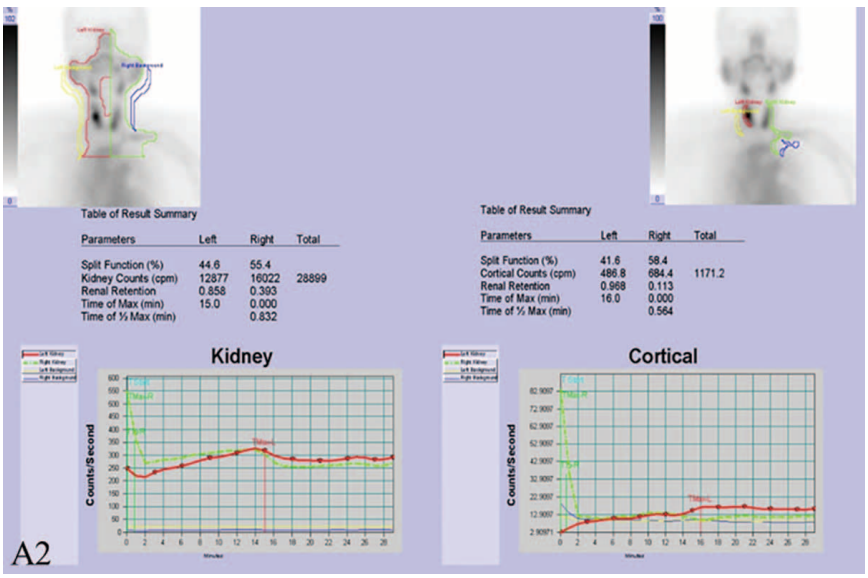


Figure 5. *Microscopy of salivary gland biopsy material. No signs of acinar atrophy or inflammatory infiltration in the gland parenchyma are demonstrated. Morphological activity index 0.*





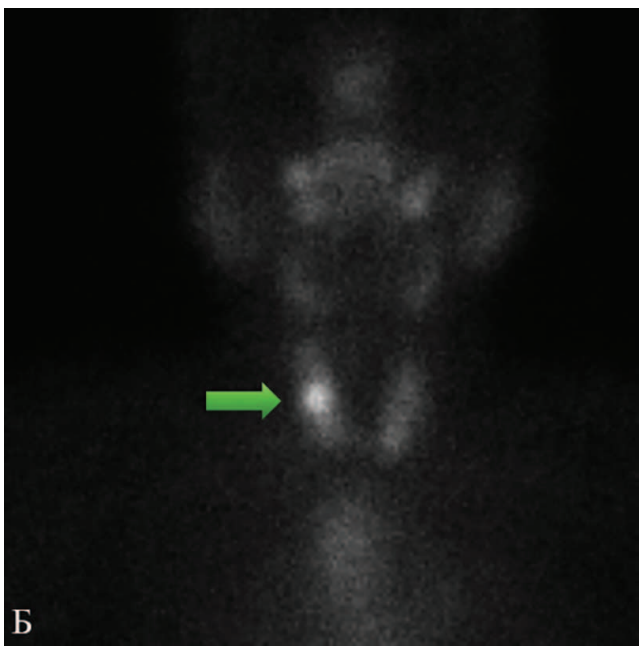


Figure 6. *Scintigraphy of salivary glands with lemon juice loading. A1,2 — no signs of dysfunction of the parotid and submandibular salivary glands. B — a focus of radiopharmaceutical hyperfixation is visualized in the projection of the middle third of the right lobe of the thyroid gland (green arrow).*

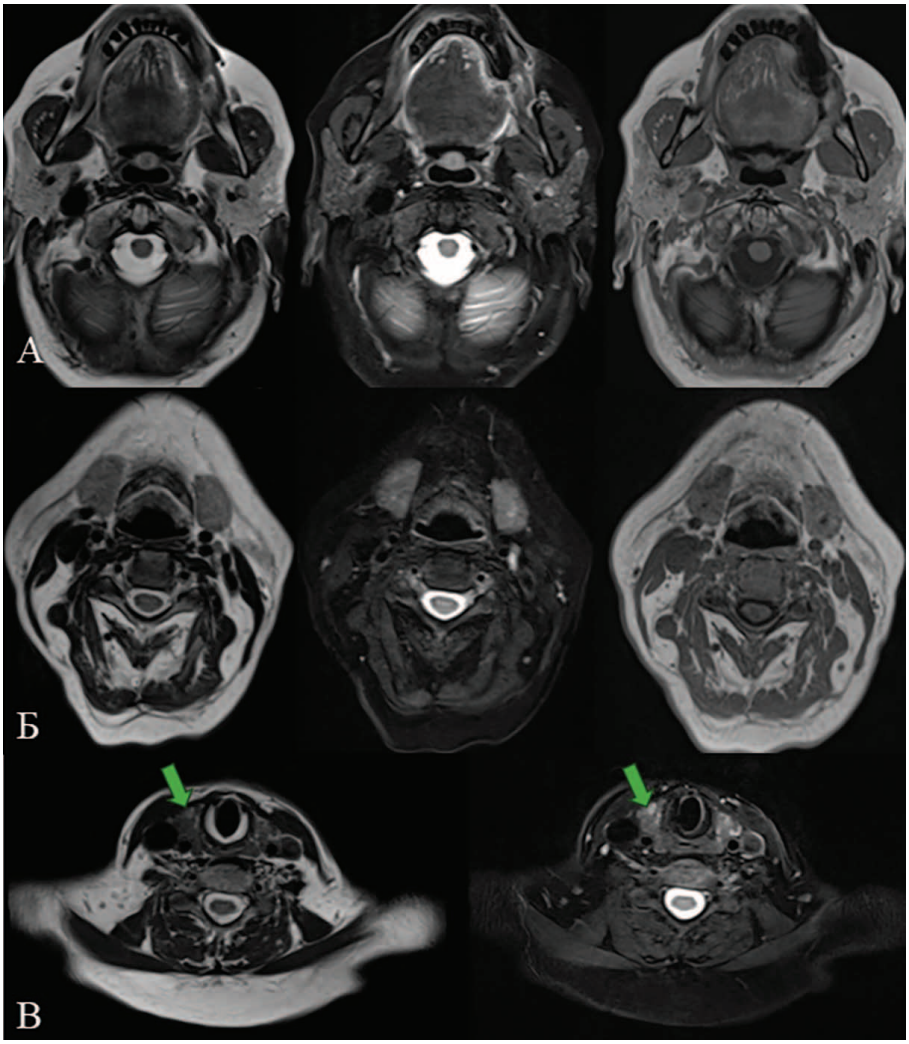


Figure 7. *MRI of the soft tissues of the neck at the level of the parotid salivary glands (A), at the level of the submandibular salivary glands (B), at the level of the thyroid gland (C), T2-weighted image pulse sequences, T2-weighted image with signal suppression from fat tissue and T1-weighted image, axial projection: the salivary glands appear symmetrical, not enlarged, have clear contours and a uniform structure; a hyperintense nodule is visible in the right lobe of the thyroid gland (green arrow).*

Discussion

Overlap syndrome is a concept describing an overlap between symptoms of several diseases in one patient. The patient indeed meets the criteria for several pathologies, hence a clear diagnosis is challenging. According to the 2016 ACR/EULAR classification criteria, a diagnosis of Sjögren's syndrome is established when the total score is 4 or higher. These criteria are applicable to patients who have at least one symptom of ocular or oral dryness, as assessed by the AECG questionnaire, or who have positive findings in at least one domain of the ESSDAI suggestive of Sjögren's syndrome, provided that no exclusion criteria are present (e.g., previous head and neck radiotherapy, hepatitis C, HIV, sarcoidosis, or amyloidosis) [7]. ESSDAI is the Sjögren's Syndrome Disease Activity Index developed by EULAR, and the score of <5 indicates low disease activity [8].

In this case, the suspicion of SS was justified, as in addition to mucosal dryness, the patient had positive findings in several ESSDAI domains, namely pulmonary involvement (3 points) and haematological involvement (2 points), indicating that the disease activity was not low. According to the 2016 EULAR/ACR classification criteria, the patient scored 4 points, even without corneal and conjunctival staining, which was not performed; therefore, the diagnosis of Sjögren's syndrome was considered justified. However, given the presence of anticentromere antibodies CENT-B, Raynaud's phenomenon, scleredema and oesophageal dysfunction, the secondary nature of SS, caused by limited CTD, cannot be ruled out.

A study based on the French National Health Insurance Database demonstrated that among connective tissue disorders (CTDs) associated with SS, systemic lupus erythematosus (SLE) accounted for 28 % of cases, rheumatoid arthritis for 53 %, and SSD for 13 % [9]. Groups with various CTDs demonstrate some differences. Patients with SLE and SS have the following characteristics: relatively late onset of the disease; high incidence of Raynaud's phenomenon and joint symptoms; as well as a high positive response to autoantibodies (especially anti-SS-A/SS-B antibodies). The most common symptom is oral sores [10].

SSD is also a multisystem autoimmune connective tissue disorder characterised by microvascular injury, dysregulation of both adaptive and innate immunity, and progressive fibrosis of the skin and internal organs.

Common clinical manifestations of SSD include Raynaud's phenomenon, skin thickening, calcinosis, telangiectasias, gastroesophageal reflux disease, gastrointestinal dysmotility, arthritis, interstitial lung disease, and pulmonary hypertension. Among these manifestations, Raynaud's phenomenon, characterised by vasospasm of the fingers, is an early clinical sign that typically precedes the development of fibrotic changes, suggesting that vascular involvement is an early manifestation of the disease and plays a key role in its initial pathogenesis. Pulmonary hypertension is usually a later sign of SSD, which manifests 10–15 years after diagnosis [11]. However, in the present case, upon hospital admission the patient did not present with Raynaud's phenomenon and did not have any typical complaints. Similar to SS, SSD is more common in women than in men, with the women-to-men ratio being 3–4:1; however, in men SSD results in poorer outcomes [12].

According to the WHO classification, CTD-associated PAH is included in group 1 of pulmonary hypertensions. Among the group 1 subtypes associated with connective tissue diseases, SSD accounts for approximately 75% of all cases of CTD-associated PAH [13]. PAH has been reported to occur in 8–12% of patients with SSD and represents one of the leading causes of mortality in this population. Together with pulmonary fibrosis, it accounts for up to 60% of all SSD-related deaths [14]. The median survival is approximately 4 years. Studies have demonstrated that the combination of early disease detection through improved screening recommendations and the use of PAH-specific therapies improves survival in patients with SSD-associated PAH, a condition that is otherwise associated with a poor prognosis [15].

It appears that SS and SSD in the present case are the elements of one pathological autoimmune process. A combination of these pathologies has been described in literature sources. Of particular interest is the study by Drosos et al., which described a cohort of 23 patients with CREST syndrome who underwent clinical, histopathological, and serological evaluation for the presence of Sjögren's syndrome. Fourteen patients were found to have positive findings consistent with Sjögren's syndrome. No significant differences were observed between these patients and the remaining nine individuals. In addition, the characteristics of patients with CREST syndrome were compared with those of 29 randomly selected patients with primary SS. Parotid gland enlargement was observed significantly more frequently in patients with primary SS than in those with CREST syndrome ($p < 0.01$). Virtually none of the patients with concomitant CREST syndrome and SS had detectable anti-Ro(SSA) or anti-La(SSB) antibodies [16]. However, in the study by Oddis et al., anti-SSA(Ro) antibodies were identified in the serum of five out of six patients with the CREST variant of systemic scleroderma and features of SS [17]. If the presence of SS in our patient is excluded and the condition is considered a "pure" form of SSD with an initial presentation dominated by visceral manifestations, particularly PAH, such a presentation would be uncommon and would also be of considerable practical interest to clinicians.

Conclusion

The treatment outcomes of SSD-associated PAH remain unsatisfactory compared with those observed in patients with SSD overall. Therefore, new diagnostic and treatment approaches are required. Given the substantial role of specific components of the immune system in disease pathogenesis, a promising therapeutic approach in the future will likely involve the combination of targeted immunomodulation with combination vasodilator therapy. Prospective studies involving patients with SS, SSD and PAH have not yet been conducted. Therefore, studies focusing on the early initiation of therapy would be important to determine whether vasodilators may exert disease-modifying effects and whether their use should be started earlier, before overt signs of organ damage develop. Clinicians should maintain a high index of suspicion and carefully evaluate patients with PAH for the possible presence of both SSD and SS, as these conditions may remain undiagnosed during routine assessment. An erroneous diagnosis of idiopathic PAH may deprive patients with an underlying connective tissue disease of the opportunity to receive immunosuppressive therapy and to benefit from the most appropriate combination of vasodilator agents.

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