A 52-year-old woman was diagnosed as having limited cutaneous systemic sclerosis (lcSSc) in June 2003. The cutaneous impairment of systemic sclerosis (SSc) was characterized by sclerodactylly, telangiectasia, pitting scars and calcinosis cutis. Systemic manifestations of lcSSc included: Raynaud’s phenomenon and esophageal impairment characterized by low pressure in the lower esophageal sphincter and decreased peristalsis in the lower two-thirds of the esophageal body on manometry. Autoantibody screening tests were positive for antinuclear antibodies (1:1200) with anticentromere antibody. Other tests, including pulmonary function tests (PFT), computed tomographic (CT) scan of the lungs and echocardiography, were within normal limits. She received therapy with combined diltiazem and omeprazole.

In October 2009, the patient presented with a 1-month history of daily severe headache, which was refractory to common analgesics. The headaches worsened abruptly upon standing and improved in the supine position. On admission, the patient had no fever. There was no nuchal rigidity and neurological examination was normal. General physical examination revealed necrotic digital ulcers involving the second and third left fingertips. Laboratory studies disclosed the following: C-reactive protein: 3 mg/l, hemoglobin level: 13.4 g/dl, white blood cell count: $6.4 \times 10^9$/l, platelet count: $158 \times 10^9$/l. Other routine biochemical tests, including renal and liver tests, were normal. Brain magnetic resonance imaging (MRI) showed thickened meninges with diffuse gadolinium enhancement and bilateral subdural hygromas (Figure 1). Spinal MRI was within normal limits. The diagnosis of spontaneous intracranial hypotension syndrome was made. Because the patient’s symptoms did not improve despite conservative therapy (hydration, best rest and analgesics), epidural blood patch was applied, which resulted in gradual disappearance of the headache. At 9-month follow-up, the patient is asymptomatic and neuroimaging findings were normal.

SSc is a systemic inflammatory disorder, affecting the skin and other organs. The disorder is characterized by three histopathological features: (i) perivascular and tissue infiltration of mononuclear inflammatory cells, (ii) increased synthesis and excessive deposition of collagen within skin and internal organs during the course of SSc and (iii) both structural and functional vascular lesions. Vascular changes in SSc primarily involve small arteries (from 500 to 50 µm in diameter) and capillaries; histological microvascular features include: concentric intimal proliferation, thickening of the media and abnormal telangiectasia in the vasa vasorum within the adventitia, as well as intimal fibrosis associated with vessel narrowing and obliteration in more advanced SSc. The pathogenesis of SSc still remains unknown, although endothelial dysfunction has been suggested as a key element of the disease process.

Whereas systemic complications of SSc involve frequently the lungs and the gastrointestinal tract, central nervous system impairment is considered to be uncommon in SSc. SSc-related central nervous
system impairment has been reported to result in: (i) neuropsychiatric manifestations, including loss of memory, disorientation, depression, hallucinations, reduced mental acuity; and (ii) intracerebral calcifications, transient ischemic attacks, ischemic stroke or hemorrhage. Spinal impairment is also rare in SSc, resulting in spinal cord compression by ectopic paraspinous or intraspinous calcinosis.

We report, to the best of our knowledge, the first case of spontaneous intracranial hypotension syndrome associated with SSc. Spontaneous intracranial hypotension is a severe syndrome, which is caused by reduced intracranial fluid pressure due to cerebrospinal fluid leakage; it is characterized by orthostatic headache, i.e.: (i) appearing within minutes of change in the body posture from supine to standing position; and (ii) relieved by the supine position. The pathological mechanisms of spontaneous intracranial hypotension syndrome in our SSc patient remain unknown. Indeed, the morphology of dura has not been described previously in SSc patients, as it has in other tissues being affected by SSc. However, in our patient, we suggest that spontaneous intracranial hypotension syndrome may be due to: (i) vascular damage causing a non-inflammatory microangiopathy of the vasa nervorum and a final ischemic dura injury. Indeed, we observed that clinical deterioration of vascular symptoms (i.e. severe Raynaud’s phenomenon and digital ulcers) occurred concomitantly with spontaneous intracranial hypotension syndrome in our patient. Our findings therefore suggest a possible vascular pathogenic link between the two diseases and (ii) alterations of the connective tissue integrity (e.g. abnormalities of collagen metabolism, proliferation of specific fibroblast subpopulations) which may be, in part, explained by defects in a major component of extracellular microfibrils: fibrillin-1; numerous microsatellites alleles near the fibrillin-1 gene have, in fact, been described in SSc patients. Interestingly, patients with Marfan syndrome, who also exhibit fibrillin-1 gene mutation, have also been reported to develop spontaneous intracranial hypotension syndrome. Taken together, our findings raise the question of an association between SSc and spontaneous intracranial hypotension syndrome as part of a continuum, suggesting that spontaneous intracranial hypotension syndrome may be included within the spectrum of SSc-related neurological complications.

Finally, our findings emphasize the importance of recognizing neurological complications at an early stage in SSc, resulting in accurate diagnosis and appropriate management, and therefore decreasing the risk of both morbidity and severe sequelae in these patients. Moreover, we also suggest that when a diagnosis of spontaneous intracranial hypotension syndrome is made, search for underlying and undiagnosed SSc should be undertaken, including clinical examination, antinuclear antibody studies (especially for anticentromere and anti-Scl 70 antibodies) and nailfold capillaroscopy.

Conflict of interest: None declared.

References


