Seizures in a patient with diffuse scleroderma

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A 31-year-old black woman, with a nine-year history of systemic sclerosis, was admitted with an episode of jerking movements of both upper extremities, followed by unresponsiveness. In the emergency room, she had an episode of generalised tonic-clonic seizures. Her husband stated that she had never had seizures prior to these two episodes and had no headaches, nausea, vomiting or prior neurological disease. On examination, she was found to be drowsy and disoriented but would move all four limbs on painful stimuli. She was afebrile with a respiratory rate of 20/min and a blood pressure of 172/78 mmHg. Fundus examination showed no evidence of any haemorrhage, exudate or papilledema.

She exhibited a characteristic facies of scleroderma with marked tightness of the skin over the nose, ears, forehead and neck. She also had extensive skin tightness, thickening and non-pitting induration involving the distal parts of both upper and lower extremities with deformities of both hands. Signs of meningeal irritation were absent and she did not have any focal neurological deficit.

The results of laboratory studies on admission and those carried out about one year earlier are shown in the table. The peripheral smear is shown in figure 1. Bone marrow biopsy revealed markedly hypoplastic marrow predominated by fat cells with occasional megakaryocytes. Serological studies showed positive antinuclear antibodies (titer 1:640), negative DsDNA, anticardiolipin antibodies and rheumatoid factor. Computed tomography (CT) scan of the head was normal and studies of the cerebrospinal fluid did not reveal any evidence of infection. Over the next three days her platelets dropped to $59 \times 10^9/l$ with a drop in haemoglobin to 7.6 g/dl. Lactate dehydrogenase increased to 1840 IU/l. Renal function also rapidly deteriorated with blood urea nitrogen 44 mg/dl and creatinine 3.1 mg/dl.

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Figure 1 Peripheral blood smear of patient

Table Laboratory findings (nd = not done)

	On admission	1 year earlier
haemoglobin (g/dl)	12.8	14.1
haematocrit (%)	38	44
platelets ($\times 10^9/l$)	114	290
prothrombin time (s)	11.5	nd
partial thromboplastin time (s)	22.5	nd
blood urea nitrogen (mg/dl)	29	7
creatinine (mg/dl)	1.3	0.7
lactate dehydrogenase (IU/l)	809	nd
reticulocyte (%)	3.5	nd
haptoglobin (mg/dl)	26	nd
D-dimer	normal	nd

Questions

- 1 What does the blood smear show?
- 2 What is the most likely diagnosis?

Figure 2 Kidney tissue obtained at autopsy showing patchy haemorrhage in the tubules and interstitium secondary to thrombotic occlusion of vessels

Figure 3 Kidney tissue obtained at autopsy showing glomerulus with abundant microthrombi

Answers

QUESTION 1

The peripheral smear shows a moderate number of schistocytes, many polychromatophils, and a decreased number of platelets.

QUESTION 2

Thrombotic thrombocytopenic purpura (TTP). The diagnosis of TTP was made in view of her neurological status, microangiopathic anemia, thrombocytopenia, mild renal impairment and normal coagulation profile and D dimers. The patient expired after four weeks hospitalisation. On autopsy the findings were consistent with scleroderma and TTP (figures 2 and 3).

TTP in patients with scleroderma

TTP usually develops in previously healthy persons. In about 15% of cases the syndrome is associated with an underlying disorder, often an infection or connective tissue disorder. The association between TTP and scleroderma is now firmly established and there have been a few case reports in the literature.^{1,2}

In patients with scleroderma, histologic studies show endothelial injury in the large vessels and capillaries. Various endothelial cell cytotoxic factors could lead to endothelial damage in systemic sclerosis³ and may explain the association between TTP and scleroderma.

CLINICAL FEATURES

TTP is characterised by the pentad of haemolytic anemia, thrombocytopenia, neurological symptoms, fever, and renal dysfunction.^{4,5} Onset is usually abrupt. The most common initial manifestations are neurologic abnormality and bleeding. Anemia and thrombocytopenia typically are severe at presentation. Fever is uncommon. Headache, confusion, stupor, coma, hemiparesis, cranial nerve palsy and histopathologic demonstration of lesions of TTP in gingival biopsy. Bone marrow biopsy is often required.

TREATMENT

Plasmapheresis is the treatment of choice for TTP. The therapeutic effects of plasmapheresis in the critically ill patient with TTP are dramatic. Long-term follow-up of TTP patients treated with plasmapheresis is limited.⁵ Other therapeutic measures, for example splenectomy, infusion of prostacycline, antiplatelet drugs and corticosteroids have been used with disappointing results.

Thrombotic thrombocytopenic purpura

- haemolytic uremic syndrome
- idiopathic thrombocytopenic purpura
- disseminated intravascular coagulation
- paroxysmal nocturnal haemoglobinuria
- Evan's syndrome

PROGNOSIS
Before the introduction of plasmapheresis, TTP was fatal in more than 80% of patients within three months. Now about 80% of the patients treated with exchange plasmapheresis survive the initial episode of TTP.⁶ Thus, early recognition in various clinical settings and prompt, appropriate treatment is of paramount importance.

Final diagnosis
Thrombotic thrombocytopenic purpura associated with scleroderma.
Keywords: thrombotic thrombocytopenic purpura, scleroderma

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5 Naild GH. Haemolytic-uraemic syndrome in practice. *Lancet* 1994; **343**: 398–401.

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Anaemia in a child

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A 16-year-old girl was admitted with pallor, fatigue, febrile episodes, and weight loss over a five-month period. On physical examination

she was a thin, markedly pale girl, with a temperature of 39°C and scleral jaundice. There was no significant peripheral adenopathy. Her spleen was palpable 12 cm below the left costal margin and liver was palpable 5 cm below the right costal margin. Initial laboratory data are given in the box.
On abdominal ultrasonography, hepatosplenomegaly and multiple para-aortic, paracaval, splenic hilar lymphadenopathies were determined. On abdominal computed tomography (CT) there was a nodular pattern in the liver and spleen.
After admission to the hospital, fever up to 39°C persisted for 13 days and laparotomy and wedge biopsy from the liver, omentum and abdominal lymph nodes was performed.

- Questions**
- 1 What type is the anaemia?

2 What is the diagnosis?

3 What treatment options are available in the acute phase?

4 What is the long-term strategy in treating this condition?

Laboratory data	
• haemoglobin (g/dl)	6.6
• haematocrit (%)	23.1
• white blood cells (× 10 ⁹ /l)	1.9
• neutrophils (%)	77
• lymphocytes (%)	20
• monocytes (%)	3
• reticulocytes (%)	10
• platelets (× 10 ⁹ /l)	135
• erythrocyte sedimentation rate (mm/h)	115
• serum bilirubin (mg/dl)	
total	1.8
direct	0.9
• direct Coombs	positive with IgG
• haptoglobulin (mg/dl)	< 30
• bone marrow	normal

Box 1

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