**The Interesting Case**

**Intriguing presentation of scleroderma renal crisis (scleroderma renal crisis sine scleroderma sine hypertension)**

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Introduction

Systemic sclerosis (SSc) is a rare autoimmune disease, the clinical hallmark of which is fibrotic skin induration (scleroderma). Current classification divides it into two variants, systemic sclerosis with limited scleroderma (lSSc) and systemic sclerosis with diffuse scleroderma (dSSc), determined by the extent of skin involvement [1]. Clinically, the diffuse form differs from the limited one by more widespread skin induration (truncal and extremities proximal to elbows and knees) and by earlier and more frequent visceral involvement. Of the latter, kidney disease in its most explosive form, aptly termed scleroderma renal crisis (SRC), is justifiably a most feared complication. The syndrome of SRC is characterized by the abrupt onset of malignant hypertension accompanied by rapidly progressive renal failure. It usually develops in patients with dSSc in whom aggressive evolution of scleroderma is evident. SRC has, however, been rarely reported to occur in the absence of either skin involvement [2–5] or hypertension [6,7].

We herein report a case of SRC who presented with advanced renal failure prior to the development of cutaneous manifestations and elevated blood pressure. Consequently, initial diagnosis was delayed and eventually confirmed by renal biopsy and the finding of anti Scl-70 antibody.

Case

A 69-year-old Arab woman was admitted with dyspnoea and mild peripheral oedema. She had been well until about a year before admission when she began to complain of arthralgia affecting mainly her wrists and small joints of the hands. For the last several months she had experienced difficulty in swallowing and anorexia with a resultant weight loss of 20 kg. Despite these symptoms, she did not seek medical attention until her current hospitalization. Physical examination revealed an, as yet, obese woman of body weight 80 kg and height 1.65 m. She was tachypnoeic with bilateral basal crepitations and +2 ankle oedema.

There were signs of arthritis of the wrists and metacarpophalangeal joints with flexion contractures of the fingers and marked wasting of the interossei. No sclerodactyly or other evidence of scleroderma was seen. Diffuse muscular tenderness was noted. Fundoscopy was normal. Laboratory data showed an ESR of 95 mm in the first hour (Westergren), serum haemoglobin 12.0 g/dl, WBC 7400/mm³ with a normal differential count, urea 72 mg/dl, creatinine 2.5 mg/dl, total protein 6.6 g/dl with an albumin of 2.8 g/dl, LDH 659 U/l, CPK 245 U/l with an MB fraction of 13.8% and normal transaminases. Urinary output was 2000 ml/day. Urinalysis revealed proteinuria (0.5 g/day) with a bland urinary sediment. Chest X-ray showed pulmonary congestion without cardiomegaly.

Treatment was initiated as for acute left heart failure, possibly due to an acute coronary event. On echocardiography the left ventricle was of normal size and contractility. Following diuretic therapy, the patient’s dyspnoea improved. A week after admission, serum creatinine remained stable at 2.5 mg/dl.

Renal biopsy (under fluoroscopy) was performed in conjunction with multiple serological tests. On biopsy, there were 38 glomeruli of essentially normal structure except for an ischaemic appearance (mildly contracted tuft with wrinkling of the basement membrane) (Figure 1). Immunofluorescence was negative and there were no deposits on electron microscopy. The main pathology centered on the blood vessels. Interlobular arteries showed a marked narrowing of the lumen due to a concentric, mucinous intimal thickening (Figure 2). In the walls of several arterioles fibrinoid necrosis was
Fig. 1. Glomerulus showing a mildly contracted tuft and wrinkling of the basement membrane. All 38 glomeruli in the biopsy were of similar appearance (PAMS, magnification × 250).

Fig. 2. Interlobular artery, almost totally occluded by a concentric mucinous intimal thickening (H&E, magnification × 100).

seen with their lumen totally occluded by fibrin thrombi. Enalapril was begun. Following the biopsy, the patient’s renal function rapidly deteriorated necessitating the onset of dialysis 3 weeks after admission. In parallel, both hypertension (180/100 despite ACEI treatment) and skin changes became manifest. Sclerodactyly and facial skin sclerosis evolved at an alarming pace. Nail fold capillaroscopy, at this stage, showed tortuous dilated vessels typical of scleroderma. ANF was positive at a titre of 1/40 and anti Scl-70 antibody at an index value of 6.8 (normal <1.1). Anticentromere antibodies were negative. Currently, the patient continues maintenance haemodialysis.

Discussion

The mode of presentation and disease course of systemic sclerosis are highly variable. The commonest early manifestations of SSc are Raynaud’s phenomenon and skin involvement, present in over 90% of patients [8]. The cutaneous changes which constitute the distinctive clinical feature of the disease, usually
precede visceral involvement. Of the multiple organ systems which can be affected: gastrointestinal, lungs, heart and kidneys, the latter, in particular SRC carries the worst prognosis. SRC is a medical emergency characterized by the precipitous onset of malignant hypertension and rapidly progressive renal failure. Its incidence in patients with SSc, ranges from 10–25% [9,10]. It usually develops early in the course of the disease with greater than 70% of cases occurring within 4 years of diagnosis [11]. However, in 5–10% of cases, SSc is not diagnosed prior to the development of SRC [11]. Typically, SRC is encountered in patients with diffuse cutaneous systemic sclerosis. In fact, the best predictor of SRC is the rapid progression of skin changes in patients with dSSc [11].

Contrary to the above, SRC has occasionally been reported to occur in the absence of or with only minimal skin involvement [2–5]. Such an occurrence is decidedly rare. Of 140 patients withSRC by Helfrich et al. [6], only 3% had limited cutaneous involvement. SRC has also been documented in the absence of concomitant hypertension [6,7]. In Helfrich’s series, 15 (11%) patients were normotensive. Our case is unique in that SRC developed prior to both the onset of sclerodermatous skin changes and an elevated blood pressure. Although the patient’s symptomatology suggested a multisystem disease compatible with SSc (arthritis, gastrointestinal, cardiac and renal manifestations), in the absence of scleroderma, the diagnosis was not initially entertained.

Rather, coronary insufficiency and possibly polymyositis (in view of the raised CPK-MB levels and marked myalgia), were considered. Renal biopsy was instrumental in establishing the correct diagnosis confirmed by the presence of anti Scl-70 antibodies. These antibodies, directed against topoisomerase I, a DNA gyrase, are relatively specific for dSSc, being found in 20–40% of cases [12]. Recently, anti-RNA polymerase III (RNAP) antibody has been reported to be a more sensitive serologic marker [13]. We did not, however, assay for anti RNAP.

Within 2 weeks after fluoroscopy guided biopsy, our patient’s renal function deteriorated to end stage kidney disease. Although this accelerated decrease of GFR might represent the natural course of SRC, we cannot exclude contrast dye induced injury as a precipitating insult. The vasoconstriction brought about by contrast dye may well have delivered the final blow to the already severely compromised renal perfusion seen in SRC.

It is interesting to note that pari passu with the rapid progression of renal failure in our patient, cutaneous changes quickly evolved. Such a course has previously been described [3,14] with skin thickening developing over as short a period as 5–10 days [14], similar to our case.

Nailfold capillaroscopy, a simple, non-invasive technique is valuable in the diagnosis of SSc. The prevalence of abnormal nailfold capillaries in SSc is greater than 85% [15]. The characteristic pattern in scleroderma and dermatomyositis consists of dilated capillaries frequently bordering avascular areas. A tortuous or ‘meandering’ appearance has been reported to occur in both: ‘SRC sine scleroderma sine hypertension’.

References

Fig. 3. Nailfold capillaroscopy showing dilated, tortuous capillaries bordered by avascular areas (see text) (dissecting microscope, magnification × 32).


