

## Nephrotic Syndrome Heraldng Scleroderma

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### ABSTRACT

#### Background

Systemic Sclerosis (SSc) is a multisystem connective tissue disorder of unknown aetiology characterized chronic inflammation, deposition of collagen and other macromolecules in extracellular matrix of tissues. Renal affectation in SSc is usually rare. In most cases Scleroderma precedes the renal disease. The finding of Nephrotic syndrome in Scleroderma is most often due to complication of drug management or amyloidosis. We hereby present a case of nephrotic syndrome preceding diffuse cutaneous systemic sclerosis.

#### Case

MB is a 17-year-old female who presented with 3 months history of generalized body swelling, a week after a febrile illness. She had taken Artemisinin combination therapy, otherwise no other drug history. She had no other systemic symptoms and her past medical history was unremarkable. Examination revealed mainly facial and lower limb oedema, otherwise no other significant finding. Her chemistry revealed 24-hour urine protein 6.1g, Serum albumin 26g/L, and dyslipidaemia. Her renal biopsy result showed features of Minimal Change Disease. She had 6 months course of Prednisolone and remitted. Seven months post treatment, she developed features of diffuse cutaneous systemic sclerosis, and has been on treatment till date. No other renal involvement.

#### Conclusion

Most cases of Nephrotic syndrome associated with Systemic Sclerosis occurred as complication after frank features of SSc have emerged unlike the index patient. Hence the need for high index of suspicion.

**Keywords:** Systemic sclerosis, Nephrotic syndrome, Minimal change disease



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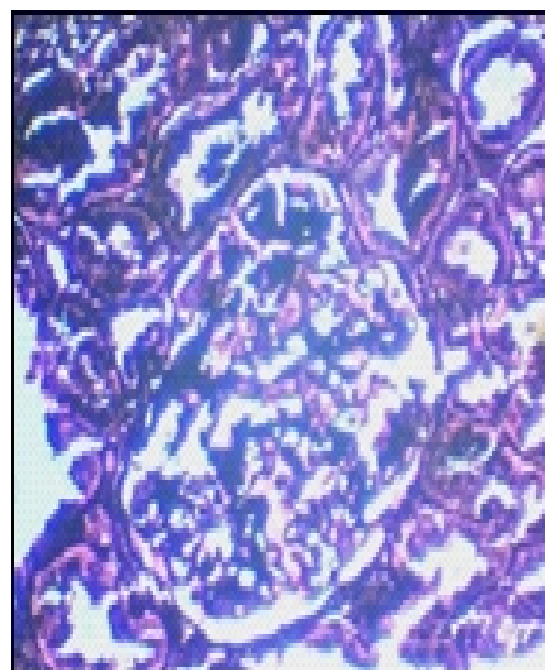
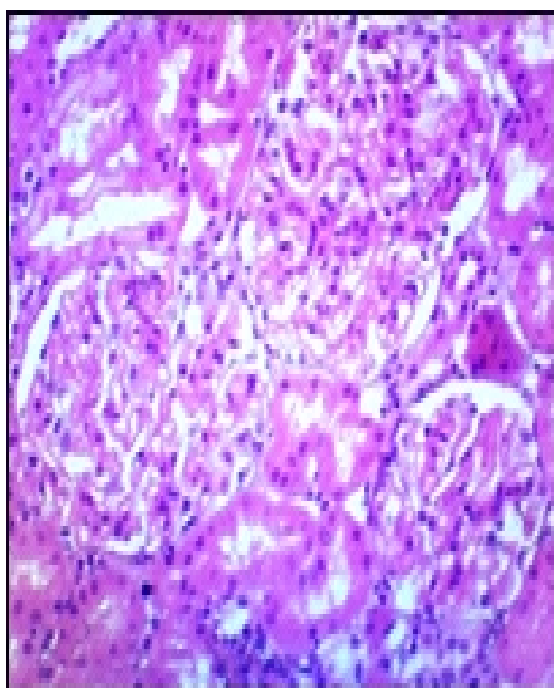
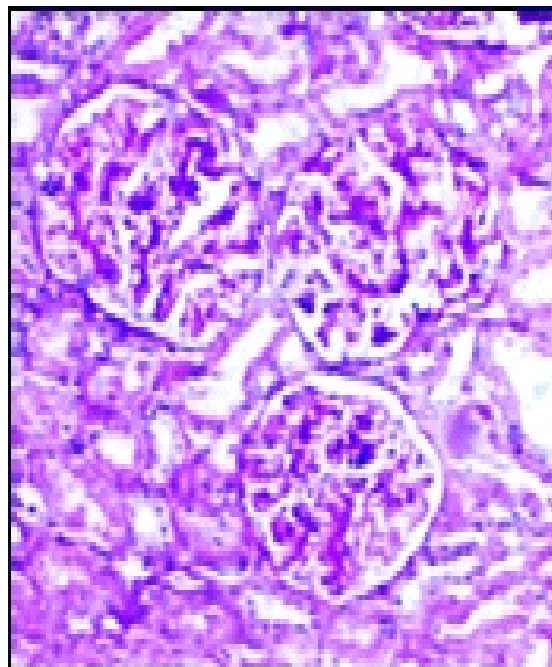
## BACKGROUND

Systemic Sclerosis (SSc) is a multisystem connective tissue disorder of unknown aetiology characterized chronic inflammation, deposition of collagen and other macromolecules in extracellular matrix of tissues, resulting in fibrosis, and obliterative vasculopathy, involving skin and multiple organs such as lungs, heart, kidney and gastrointestinal system. Renal involvement in SSc is usually rare.(1) Renal involvement in scleroderma can be divided into scleroderma renal crisis (SRC) and non-renal crisis. It ranges from less severe renal abnormalities, to hypertension, proteinuria and a rise in serum creatinine (in 45-60% of patients), to overt life-threatening scleroderma renal crisis (SRC)(2). Risk factors implicated in Scleroderma renal crisis include anaemia, new onset cardiac events, steroid use (>15mg prednisolone/day), cyclosporin therapy, diffuse skin disease, rapidly progressive skin disease, Modified Rodnan skin sore, large joint contractures, presence of anti-RNA-polymerase antibody, and <4 years since scleroderma onset. These risk factors may relate to disease severity, rather than having a causative role in pathogenesis of the renal crisis.(1) In most cases Scleroderma precedes the renal disease.(2) The finding of Nephrotic syndrome in Scleroderma is most often due to complication of drug management or amyloidosis. Typical renal complication of Scleroderma is arterial hypertension with or without proteinuria, not full blown Nephrotic syndrome.(1)(3) We hereby present a case of nephrotic syndrome preceding diffuse cutaneous systemic sclerosis because of its rarity and management challenges.

## CASE REPORT

MB is a 17-year-old female who presented with 3 months history of generalized body swelling, a week after a febrile illness. She had taken Artemisinin combination therapy, otherwise no other drug history. No associated change in urine volume or hematuria. No history of joint pains or skin rashes. No preceding history sore throat. No other history of note- no diabetes or hypertension. No alcohol, cigarette or substance use. Examination revealed mainly facial and lower limb oedema. No lymph node enlargement. Her blood pressure was 120/80mmHg. Other examinations were unremarkable. Her lab results were as follows: 24 hour urine protein 6.1g, Serum albumin 26g/L, Urine microscopy: no rbc or wbc, Total cholesterol 6.2mmol/L, Creatinine 59 µmol/L. Full blood count: wbc  $6.0 \times 10^9/L$ , Hb 11.8g/dL, PLT  $402 \times 10^9/L$ . Hepatitis B and C negative, non-reactive to HIV, High Serum C3 350 g/dl (NR=101-182). Normal C4, Antinuclear antibody positive (1.81). Renal histology showed normal glomeruli with resorption granules and occasional calcified cast. The tubules, interstitium and blood vessels were unremarkable. Immunofluorescence to C3 weakly positive but negative to IgG, A and M. The pathological assessment was Minimal Change Disease. She had 1mg/kg of oral Prednisolone and attained remission at 4<sup>th</sup> month of induction, thereafter dose of Prednisolone was tapered over 6 months. Other medications given were Tabs Irbesartan 300mg daily, Tabs Frusemide 40-80mg daily and Tabs Atorvastatin 20mg daily. Seven months later she developed progressive thickening of skin over the face and limbs from digits to the proximal to the elbows and knees noticed within a month. Has associated tightening of the oral cavity.

All peripheral pulses were palpable and of good volume. Her blood pressure and serum creatinine had remained normal; average Creatinine range of 60-80 $\mu$ mol/l and she remained in remission, 24-hour urine protein of 0.25g. Echocardiography showed essentially normal ventricular geometry, normal systolic and diastolic function and normal pulmonary pressure. Following Rheumatology review, a diagnosis of diffuse cutaneous systemic sclerosis (dcSSc) was made based on 2013 ACR/EULAR classification criteria.(4) Consequently, she was commenced on Tabs Hydroxychloroquine sulfate 200mg daily. Tabs Azathioprine 25mg bd, tabs Rabeprazole 20mg daily, in addition to skin moisturizers. She is currently on follow up and stable



Sections show 3 closely disposed glomeruli with unremarkable capillary tufts and peripheral glomerular basement membranes



**Pictures of the patient's different areas of skin involvement**



## DISCUSSION

Systemic sclerosis is said to be a rare disease in both developed and developing countries. (5)(6) Clinically patients are classified Limited and Diffuse subset based on skin involvement. The index patient had diagnosis of diffuse cutaneous systemic sclerosis (dcSSc) based on her skin involvement proximal to the elbows and knees. The dcSSc is the commoner presentation among Africans. (5) Although the disease is generally commoner in males with male: female of 5.4:1 in African population(5), the index patient is female, hence uniqueness of the case. The cardinal features of Scleroderma renal crisis, SRC, comprise a new onset of significant systemic hypertension ( $>150/85\text{mmHg}$ ) and decreased renal function [ $\geq 30\%$  reduction in estimated glomerular filtration rate (eGFR)]. While a minority of patients may appear normotensive, their blood pressure will

invariably be increased from baseline and accompanied by other manifestations characteristic of SRC.(7). The index patient presented with nephrotic syndrome. No evidence of deteriorating eGFR or significant variation of blood pressure nor hypertension. Hence there no clearly defined SRC features. Renal complications associated with Scleroderma are said to be commoner in females (7)(1) with dcSSc. (7) Although our patient is a female with diagnosis of dcSSc, but her presentation was atypical. The usual age of presentation is 30 to 60 years, but our patient presented at the age of 17 years. Use of steroid like the Prednisolone > 15mg/day is a risk for SRC. Although the patient had been exposed to high steroid dose for her initial treatment of MCD, but renal complication associated the dcSSc are not typical of SRC. Most of the reported cases of Nephrotic syndrome associated with Systemic Sclerosis occurred as complication after frank features of SSc have emerged.(1) This patient manifested with feature of Scleroderma seven months post diagnosis of Nephrotic syndrome. It is a known fact that about 20% of SRC may precede SSc.(7) but the preceding renal disease in this index patient are not those of SRC. A few reports of nephrotic syndrome preceding or associated with SSc exist, but mostly their histological findings were Focal segmental glomerulosclerosis(8) and Membranous nephropathy(9)(2).The histological finding of the index patient was Minimal Change Disease on light microscopy.

## CONCLUSION

Though Nephrotic syndrome have rarely being reported in association with systemic sclerosis, cases could forerun or develop in patients with systemic sclerosis. Hence the need for high index

of suspicion to allow for early diagnosis as well to forestall possible renal damage.

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