Sudden Renal Failure in a Scleroderma Patient: A Clinical Dilemma

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Abstract

Scleroderma is a connective tissue disease which may present with renal crisis. But sometimes, acute renal failure in scleroderma may be due to a second pathology. We here present a case of a 35 year old woman with systemic sclerosis, who presented with acute renal failure. She was started treatment as a case of scleroderma renal crisis. But her condition continued to deteriorate and she also developed some cutaneous vasculitic lesions. Her urine also had active sediments. Finally, serology and kidney biopsy established the renal lesion as stage IV lupus nephritis. She responded to immunosuppressive regimen for lupus with rapid improvement of kidney function. Such overlap of scleroderma with lupus is very rarely reported.

Introduction

Scleroderma is a multi-systemic connective tissue disorder which can cause acute renal failure. The condition is called scleroderma renal crisis and it often has a poor prognosis.[1] Thus, development of renal failure in a patient of scleroderma is often an adverse prognostic marker and requires immediate management.

However, acute renal failure in scleroderma patients can also be caused by other overlapping disorders. Timely differentiation of the etiology in such cases is vitally important as the management of these other disorders with renal failure is widely different from scleroderma renal crisis. We here present such a case of renal failure in a scleroderma patient, which presented to us as a clinical dilemma.

The Case Report

A 35 year old woman was admitted with rapidly progressive dyspnea and anasarca for 15 days. She had progressive oliguria and at the time of admission, her urine output was 200 ml/day. She also had intermittent fever and arthritis of small joints. In the past, this woman had been diagnosed as diffuse systemic sclerosis (dSSC) but except for NSAIDs for her arthritis, she was not receiving any therapy. She had had occasional episodes of Raynaud's phenomena but did not take any treatment for it. At the time of admission, she was receiving some herbal treatment.

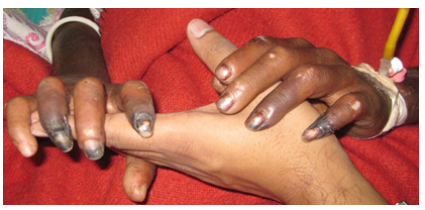

Fig. 1: Digital gangrene in both hands of the patient

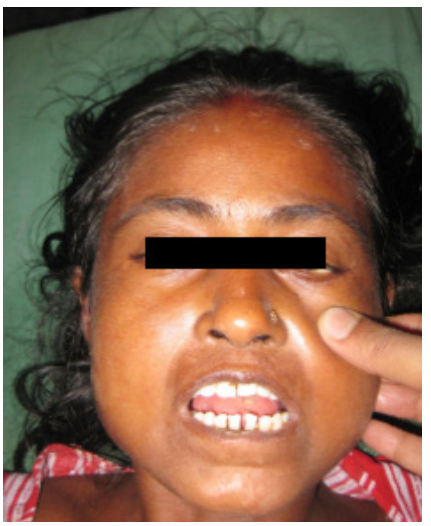

Fig. 2: Tightening of facial skin with decreased mouth opening

On examination, the patient was found to have a pulse rate of 120/minute and blood pressure of 180/96 mm of Hg in both the arms. Her hands showed digital gangrene with pseudoclubbing (Figure 1) and there was skin tightening in the face (Figure 2). She had mild pallor, pedal edema and generalized muscle tenderness. The respiratory rate was 32/minute and SaO2 was 95% in room air. Examination of the thorax revealed decreased breath sound with percussion dullness in right lower zone, suggestive of pleural effusion.

Initial investigations revealed hemoglobin level of 8.1 gm/dl, total leukocyte count of 13700/cmm (neutrophil 81%) and platelet count of 2.34 lakh/cmm. The ESR was 120 mm in the 1st hour. Blood urea was 154 mg/dl and creatinine 3.2 mg/dl. Serum sodium was normal and potassium level was 5 mEq/L. Peripheral blood smear examination revealed anisocytosis with polychromasia. The reticulocyte count was 6.3 %. Routine urine examination showed protein 2+, plenty of WBCs/hpf and 8-10 RBCs/hpf; there were no casts or crystals. Ultrasonography of kidneys showed only mild intra-renal edema. Repeat serological tests showed Anti-Nuclear factor to be positive (1:640) with a speckled pattern and Anti-Scl-70 to be moderately positive.

The patient was at first diagnosed as a case of scleroderma renal crisis and started on ACE inhibitors (Enalapril 5 mg BD). Also, calcium channel blockers were given for the hypertension. But the condition continued to deteriorate and on the 3rd day, she had complete anuria with severe anasarca. The urea/creatinine on day 3 was 196/4 mg/dl respectively. She was started on hemodialysis.

However, on the 4th day, the patient was noticed to have some skin lesions (Figure 3) on her feet and legs, which

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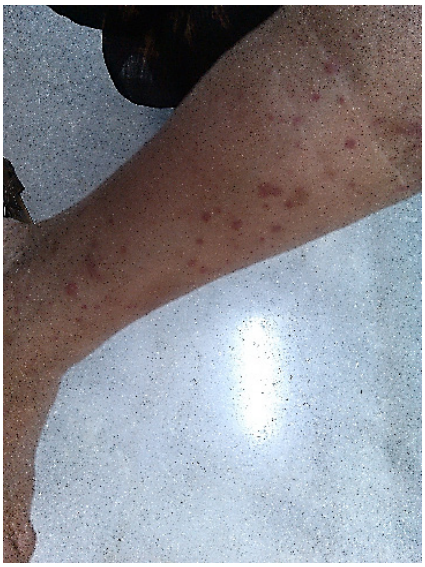

Fig. 3: The vasculitic skin rashes of the patient

were diagnosed as cutaneous vasculitis. The next day, she also developed a few similar lesions on her trunk. In view of these lesions, some further tests were done which revealed positive anti ds-DNA (1:160). Complement levels were also low (C3: 60 mg/dl; C4: 6 mg/dl). The patient was immediately given pulse methylprednisolone (1 g for 3 consecutive days) followed by first dose of cyclophosphamide (750 mg/m^2). There was rapid decline in the urea/creatinine levels with levels 98/1.5 mg/dl on day 4 after starting methylprednisolone. The edema and pallor also decreased markedly. 24 hour urinary protein came as 4.2 gm. After stabilization, a kidney biopsy was done which revealed WHO class IV Lupus nephritis with activity index 6/24. IgG, IgM, C3 and C1q deposits were found in subendothelial and subepithelial locations. Anti U1-RNP and ANCA were negative. Thus, the case was finally diagnosed as overlap of SLE with class IV nephritis in a case of systemic sclerosis. The patient was started on oral steroids (1 mg/kg) with cyclophosphamide according to NIH protocol. In follow up, she has maintained a stable kidney function. There has been no new skin lesions.

Discussion

The guidelines for management of individual connective tissue disorders (CTD) are now established with a fair degree of consensus. But often clinicians are faced with patients having overlapping features of more than one CTD. While some of these entities (like rhupus or mixed connective tissue disorder) are well defined, some others are often ill defined and may present a diagnostic and therapeutic challenge[2]. Often, for these "overlap" syndromes, there is no particular guideline and management is determined by the presenting features.

Scleroderma (SSC) can sometimes have overlap with other CTDs. Rheumatoid arthritis, Sjogren's syndrome and myositis have been reported to overlap with SSC.[3] Overlap with SLE is comparatively rare.[3] The autoantibodies found in SSC, like Scl-70, may also appear in other connective tissue disorders like SLE.[3] Hence, only the presence of autoantibodies is not a definitive proof of the presence of a particular CTD. Proper clinical features (like the renal failure in our case) must also be present for diagnosis.

Cases with SSC/SLE overlap has been reported rarely from other parts of the world. A case from China reported a 15 year old boy who had SSC to start with and then developed pleural effusion and polyarthritis.[4] However, renal involvement was not detected. Another case was reported from Canada where SLE/SSC overlap presented with orchitis due to vasculitis.[5] In our case, besides the renal involvement, cutaneous vasculitis was also present. In general, cutaneous vasculitis is not a common feature of SSC. Presence of such lesions should prompt a search for other second concomitant disorders.[6]

In our case, there were certain subtle clues to suggest a diagnosis other than scleroderma renal crisis. The first was the ESR. SSC is the only CTD where the ESR remains normal. Even in renal crisis, it may remain normal.[7] Thus, highly raised ESR in a scleroderma patient may be an indication of some second pathology. The peripheral blood picture was not helpful because fragmented RBCs causing anisocytosis may be found in scleroderma renal crisis (as it is predominantly a microangiopathic crisis) as also in SLE due to haemolytic anemia. Another clue was the urine report. In our patient, significant active sediments and proteinuria were present. But, in scleroderma renal crisis, usually proteinuria is mild as the glomeruli are relatively spared.[8]

Some authors have reported ANCA-associated renal disease in SSC.[9] Hence, a full autoimmune serology must be done in suspected scleroderma renal crisis to rule out secondary disorders. Sometimes, kidney biopsy remains the only way of differentiation. Typically, SSC crisis shows sparing of glomeruli with fibrinoid necrosis of vessels.[8] But, in SLE and other vasculitis, the glomeruli are invariably involved with or without immune deposits.

Coexistence of SLE and scleroderma may present a therapeutic dilemma. Steroids are often used for SLE but that may precipitate a scleroderma renal crisis. Thus, treatments have to be individualized and often, frequent changes of treatment may be needed.

Conclusion

We present this case to sensitize clinicians to this rare overlap syndrome. Elucidation of the exact aetiology of renal failure in such cases is important as the therapy varies widely for scleroderma renal crisis and SLE nephropathy.

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