# PATIENT WITH SYSTEMIC SCLEROSIS AND SECONDARY SJÖGREN SYNDROME COMPLICATED BY CRYOGLOBULINEMIC GLOMERULONEPHRITIS AND VASCULITIS

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**Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by vascular alterations and autoimmune activation leading to widespread organ fibrosis. SSc microangiopathy includes loss of small vessels and proliferative obliterative vasculopathy; however, vascular inflammation indicating association with systemic vasculitis is rare.**

**A 67-year-old man with diabetes mellitus type I and SSc presented with fatigue, abdominal pain, occasional diarrhea, anemia, purpura of arms and legs, and worsening renal function (serum creatinine from 170 to 270 umol/l in the last 3 months). Urine examinations showed only mild hematuria with scarce erythrocytic casts and low proteinuria, which tended to indicate tubulointerstitial disease. ANA was positive, ENA was negative and ACMA antibodies were present. ANCA was negative but mixed cryoglobulinemia 1857 mg/l (IgG and IgM) was noticed. C4 component of complement was lowered. Serology tests for hepatitis B and C were negative. Skin biopsy suggested immune complex vasculitis.**

**Renal biopsy revealed diffuse proliferative and exudative immune complex glomerulonephritis with double contour formation and diffuse necrotizing vasculitis of small interlobular arteries and arterioles, and acute tubular injury** *(Figure 1,2,3)***. Ultrastructurally, there were not only subendothelial and mesangial deposits consistent with cryoglobulinemic glomerulonephritis but also glomerular chronic thrombotic microangiopathy related to SSc** *(Figure 4)*.

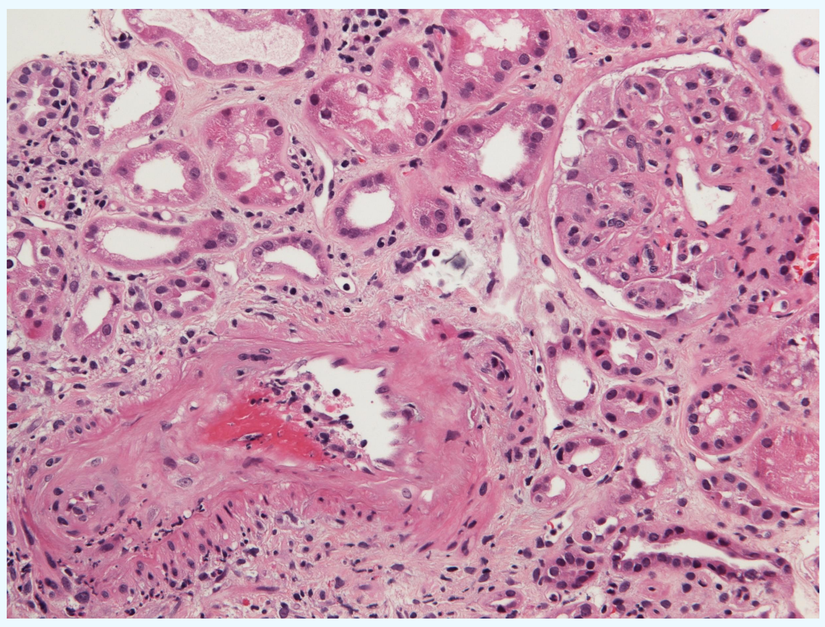

*Figure 1:* Proliferative immune complex glomerulonephritis and diffuse necrotizing vasculitis of small interlobular arteries and arterioles (HE, x200)

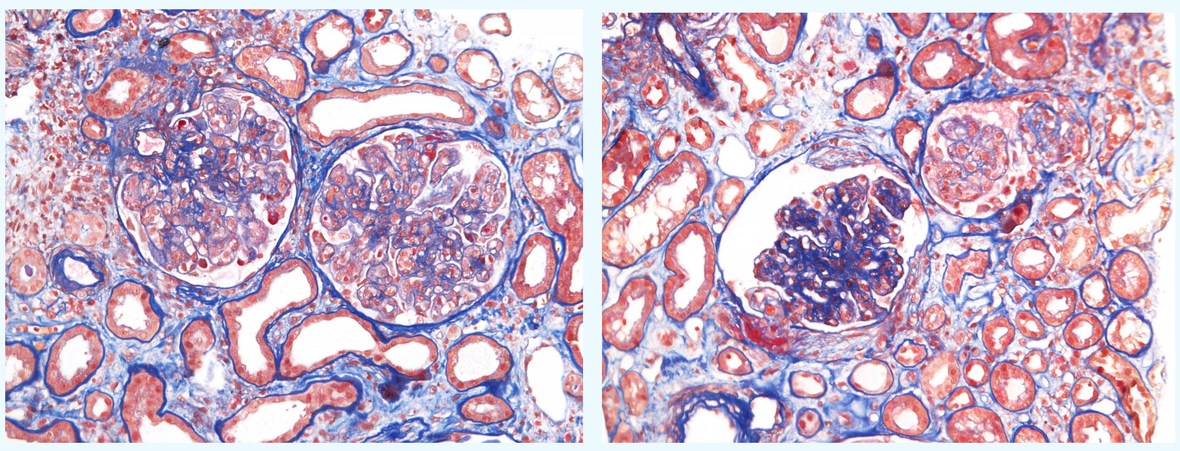


*Figure 3: Glomerular immune deposits ( IgM⁺, C3⁺ ) consistent with* cryoglobulinemic glomerulonephritis.

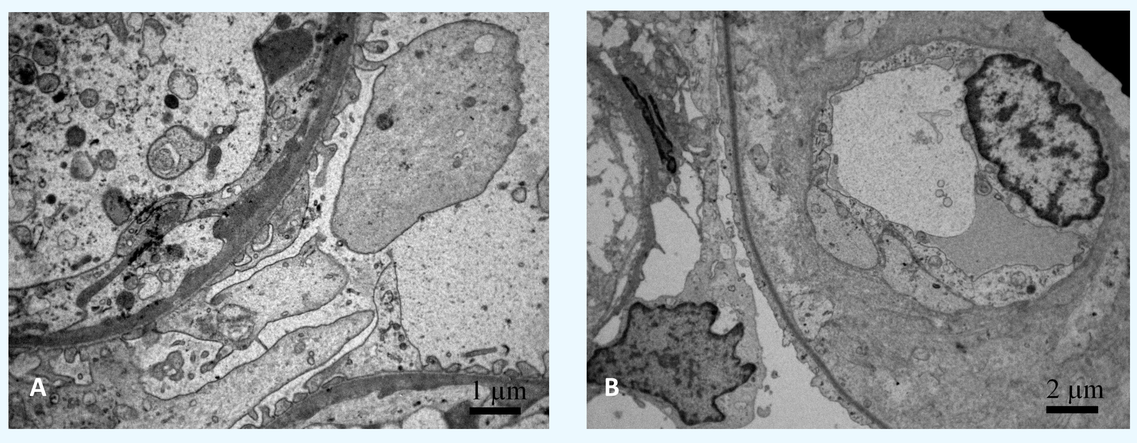


*Figure 4*: Subendothelial deposits consistent with cryoglobulinemic glomerulonephritis (A) and glomerular chronic thrombotic microangiopathy related to SSc (B).

**After treatment with plasmapheresis, rituximab and methylprednisolone pulses, renal function improved but proteinuria transiently increased into the nephrotic range and laboratory signs of thrombotic microangiopathy occurred, so the dosage of methylprednisolone was quickly diminished.**

**Seven months later, when renal function worsened again (serum creatinine 330 umol/l, cryoglobulins 250 mg/l), kidney re-biopsy revealed residual immune complex glomerulonephritis and chronic thrombotic microangiopathy without active vascular lesions, but marked interstitial fibrosis and tubular atrophy developed. Biopsy of small salivary glands confirmed secondary Sjögren's syndrome.**



*Figure 2*: Proliferative and exudative immune complex glomerulonephritis with double contour formation and necrotizing vasculitis of arteriole causing glomerular collapse (trichrome stain, x200)

**Conclusions:**
**SSc patients with suspicious small vessel vasculitis should undergo appropriate clinico-serological investigation, including cryoglobulins detection.**
**In SSc patients, worsening of renal function might be associated with cryoglobulin-related vasculitis and glomerulonephritis, even in the absence of marked hematuria and proteinuria, which could be confirmed only by renal biopsy.**

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