Progressive systemic sclerosis: a rare form of presentation

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Abstract

The authors report a case of a 28 years old woman, admitted to hospital by malignant hypertension, retinopathy grade IV and intracranial hypertension, associated with polyarthralgia, Raynaud's phenomenon, microstomia, sclerodactyly and acute renal failure.

After complete evaluation, we have excluded other causes of secondary hypertension and diagnosed progressive systemic sclerosis with multisystem involvement (kidney, skin, lung, esophagus and retina), that had a rare forme of presentation scleroderma renal crisis (10% of cases) having started emergency antihypertensive treatment with ACE inhibitors (captopril 150 mg daily), nifedipine (60mg daily) and dialysis. We emphasize this clinical case because it is a rare disease (2.7 new patients/million/year) that had a rare form of presentation with a total recovery of the renal function after three months of haemodialysis. She is at the present date with normal blood pressure without any treatment.

Key words: scleroderma renal crisis, progressive systemic sclerosis, secondary hypertension.

Introduction

Progressive systemic sclerosis (PSS) is a generalized disease of the connective tissue, which is characterized by inflammatory, vascular and fibrotic alterations of the skin and multiple organ systems, particularly the lung, heart, kidney and digestive tract.[1] The pathogenesis is still unclear, but the clinical manifestations are the result of endothelial lesion of the cells with intimal proliferation, fibrosis and vascular obliteration. This is due to three main factors: Alterations in collagen synthesis, alterations in the capillaries, and immunological aspects.[2]

It is a rare disease (2.7 cases/million/year)[2,3] for which the therapeutic options are limited (symptomatic), giving it a reserved prognosis. Renal disease is a potential fatal complication of scleroderma. The manifestations of renal involvement habitually occur four years after the start of the extra-renal symptoms.[3,4,5] Studies carried out on autopsies suggest that around 80% of patients have primary histological alterations in the interlobular arteries and glomeruli. However, only 50% present clinical or laboratory manifestations of renal dysfunction, such as slight proteinuria, slight increase in plasma creatinine, or hypertension. The majority of these patients have a good renal prognosis. However, around 10% develop severe renal disease (renal crisis of scleroderma)[3,5] which is characterized by: acute renal insufficiency, usually in the absence of previous renal disease; moderate to severe arterial hypertension, due to activation of the renin-angiotensin system by kidney ischemia; normal urinary sediment or with slight proteinuria, and some cells or cylinders.

The clinical case presented here was preceded by extra-renal complaints nine months before admission, which were not clinically valued, manifesting as severe arterial hypertension in a young woman, whose diagnosis, after exhaustive study, was progressive systemic sclerosis with multisystemic involvement. After the onset of the renal crisis of scleroderma, she had a good prognosis after three months of haemodialysis (HD) with complete recovery of renal function.

Clinical case

Woman aged 28 years, White, cleaner, of low socio-cultural background, who around 9 months before admission reported the appearance of polyarthralgias of the hands, knees and tibiotarsal joints, accompanied by marked functional impotence and Raynaud's

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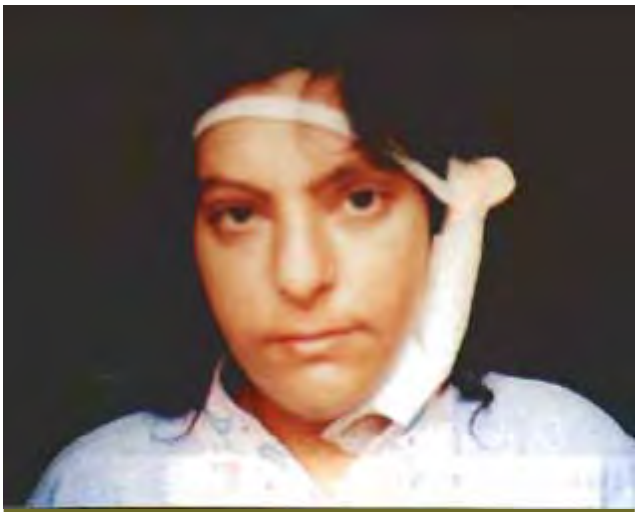


Typical appearance of scleroderma, microstomia

FIG. 1

Sclerodactyly.

FIG. 2

phenomenon. Three months afterwards, she reported intense frontal migraines, which did not ease with analgesics (acetylsalicylic acid), and which were associated, one week before admission, with a progressive decrease in visual acuity, nausea, and marked weight loss (20 kg in a month).

On observation, she appeared depressed and thin, with atrophy of the muscle masses, dry, thick skin with limited opening of the oral cavity (microstomia) *(Fig. 1)*, sclerodactyly, inability to extend the fingers *(Fig. 2)* and arterial hypertension (190/140 mmHg). Ophthalmological exam showed a decrease in visual acuity (Right eye vision, fingers to 1.5 m and left eye vision fingers to 2.0 m), ocular fundus with exuberant bilateral papillary edema, flame-shaped peripapillary hemorrhages, disperse cotton wool spots next to vascular arcades, marked edema of the posterior pole with bilateral macular star. These alterations are compatible with grade IV hypertensive retinopathy, associated with severe ischemic and exudative lesions of the retina, attributable to the phenomenon of vasculitis.

The analytical parameters *(Table 1)* showed rapidly progressing renal insufficiency, intravascular haemolysis and hyperreninism.

The serum levels of cortisol, catecholamines, aldosterone, T3 and T4 and TSH were normal, as were the 24-hour urine levels of metanephrines and *vanillylmandelic* acid.

The immunological study revealed positive APLA (1/80) with a mottled pattern, without extractable nuclear antigens, namely: anti-DNA; anti-SSA; anti-SSB; anti-SM; anti-histone; anti-SCL70; anti-centromere; ANCA. Antiphospholipid Antibody (APLA) IgM and IgG negative. The levels of complement fractions C3, C4 and CH50 were considered within the normal limits.

ECG: left ventricular hypertrophy by voltage criteria; echocardiogram type M and bidimensional: normal, chest x-ray, Postero-anterior: reinforcement of the bronchovascular reticulum in the bases and derivation of the left ventricular arch; proofs of respiratory function: Slight restrictive ventilatory alteration, accentuated decrease in CO transfer compatible with pulmonary impairment of the connectivitis; fluorescein angiogram of the retina *(Fig. 3)*: Diffuse papillae, areas of retinal ischemia surrounded by corresponding edema, and microeffusions of the retina, retinal masking effects corresponding to retinal hemorrhages – in conclusion, alterations suggestive of grade IV hypertensive retinopathy, associated with extensive areas of delayed choroid filling, due to probable hyalinization of the choroid veins (a common lesion in scleroderma).

Skin biopsy *(Fig. 4)*: atrophy of the epidermis, thickening and hyalinization of the collagen bundles, decrease in the vascular bundle and narrowing of the lumen, subcutaneous cell tissue with fibrosis of the septa and incarceration of the adnexal structures - in conclusion, cutaneous sclerosis consistent with a

TABLE I

Laboratory values

	16/02/94	02/03/94	18/03/94	24/03/94	31/03/94	14/04/94
Red blood cells (cel/mm^3)	4,450,000	3,240,000	2,800,000	2,820,000	2,440,000	3,110,000
Hemoglobin (g/dL)	13.5	10.3	8.5	8.7	8.1	10
Morphology	N	N	aniso	aniso	aniso	aniso
White blood cells (cel/mm^3)	14,000	10,600	14,500	9,800	8,500	9,000
Neutrophils (%)	85	79	75	81	76	84
Lymphocytes (%)	13	17	19	14	21	13
Platelets (cel/mm3)	65,000	218,000	110,000	191,000	176,000	182,000
Urea (mg/dL)	68	130	198	57	168	193
Uric acid (mg/dL)	4,7	7,7	7,3	—	8,2	7,5
Creatinine (mg/dL)	1,7	4,1	6,8	4,7	6,1	6,3
Creat. clearance (mg/min)	45	19,3	11,3	16,4	12,6	12,2
Calcium (mg/dL)	8,7	9,4	9,6	7,5	8,9	9,2
Phosphorus (mg/dL)	4,3	—	6,6	3,4	5,1	6,9
Sodium (mEq/L)	138	142	133	130	135	140
Potassium (mEq/L)	3,4	3,9	3,3	2,9	3,8	4,9
Chloride (mEq/L)	93	93	89	84	101	114
TBIL (mg/dL)	1,69	0,42	—	0,67	0,53	—
DBIL (mg/dL)	0,52	—	—	0,35	0,36	—
LDH (mg/dL)	1395	475	—	656	501	—
PT (%)	90	—	120	—	—	120
PPT (seg)	24	—	34	—	—	35
Fibrinogen (mg/dL)	386	—	609	—	—	522
Cholesterol (mg/dL)	204	—	212	—	—	266
Triglyceride (mg/dL)	283	—	308	—	—	477
Plasma renin (ng/dL)	—	—	32	—	—	40

diagnosis of scleroderma.

Abdominal and renal echography: kidneys with normal dimensions (diameter 10cm/diameter 11.5cm), with a decrease in right parenchyma--complex differentiation on the right, with a certain heterogeneity of same, slight dilation of the right excretory tree (around 8mm in antero-posterior diameter of the pelvis).

CAT-scan of the abdomen: pancreas, spleen, kidney and suprarenal glands without any morphological changes worth noting.

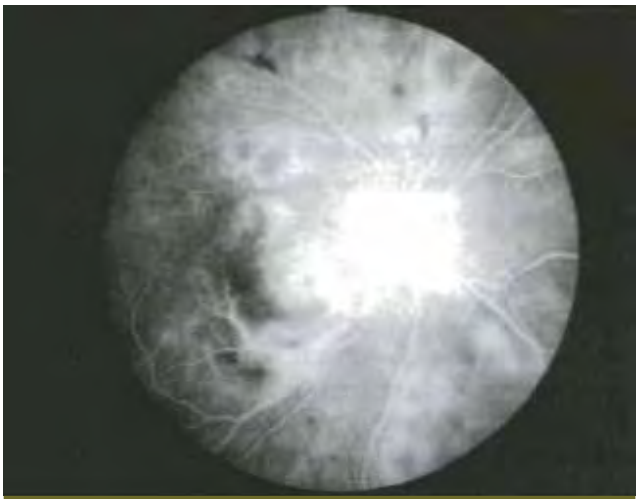
Selective renal arteriography: absence of stenosis of the renal arteries; multiple vasospastic intrarenal phenomena, manifested as renal ischemia *(Fig. 5)*.

Renal biopsy: Ischemic glomeruli with global and diffuse wrinkling of the glomerular capillary walls, leading to condensation of the capillary bulk, wrinkling of the tubular basal members; interstitium with medial fibrosis and infiltrate scarcity: Veins with slight to medium thickening of the arterial intima, with preeminence of endothelial cells in the vascular lumen, without replication of the internal elastics or thromboses. In conclusion: Severe ischemic kidney secondary to scleroderma, hemolytic--uraemic syndrome or malignant HTA *(Figs. 6 and 7)*.

Upper endoscopy: Antral mucosa with marbled appearance, bulb and duodenum unaltered.

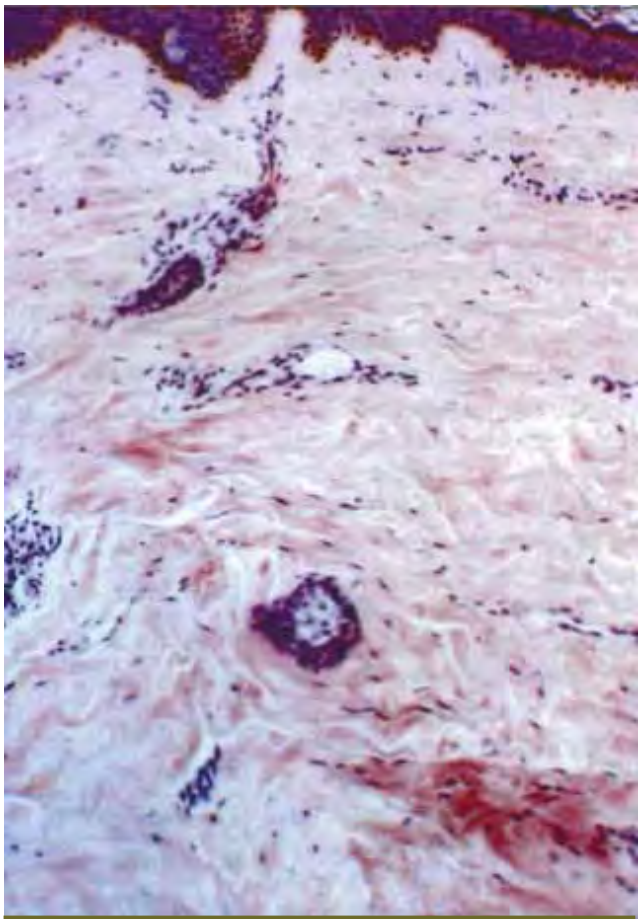
Gastric biopsy: low grade superficial chronic gastritis

Esophageal manometry: lower esophageal sphincter with pressure at rest of 23.25/3.1 (mmHg/KPa) (N: 37.55 ± 17.66/5.0 ± 1.1) with complete relaxation; body of the esophagus with total aperistalsis, absence of contractions and simultaneous contractions – in



Fluorescein angiography.

FIG. 3



Skin biopsy: Atrophy of the epidermis, thickening and hyalinization of the collagen bundles, with decrease in vascular pattern.

FIG. 4

conclusion, total aperistalsis of the body of the esophagus.

Medical therapy was initiated with nifedipine (30 - 60 mg/day), captopril (25 - 150 mg/day) for control of hypertension, followed by aluminum hydroxide and anti-reflux therapy with metoclopramide for to the associated dyspeptic complaints; therapy was also administered with D-penicillamine (150 mg/day) in an attempt to prevent the progress of the pulmonary and cutaneous lesions, as well as a short period of corticotherapy (methylprednisolone) for a complication of pericarditis.

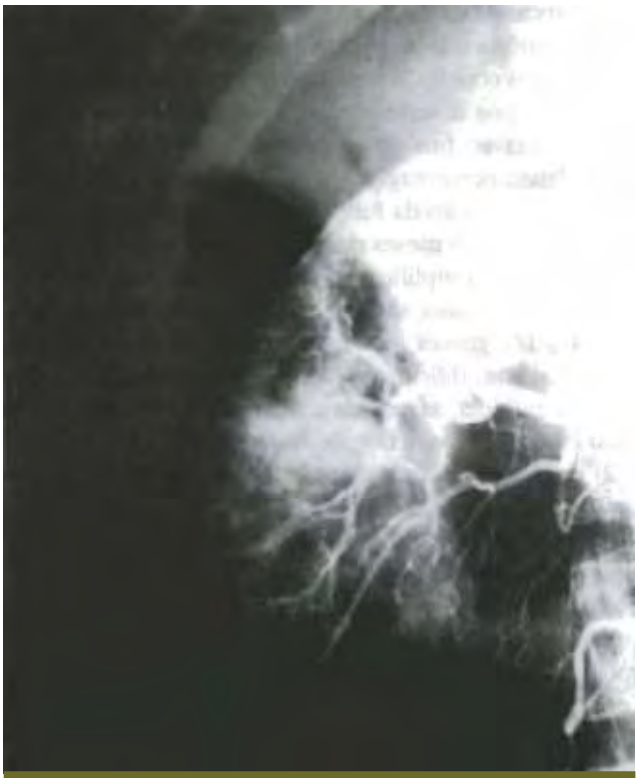
Fluoxetine was also prescribed (20 mg/day) by the psychiatric clinic. On the 15th day of hospitalization, due to the onset of a clinical and laboratory condition of acute renal insufficiency, a program of HD was begun.

The patient is now clinically stabilized, without signs of renal insufficiency, and with normal blood pressure, although all the therapy has been suspended.

Discussion and conclusions

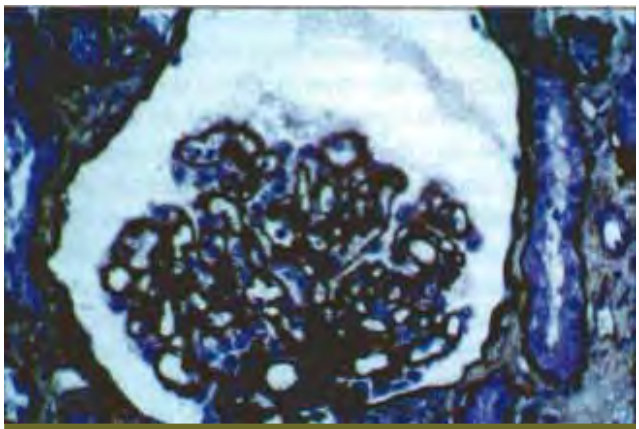
The patient presented a typical clinical condition of scleroderma, which has not been diagnosed to date, with extra-renal (joint) complaints for the past nine months or so. She was admitted with malignant arterial hypertension, associated with a severe sight defect, and onset of acute renal insufficiency. A complete analytical study was performed to exclude other secondary forms of arterial hypertension, notably, phaeochromocytoma, hyperthyroidism, primary hyperaldosteronism, stenosis of the renal artery, etc.

We conclude that the patient has PPS, with multisystemic involvement – of which 2.7 cases/million/year being described[2] - which in this case is manifested in a rare form – renal crisis of scleroderma (10% of cases of PPS)[3,4,5,6] – with acute oliguric renal insufficiency, malignant arterial hypertension and hyperreninism, leading to the urgent start of haemodialysis. Medical therapy with nifedipine was administered in increasing doses, with improvement in the Raynaud's phenomenon and reasonable control of blood pressure when associated with captopril (150 mg/day). During hospitalization, a complication of



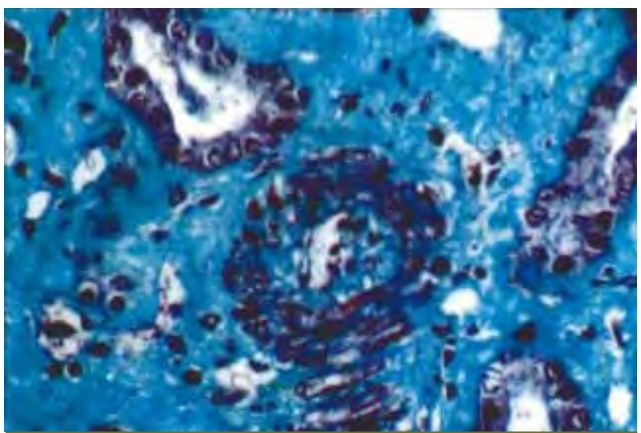
Multiple vasospastic phenomena manifested as renal ischemia.

FIG. 5



Renal biopsy: Ischemic glomeruli with global wrinkling and diffusion of the glomerular capillary walls, leading to condensation of the capillary bulk.

FIG. 6



Interstice with medial fibrosis and rare infiltrate; veins with slight to medium thickening of the arterial intima.

FIG. 7

fever was observed (ITU/catheter infection) which was treated with amoxicillin for 15 days. The aspects of the renal histology are non-specific, manifested as fibrin thrombi and areas of fibrinoid necrosis in the acute phase, evolving to a concentric thickening of the interlobular arteries ("onion skin") similar to the vascular lesions observed in other organs, [4,5,6,7] leading to a differential diagnosis with hemolytic-uraemic syndrome, thrombotic thrombocytopenic purpura, malignant idiopathic nephrosclerosis (due to accelerated hypertension), rejection of chronic transplant and lupic anticoagulant. These diagnoses were also excluded by the laboratory tests and clinical signals of the disease, notably, microstomia, sclerodactyly and thickening of the skin.

The therapeutic options of PPS associated with renal insufficiency are: angiotensin-converting enzyme inhibitors (ACEi), chronic HD and renal transplant, the results of which are very discouraging due to the observation of relapse of the patient in the transplanted kidney.[8,9,10,11]

The prognosis is reserved, and it is seen that in cases treated with ACEI, the survival rate at the end of 6 months is 56%; in patients submitted to chronic HD in patients submitted to chronic HD, the survival rate at the end of the period is not more than 8%. In a small percentage of patients, recovery of renal function was achieved with ACEI therapy after 13 – 15 days of the start of HD, this clinical case being typical of this type evolution.

In the present case, some particularly serious aspects are highlighted:

1) malignant arterial hypertension, which was difficult to control with multiple medical therapies, associated with grade IV hypertension retinopathy with severe sight defect.
2) Acute renal insufficiency, which led to the urgent start of a haemodialysis program.
3) Multisystemic effects of the disease (retina, skin, kidney, esophagus, lung).

Despite this, the clinical evolution was favorable after the haemodialysis program (3 months), and the patient is now in follow-up at an external clinic, clinically asymptomatic, with good renal function and not receiving any treatment. ■

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