中文題目：類固醇引起之硬皮病腎危象/重疊症候群併發高血壓腦病變

英文題目：Posterior reversible encephalopathy syndrome triggered by steroid-induced scleroderma renal crisis in a patient with systemic sclerosis/ Sjogren's overlap syndrome

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Introduction

Scleroderma renal crisis (SRC) is a fatal complication of systemic sclerosis and a medical emergency(1). It requires prompt diagnosis and urgent control of hypertension within 72 hours to prevent irreversible damage to the kidney and other organs, including the brain, leading to posterior reversible encephalopathy syndrome (PRES). To our best knowledge, scleroderma renal crisis/Sjogren overlap syndrome, complicated by posterior reversible encephalopathy syndrome, is rare. Hence, this case was selected for a detailed presentation and discussion.

Case presentation

This 66-year-old female patient took cortisone for adrenal insufficiency and three months later, new onset of hypertension, headache, and acute change in mental status were noted with spontaneous recovery on the next day. Neurological examination and brain CT revealed no significant findings. Cortisone was discontinued for suspected steroid-related psychosis. Instead, incidental findings of acute kidney injury: KDIGO stage 3 (creatinine: 3.26mg/dL) with proteinuria (Urine Protein / Creatinine Ratio: 1527) were noted.

She was admitted to the nephrology ward for further survey. On admission, the patient had leg edema 2+, but otherwise normal physical examination. Laboratory data showed normal hemogram, albumin, and lipid profiles with creatinine slightly improved from 3.37 mg/dl to 2.82 mg/dl after discontinuing cortisone. Urinalysis showed no erythrocytes, pyuria, or casts but had proteinuria 3+. Renal ultrasound disclosed no hydronephrosis. She had positive ANA (≧1:5120) with the cytoplasmic dense fine speckled pattern but negative for C3, C4, ASLO, C-ANCA (Anti-PR3), P-ANCA (Anti-MPO), Cryoglobulin, and Anti-GBM Ab. Renal biopsy reported focal segmental glomerulosclerosis (FSGS). Oral prednisolone 10 mg daily was titrated up to intravenous methylprednisolone 10mg Q12H.

Ten days after admission, she suffered an episode of generalized tonic-clonic seizure with upward gaze, stupor, with malignant hypertension but no focal neurological deficits. She was transferred to the intensive care unit after endotracheal intubation. IV nicardipine was used and

hypertension was under control within 3 days. Brain CT, lumbar puncture, and EEG were insignificant. Brain MRI disclosed multifocal T2/FLAIR hyperintensities in bilateral occipital white matter, without mass effect. CSF study ruled out Neuromyelitis Optica, Multiple Sclerosis, and limbic encephalitis. Posterior reversible encephalopathy syndrome (PRES) was impressed clinico-radiologically by the neurologist.

High-dose intravenous methylprednisolone 250 mg daily was prescribed for suspected RPGN which further deteriorated renal function. Hence, methylprednisolone was tapered off and hemodialysis was commenced. Therapeutic plasma exchange was also given for 3 days but a poor response in renal function recovery pointed out RPGN was unlikely.

Second-time renal biopsy showed progressive segmental sclerosis of the glomerulus, prominent tubular atrophy (50%), and interstitial fibrosis. One muscular artery showed marked arteriosclerosis prominent fibrointimal concentric proliferation (so-called onion-skin appearance)(Figure 1). The immunofluorescent study showed no deposition of IgG, IgA, IgM, C3, and C1q. Here, marked pathology changes compared to first-time biopsy were noted after high-dose steroid therapy.

New onset of sclerodactyly of both hands, peri-ungual changes with Raynaud's phenomena were noted and rheumatologist impressed systemic sclerosis under 2013 ACR/EULAR criteria. Together with renal biopsy, scleroderma renal crisis (SRC) was diagnosed. Anti-Scl-70 antibodies were negative as it was collected the day after plasma exchange. Anti-RNA polymerase III was not tested for unavailability at the local hospital. Serum markers ruled out SLE. Overlap syndrome of SRC and Sjogren syndrome (history of dry eyes, positive Anti-Ro Ab and positive Schirmer's test) was impressed. Hypertension was controlled with an ACE inhibitor: captopril. Steroid was discontinued, but renal function did not recover despite hemodialysis.

During the course of the ICU stay, the patient had repeated bouts of ventilator-associated Pneumonia and fungemia. Patient expired after one month of hospital stay.

Discussion

Systemic sclerosis (SSc) is a serious immune-mediated rheumatic disease characterized by vasculopathy, inflammation, and fibrosis affecting systemically including scleroderma renal crisis (SRC) (1). SRC is one of the fatal complications of scleroderma (mortality of 20% at 6 months*)* with a prevalence of 4.9%(2). In up to 75% of cases, scleroderma renal crisis develops within the first 4 years (median duration: 8 months) from the diagnosis(3) but can also remain subclinical and be an initial presenting feature of scleroderma(4), as in the case of our patient. High-dose corticosteroids (> or =15 mg/day prednisone or equivalent) are significantly associated with scleroderma renal crisis(5).

Regarding our patient, she had repeated episodes of worsening renal function after steroid use. Together with clinical and typical renal biopsy findings, scleroderma renal crisis was impressed. Sclerodactyly presented late in the course and SRC is the earliest presentation noted in this patient. Renal biopsy may not be required to diagnose SRC but it can help to differentiate and rule out other possible differential diagnoses. Anti-Topoisomerase I antibody (anti-Scl-70) was negative possibly due to the low positive rate of anti-Scl-70. She also has Sjogren syndrome and a recent retrospective cohort reported that SgS/SSc overlap (6% of SSc) had a higher mortality rate (Hazard ratio: 3.79) than non-overlap SSc since more corticosteroids were likely to be used in overlap syndrome(6).

Posterior reversible encephalopathy syndrome is a clinico-radiologically diagnosed disease caused by vasogenic multifocal edema, mainly involving occipital lobes. The mainstay of treatment is adherence to BP maintenance, seizure control, and management of underlying etiology(7) which is SRC and infection in our patient. Although hypertension was effectively controlled within 72 hours with ACE inhibitor(captopril) and nicardipine pump, she had concomitant infection with severe ventilator-associated pneumonia and fungemia which limited the recovery of consciousness and renal function, resulting in the patient's mortality.

Conclusion

In conclusion, this is a rare case of overlap syndrome with steroid-induced scleroderma renal crisis and Sjogren syndrome complicated with posterior reversible encephalopathy syndrome. From a clinical point of view, steroid-induced worsening of renal function with positive ANA and unexplained fibrosis of internal organs should raise the suspicion of SRC. General rules of organ-oriented therapy are applied to those patients.

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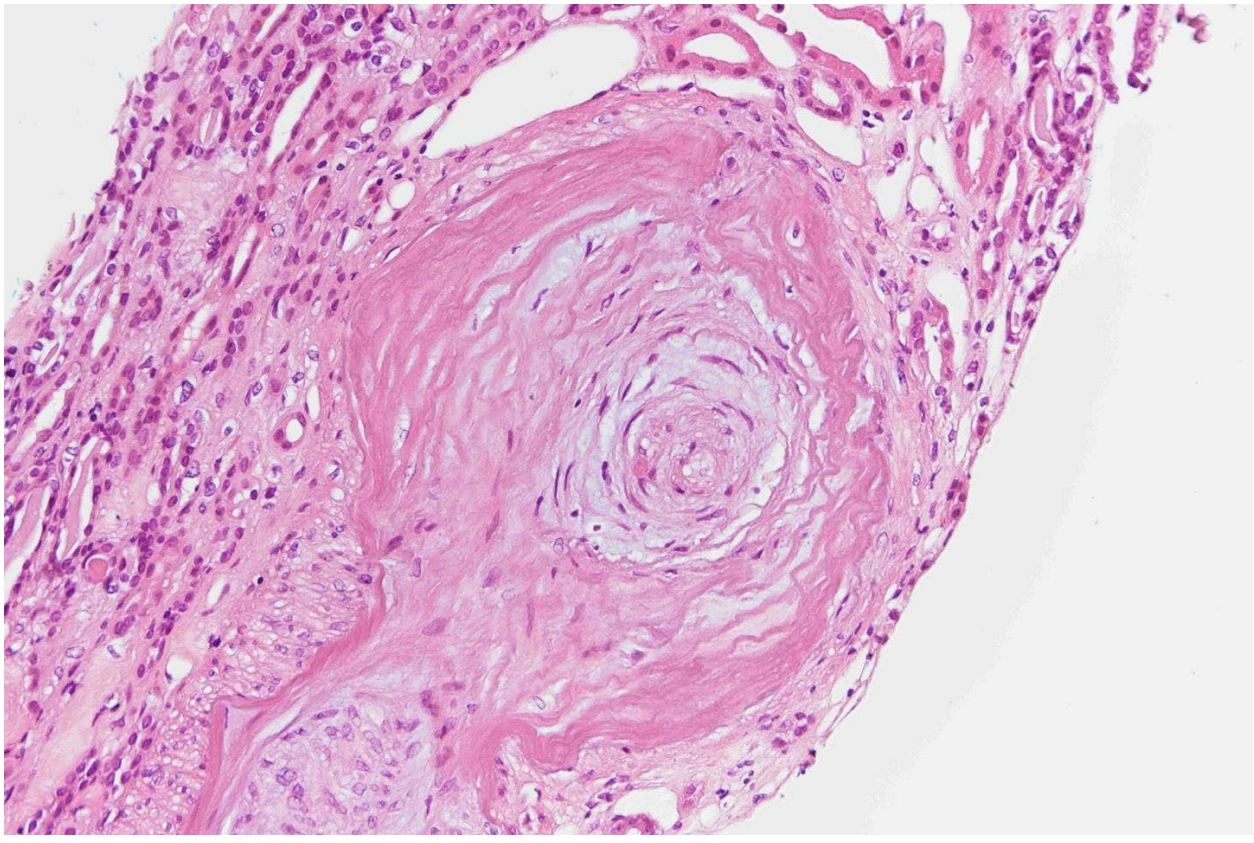

Figure 1. Renal biopsy showing the typical feature of advanced scleroderma renal crisis with muscular artery showing marked arteriosclerosis, prominent fibrointimal concentric proliferation (so-called onion-skin appearance)