

Diagnosics issues of systemic sclerosis on the example of clinical case

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Introduction

- **Systemic sclerosis (SSc)** is a rare chronic systemic disease of the connective tissue, presenting with generalized microangiopathy, immune dysregulation and activation of fibrosis.
- The frequency of SSc varies from 2.3 to 10 people per 1 million.
- Features of SSc are: high level of patient-to-patient clinical variability, multiple organ lesions and a progressive course leading to disability.
- Early diagnosis of SSc allows prescription of an adequate therapy in a timely manner, which can slow the progression of the disease and improve the quality of life of patients.



Our patient

- **Name: K. G. M.**
- **Sex: Female**
- **Age: 39 years**
- **Location: Kharkiv**
- **Occupation: Not working, disability 3d degree.**

Complaints

- **Pain and swelling of wrists** (more pronounced at night, lasts up to 5-6 hours, subside at rest), **stiffness of wrists, inability to perform fine handwork**;
- **Changing of skin color of hands (pale, bluish), chilliness and numbness of the hands and feet, aggravated in cold** (wears gloves and warm socks all the time)
- **Pain in the knee and elbow joints with stiffness up to 2 hours**;
- **Constant feeling of skin tightness especially on the face, inability to open mouth widely, changing of voice**;
- **Difficulty of swallowing of solid foods, constant heartburn**;
- **General weakness, fatigue, periodical dyspnea, decreased muscle strength, hair loss; periodical fever up to 37,5C.**
- **Also notes episodes of intermenstrual bleeding.**

Anamnesis morbi

- 2008 - after childbirth first appeared chilliness and numbness along with paleness and blueness of the fingers in the cold. Was consulted by district physician – diagnosis was not made, recommendations were to avoid hypothermia and wear gloves, treatment was not prescribed.
- 2008-2013 – state of the patient progressively deteriorated, appeared pain in wrists, shoulder, knee, elbow joints, decreased muscle strength, inability to perform fine handwork, difficulty in swallowing of solid food, feeling of skin tightness on the face, hair loss, changing of voice, weight loss.
- Jan 2013 - a severe deterioration in general state after a URVI: pain in the joints of the hands became more severe, appeared deep non-healing ulcers on the fingertips.
- Sept 2013 - was consulted by a surgeon with diagnosis: Felon of the distal phalanx of the left thumb, was treated with antibiotics but without significant effect. Was referred to rheumatologist.

Anamnesis morbi (2)

- Oct 2013 – inpatient treatment in rheumatological department of the hospital #28 with diagnosis: systemic sclerosis, stage II, subacute course, activity II stage, with damage to the skin (edema, induration), blood vessels (Raynaud syndrome, ischemia III degree), joints (polyarthrititis with predominant lesion of the hands, wrists, elbow, knee, feet joints, Röntgen changes of II degree, functional impairment I st.), esophagus (esophagitis). Was administered methylprednisolone (20 mg/day). D-penicillamin was prescribed but the patient refused to use it due to her financial issues.
- Dec 2013 – progression of Raynaud phenomenon despite of treatment and osteolysis of the distal phalanx of the left thumb.
- Patient has planned hospitalization 2 times per year. Takes constantly methylprednisolone, amlodipine, naftidrofuryl, aspirin.

Anamnesis vitae

- 1 pregnancy, 1 child. Married;
- **Not working since 2015 (previously worked as a seamstress).**
- Postponed diseases: URVI, epidemic parotitis, chicken pox in childhood, **pneumonia (May 2016);**
- **Operations: cataract of both eyes (March 2016).**
- Menses from 14 years, **episodes of intermenstrual bleeding started 1 year ago, patient didn't seek for doctor consult**
- Tuberculosis, diabetes, viral hepatitis, allergic reactions denies.
- Bad habits denies.
- Hereditary history is not burdened.
- Physical activity: sedentary lifestyle.

Objective status (1)

- General condition of the patient is of moderate severity, clear consciousness, posture is active, patient is hyposthenic;
- Weight - 50 kg, height – 164 cm. BMI – 18,6 kg/m²; t - 36.8°C.
- Skin: pale, clean, dry, tightened, mask-like facial features, expressionless, radial furrowing around the mouth, incomplete opening of the mouth.
- There is pallor, cyanosis of the skin of the hands and feet, their swelling, hardening of the skin, hypothermia. On the distal phalanges of the fingers – pitting scarring about 2-4 mm.
- Mucous membranes: pale-pink, tongue is covered with white plaque; lymphatic nodes are not palpated; peripheral pitting edema is absent.
- Thyroid gland: not palpable. There is hoarseness of voice.

Objective status (2)

- Lungs: resonance percussion sound, **harsh breathing over both lungs fields**, RR -18/';
- Heart borders on percussion are not enlarged, on auscultation heart tones are clear, loud, rhythmic; BP - 110\70 on both arms, **radial pulse is weakened**, synchronous, rhythmic at 74bpm.
- Abdomen: **epigastric tenderness on palpation**. Liver at the costal margin, painless; spleen is not palpable.
- Tapping sign - negative on both sides. Urination is free, painless.
- Musculoskeletal system:
- **Hands: hypothermia, cyanosis of the fingers. Thickening, swelling and induration of the skin, smoothed contours of the metacarpophalangeal, carpometacarpal, wrist joints, with pain on palpation, reduced muscular strength - 3 points; flexion – 70%. Defect of distal phalanx of the left thumb. Pitting scarring of the fingertips.**

Objective status (3)

- **Feet:** hypothermia, cyanosis, puffiness, thickening, induration of the skin of the toes, tenderness on palpation.
- Other joints are not visually altered, there is slight tenderness on palpation of the knee and elbow joints, soft tissue swelling is absent, skin color and skin temperature over the joints is not changed.
- Range of movements in joints – see table 1.

Table 1.

Type of movement	Wrist joints	Elbow joints	Knee joints	Ankle joints
Extension/flexion	Right: 45°/40° Left: 50°/40°	Right: 180°/40° Left: 175°/40°	Right: 180°/40° Left: 180°/40°	Right: 60° /100° Left: 60° /110°
Normal (Extension/flexion)	65°/75°	180°/40°	180°/40°	70°/130°

Objective status (4)



Pic 1. “Mouse face”



Pic 2. Raynaud phenomenon, defect of distal phalanx of the left thumb, thickening, swelling, induration of the skin, smoothed contours of the joints

Plan of survey

- Full blood count, urinalysis
- Biochemical panel (fasting plasma glucose, AST, ALT, urea, creatinine, total protein, calcium, potassium, sodium, chlorides, 25(OH)D, CRP, seromucoid, sialic acids)
- Serological panel (ANA, anti-SS-A 52/60, anti-Sm/RNP, anti-RNP, anti-Scl-70, anti-Jo-1, anti-dsDNA, ACA)
- Chest X-ray, X-ray of wrists and hands
- Upper GI tract radiography
- Upper GI endoscopy
- Ultrasound of of abdominal organs, kidneys
- ECG, EchoCG
- Rheovasography of the vessels of the upper limbs
- Consults of gastroenterologist, vascular surgeon, gynecologist

Full blood count

Options	Results	Normal range
Hemoglobin, g/L	143	130,0 – 160,0
Erythrocytes $\times 10^{12}/l$	4,56	3,7-4,7
Color index	0,94	0,85 – 1,15
Leukocytes $\times 10^9/L$	14,8	4,0 – 9,0
ESR, mm/h	17	2-15
Stab neutrophils, %	2	1-6
Segmented neutrophils, %	59	47-72
Eosinophils, %	3	0,5-5,0
Basophils, %	0	1-1,0
Lymphocytes, %	32	19-37
Monocytes, %	4	3-11

Conclusion: leucocytosis, increased ESR,

Urine analysis

Options	Results	Normal range
Specific gravity	1,013	1,001-1,040
pH	6,0	5,0-7,0
Protein, g / l	Not detected	to 0.033
Glucose	Not detected	absent
Leucocytes, cells/hpf	1-3	6-8
Epithelium, cells/hpf	1-2	≤15-20
Bacteria	Not detected	absent

Conclusion: all parameters within the normal range

Biochemical panel

Options	Results	Normal range
Total protein, g/l	78	54-78
Urea, mmol/l	2,9	1,7-8,3
Creatinine, mmol/l	0,059	0,7-1,4
Sialic acids	140	135-200
Seromucoid, U	0,130	0,13-0,2
CRP, mg/l	11	<5
FPG (fasting plasma glucose), mmol/l	5,5	3,3-5,5
AST, U	23	<41
ALT, U	24	<40
Ca, mmol/l	2,2	2,2-2,5
P, mmol/l	1,2	0,8-1,4
25(OH) D ng/ml	30,12	30,0-100,0

Conclusion: increased level of CRP

Serological panel

Options	Results	Normal range
ANA	positive	
anti-SS-A 52/60 (U1-RNP)	6,8 AI	N<1 AI
anti-Sm/RNP	8 AI	N<1 AI
anti-RNP	8 AI	N<1 AI
anti-Scl-70	0,3 AI	N<1 AI
anti-Jo-1	0,2 AI	N<1 AI
anti-dsDNA	1 AI	N<4 AI
ACA	0,2 AI	N<1 AI

Conclusion: increased levels of ANA, anti-SS-A 52/60, anti-Sm/RNP, anti-RNP

Data of instrumental survey (1)

- ECG - sinus rhythm, HR 71 bpm, **left anterior fascicular block of bundle of Hiss;**
- EchoCG: chambers of the heart are not enlarged, myocardial contractility is satisfactory, ejection fraction – 58%;
- Chest X-ray: in lungs - infiltrative lesions are absent, sinuses of the lungs without pathological changes, **there are signs of pneumofibrosis,** size and shape of the heart are normal;
- Upper GI tract radiography – **gastroesophageal, duodenogastral reflux, esophagitis, sliding axial hernia of 1st degree;**
- Upper GI endoscopy: **gastroesophageal reflux with esophagitis; duodenogastric reflux, indirect signs of axial hernia.**

Data of instrumental survey (2)

- Ultrasound of abdominal organs, kidneys - no pathological changes;
- Ultrasound of the pelvic organs: **echo signs of endometrial polyp**;
- Rheovasography of the vessels of the upper limbs: **in the left hand blood supply is reduced by 29%, mild hypovolemia**, the tone of large, medium and small arteries, arterioles and venules is normal; **in the right hand the blood supply is reduced by 34%, moderate hypovolemia**, the tone of large, medium and small arteries, arterioles and venules is normal;

X-ray of wrists and hands

Conclusion: bone defect in the distal phalanx of the left thumb, shortening, fuzziness of the adjacent interphalangeal joint plates of the left thumb with elements of marginal resorption; cystic restructuring of the heads of the metacarpal bones, patchy osteoporosis of the carpal bones.



Consults of specialists

- Consultation of gastroenterologist: gastroesophageal reflux, duodenogastral reflux, esophagitis, sliding axial hiatal hernia of 1st degree;
- Consultation of vascular surgeon: Raynaud phenomenon, chronic ischemia of IIIrd degree;
- Consultation of gynecologist: endometrial polyp, recommended surgical intervention.

Diagnostic criteria for SS (ACR/EULAR, 2013)

Item	Sub-item(s)	Score
• Skin thickening of the fingers of both hands extending proximally to the MCP joints		9
• Skin thickening of the fingers (count the higher score only)	Puffy fingers	2
	Sclerodactyly	4
• Fingertip lesions (the higher score only)	Digital tip ulcers	2
	Fingertip pitting scars	3
• Telangiectasia		2
• Abnormal nailfold capillaries		2
• Pulmonary arterial hypertension and/or interstitial lung disease	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
• Raynaud phenomenon		3
• Systemic sclerosis–related autoantibodies (maximum score is 3)	Anticentromere	3
	Anti–topoisomerase I	3
	Anti–RNA polymerase III	3

Patients with a total score equal to or greater than 9 are classified as having definite SS

Diagnosis

- **Main diagnosis:**

Systemic sclerosis, stage II (generalized), chronic course, activity of stage I, with skin lesions (edema, induration), vessels (Raynaud syndrome, ischemia of III degree), joints (polyarthrititis with predominant lesion of the joints of the hands, wrists, feet, Rö-changes of II degree, functional impairment of I degree), esophagus (gastroesophageal, duodenogastric reflux, esophagitis, sliding axial hernia of 1 degree), lungs (pneumofibrosis).

- **Concomitant diagnosis:**

Polyp of endometrium.

Treatment

Non-pharmacological treatment:

- Exclusion of physical overload, overcooling, insolation.
- Diet with limitation of mechanical and chemical irritants of the mucous membrane, stimulants of gastric secretion, substances that linger for a long time in the stomach.
- Usage of moisturizing and emollient hypoallergenic skin care products.
- Dynamic observation of a rheumatologist, vascular surgeon, gastroenterologist, ophthalmologist, gynecologist,

Treatment (2)

Drug therapy:

- Methylprednisolone 8 mg per day - constantly under the control of clinical and laboratory parameters
- Naftidrofuryl hydrogen oxalate 200 mg 3 times a day for 3 months
- Pentoxifylline 600 mg 1 time per day - 2 months
- Amlodipine 2.5 mg 1 time a day – continuously under the BP control
- Aspirin 75 mg after dinner – continuously
- Omeprazole 20 mg 1 time per day - from the 1st to the 10th day of each month

Recommendations:

- spirometry and consultation of pulmonologist;
- surgical therapy for endometrial polyp: polypectomy.

Conclusion

- **Diagnosis of systemic sclerosis in our patient was made a 5 years after the onset of symptoms mainly due to weak medical vigilance in detection of rare rheumatologic diseases, as a result late diagnosis in this case led to untimely prescribed treatment and to the disability of the patient;**
- **Thus, key factors for the early diagnosis of rare diseases are a careful history taking, attentive and accurate approach to the patient, as well as a systematic analysis of laboratory and instrumental surveys.**

**Thank you for your
attention!**

Any questions?

