

## CASE REPORT

## Spontaneous subdural haemorrhage in a patient with scleroderma renal crisis

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**SUMMARY**

A 52-year-old woman with a history of systemic sclerosis presented with new onset seizures and renal failure. The patient's history, laboratory data and pathology supported the diagnosis of scleroderma renal crisis. The patient was also noted to have a subdural haemorrhage (SDH) in the absence of trauma. This is the first report of scleroderma renal crisis associated with a spontaneous SDH.

**BACKGROUND**

Scleroderma renal crisis (SRC) is an acute complication of systemic sclerosis. Patients present with malignant hypertension and renal failure with a bland urine sediment. This complication is seen in up to 20% of patients with systemic sclerosis, particularly in patients with diffuse cutaneous disease.<sup>1</sup> It is associated with anti-RNA-polymerase III antibodies; conversely anti-scl-70 and anti-centromere antibodies are typically absent.<sup>2</sup> Renal biopsy classically reveals vascular narrowing with intimal deposition of collagen associated with 'onion-skin' hypertrophy. These pathological changes are also seen in other thrombotic microangiopathies including thrombotic thrombocytopenic purpura (TTP) and malignant hypertension. These associated conditions must often be differentiated based on clinical and laboratory grounds.

SRC is a multisystem disease affecting the haematological (microangiopathic haemolytic anaemia), cardiac (congestive heart failure, arrhythmia, pericardial effusion), pulmonary (pulmonary oedema, pleural effusion) and neurological (seizure,

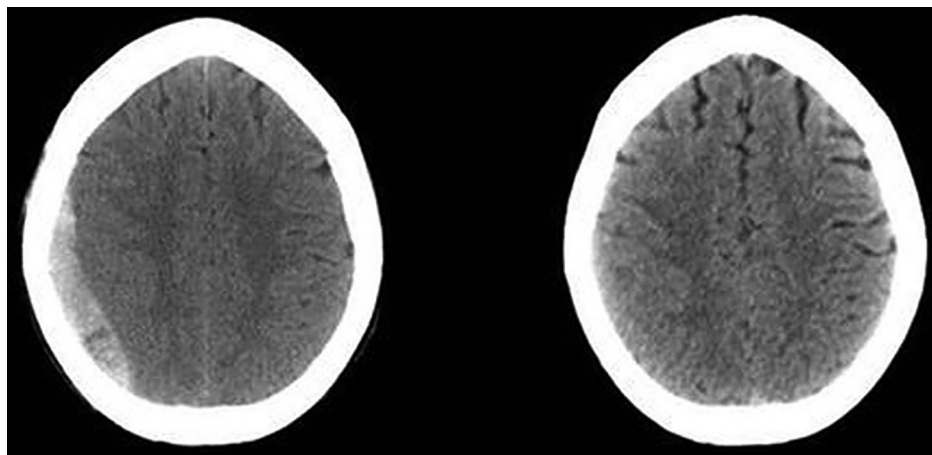
encephalopathy, papilledema) systems.<sup>3</sup> We present the first reported case of SRC associated with a spontaneous subdural haematoma.

**CASE PRESENTATION**

A 52-year-old Hispanic woman with a history of diffuse cutaneous scleroderma presented with 2 weeks of headache, lethargy and confusion. On the morning of admission, the patient had a generalised seizure, which was partially witnessed by her husband. This episode was followed by a period of non-responsiveness. There was no history of trauma nor was there any evidence of superficial injury consistent with trauma. In the emergency room, the patient was stuporous and confused. A generalised tonic-clonic seizure was observed, and the patient was intubated for airway protection. The patient's blood pressure on presentation was 171/91. Non-contrast CT imaging of the head demonstrated a subdural haematoma of the right parieto-occipital lobe (figure 1).

The patient had a history of systemic sclerosis diagnosed 4 years prior. The patient had been treated with corticosteroid therapy. Her illness was complicated by diffuse upper extremity skin thickening, Raynaud's phenomenon and dysphagia. She had a history of partial gastrectomy in the setting of a gastrointestinal bleed secondary to gastric antral vascular ectasia (watermelon stomach). She had no prior history of hypertension.

Physical examination revealed diffuse sclerotic, hypopigmented patches of skin of the proximal and distal arms sparing the trunk and extremities. In addition, calcifications of the distal fingers with

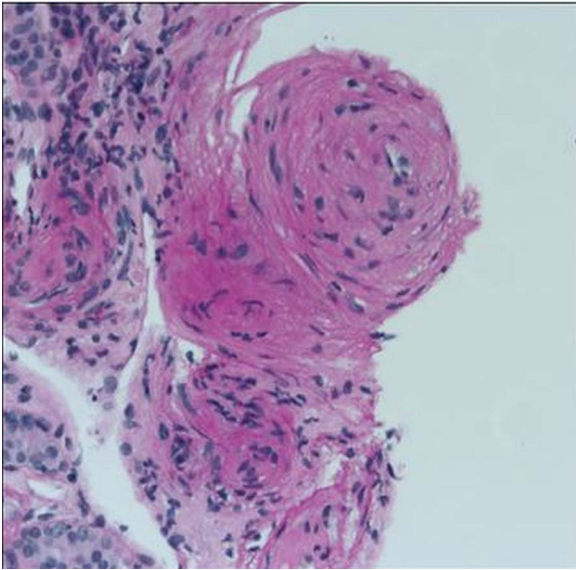


**Figure 1** CT image of head, axial view, showing 12 mm parieto-occipital subdural haematoma without evidence of midline shift (left). Follow-up image 2 months later showing complete resolution of haematoma (right).



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**Figure 2** Renal biopsy demonstrating renal arteriole with concentric 'onion-skin' hypertrophy and resultant obliteration of vascular lumen.

healed ulcerations were noted. The skin on the patient's face was tight and her hair was thin. In the emergency department, the patient was noted to be somnolent and answered questions incorrectly; however, her mental status improved quickly, so that by the time she was transferred to the intensive care unit she was responsive and interactive. She moved all four extremities to command. Her pupils were equal and reactive. Asterixis was absent. No other focal neurological deficits were noted.

Laboratory evaluation revealed a blood urea nitrogen of 102 mg/dL and a creatinine of 7 mg/dL. The patient's last documented creatinine was 0.6 mg/dL 5 months prior. Renal biopsy showed evidence of vasculopathy consistent with SRC (figure 2). While not immediately available, autoantibody profile was later found to be consistent with the diagnosis of SRC (anti-RNA polymerase III positive, anti-Scl 70 negative and anti-centromere negative).

### OUTCOME AND FOLLOW-UP

The patient's blood pressure was initially managed emergently with intravenous nicardipine and later transitioned to captopril when the diagnosis of SRC was strongly suspected. The patient's blood pressure was well controlled on ACE-inhibitor therapy. In the setting of volume overload and worsening electrolyte disturbances, haemodialysis was initiated on the second hospital day.

The patient also developed haemolytic anaemia requiring red blood cell transfusion. As thrombotic TTP presents with similar findings of renal failure, microangiopathic haemolytic anaemia and neurological dysfunction, we treated empirically for TTP with plasmapheresis until von-Willebrand factor (VWF) cleaving protease ADAMTS13 was found to be normal (10 days later). In addition, the patient's clinical course was further complicated by multiple comorbid conditions including congestive heart failure, pulmonary oedema and a large pericardial effusion requiring drainage.

She did not have further seizure activity or residual neurological deficits throughout her hospitalisation. The patient's subdural haematoma was managed conservatively and followed with serial CTs that demonstrated stability of the haemorrhage. After discharge, follow-up CT showed complete resolution

(figure 1). Unfortunately, despite ACE-inhibitor therapy, the patient continues to require haemodialysis, now 6 months after discharge.

### DISCUSSION

SRC is a devastating and life-threatening complication of systemic sclerosis.

Nearly 20% of affected patients die within 3 months despite ACE-inhibitor therapy.<sup>4</sup> Papilloedema, encephalopathy, seizures, haemolytic anaemia, congestive heart failure, pericardial effusions and flash pulmonary oedema have been reported in this condition.<sup>2,5</sup> However, an association between spontaneous subdural haemorrhage (SDH) and SRC has not been previously described.

SDH is most commonly associated with head trauma and the use of oral anticoagulants.<sup>6</sup> The pathophysiology of traumatic SDH is related to tearing of the bridging veins that cross the subdural space. Non-traumatic SDH is a well-described clinical entity that may occur in up to 2.6% of all cases of SDH.<sup>7</sup> The exact pathophysiological mechanism in non-traumatic SDH is not entirely understood but may be related to spontaneous rupture of the middle cerebral artery.<sup>8</sup> Risk factors for the development of non-traumatic SDH includes hypertension, coagulopathy and thrombocytopenia, all of which were present in our case.<sup>7</sup>

In particular, patients with renal failure on dialysis have a 10-fold increase in the rate of subdural haematoma as compared with the general population.<sup>9</sup> This association may be the result of uraemic toxins that impair platelet-endothelial interactions as well as venous hypertension in the setting of volume overload.<sup>10-12</sup> In this case, the patient had no clinical history of any fall or trauma that would account for her presentation. This was supported by the absence of any superficial skin or soft tissue abnormalities on physical examination.

Three factors may have contributed to our patient's persistent neurological symptoms including (1) hypertensive encephalopathy, (2) seizure and postictal state and (3) the presence of a SDH. Indeed, seizures are well described in SRC having been reported in 8% of patients and are likely a consequence of hypertensive encephalopathy.<sup>13</sup> The rapid improvement of the patient's mental status with antihypertensive therapy suggests a significant component of hypertensive encephalopathy and further emphasises the importance of prompt blood pressure control.

Prompt management of hypertension with ACE inhibitors remains the mainstay of treatment of scleroderma renal crisis. ACE-inhibitor therapy dramatically improves survival at 1 year to 85% compared with 15% in patients in whom no ACE-inhibitor therapy is administered.<sup>14</sup> Despite medical therapy, 20-40% require permanent dialysis.<sup>2,4</sup> Patients with anti-RNA polymerase III antibodies have a higher risk of renal crisis among all patients with diffuse systemic sclerosis and may benefit from testing at diagnosis for risk stratification.

Finally, the patient's worsening haemolytic anaemia highlights an important clinical dilemma in differentiating this syndrome from thrombotic TTP. Both diseases present with acute renal failure, thrombotic microangiopathy, thrombocytopenia, neurological dysfunction, malignant hypertension and similar pathological findings on renal biopsy. ADAMTS13 is a plasma metalloprotease responsible for cleaving the adhesive glycoprotein VWF associated with TTP. In TTP, marked ADAMTS13 deficiency is found (<10%) resulting in accumulation of highly thrombogenic multimers of VWF.

Differentiating SRC from TTP can be difficult. Initially, in this patient, empiric treatment of both SRC and TTP was initiated. Clinical findings suggestive of TTP rather than SRC include severe thrombocytopenia, fever and normal blood pressure.<sup>15</sup> Based on the clinical presentation and later a normal ADAMTS13 level, the diagnosis of TTP was excluded and plasmapheresis was discontinued. Interestingly, patients with SRC treated with ACE inhibitors and plasmapheresis may have improved outcomes compared with patients treated with ACE inhibitors alone.<sup>16</sup>

### Learning points

- ▶ Scleroderma renal crisis (SRC) is an acute complication of diffuse systemic sclerosis.
- ▶ This condition is associated with multiorgan system dysfunction including encephalopathy, seizures, congestive heart failure, haemolytic anaemia and pericardial/pleural effusions.
- ▶ Prompt initiation of ACE-inhibitor therapy improves mortality in SRC.
- ▶ Patients with diffuse systemic sclerosis should be tested for anti-RNA polymerase III antibodies at diagnosis to identify patients at higher risk for SRC.

**Competing interests** None.

**Patient consent** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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