Non-infective endocarditis with systemic embolization and recurrent stroke in systemic sclerosis

Rheumatology key message
- Non-bacterial thrombotic endocarditis with systemic embolization and stroke can occur in systemic sclerosis patients.

Sr, SSc is a rare, multisystem autoimmune disease, characterized by small vessel vasculopathy, autoimmunity and uncontrolled fibrogenesis. Patients are at risk of severe morbidity and mortality in cases of internal organ involvement with subsequent dysfunction and failure. Low-grade endocardial inflammation with valvular disease has been described but is considered a very rare phenomenon in SSc patients [1].

In 2013, a 27-year-old black female presented with a painful necrotic toe ulcer. Clinical examination demonstrated multiple digital ulcers on both hands and feet and skin fibrosis extending to the thorax and abdomen. Laboratory analysis revealed positive ANA, with the detection of anti-topoisomerase I antibodies. Capillaroscopy showed an early SSc pattern with multiple megacapillaries. Pulmonary function tests and high-resolution CT suggested early interstitial lung disease. The patient was diagnosed with rapidly progressive early dcSSc and treated with a calcium antagonist, MTX and i.v. prostaglandins for ulcer healing. Four months later the patient presented with a non-fluent aphasia and mild sensorimotor deficit. Intracerebral haemorrhage was excluded and i.v. recombinant tissue plasminogen activator was administered. On brain MRI, bihemispheric areas of diffusion restriction were documented (Fig. 1A and B). Cerebral MRI angiography showed reduced flow in a distal branch of the left middle cerebral artery without convincing evidence of vasculitis. Lumbar puncture was unremarkable. Transoesophageal echocardiography demonstrated a posterior mitral leaflet vegetation with concomitant valvular insufficiency (2/4), highly suggestive of endocarditis. This had not been identified on previous transthoracic echocardiography, nor on a recently performed cardiac MRI. Serial blood samples and cultures showed no signs of infection or inflammation. Anti-cardiolipin antibodies and lupus anticoagulant were absent.

After initial improvement, she suddenly developed a left hemiparesis with dysarthria. MRI showed new areas of ischaemia in the frontal and insular region in the right hemisphere with occlusion of an M2 branch (Fig. 1C and D). No other aetiologies for bilateral ischaemic insults were identified. The diagnosis of nonbacterial thrombotic endocarditis (NBTE) was made and treatment with low molecular weight heparin (LMWH) was initiated. At present, there is an incomplete recovery with persistent left hemiparesis.

We present the case of a non-bacterial thrombotic endocarditis with systemic embolization and recurrent stroke in a Mauritanian female with SSc. Recent evidence shows that SSc patients are at increased risk of ischaemic stroke, and this is suggested to reflect primary vascular involvement of the brain with obliterator vasculopathy, endothelial dysfunction and vasospasms, resulting in focal and diffuse hypoperfusion [2]. In our patient, there was no evidence of primary cerebral vascular involvement and the rapid recurrence of stroke in the contralateral hemisphere suggested an embolic mechanism. Myocardial and pericardial disease are frequently present in SSc patients, but endocardial involvement is considered an extremely rare event [1]. Although post-mortem studies have described endocardial vegetations in as many as 5 of 28 SSc patients [3], only a few case reports describe the presence of such vegetations in living patients. To our knowledge, there is only one case report suggesting systemic embolization from a mitral vegetation as the origin of multiple ischaemic lesions [4]. However, others challenged this case because of the presence of cryoglobulinaemia and severe anaemia.

The occurrence of this rare and severe complication in our patient might be related to her ethnic background, but this remains speculative [5]. With regard to therapy, there is no consensus in patients with non-bacterial thrombotic endocarditis. The most recent clinical practice guidelines on antithrombotic therapy and prevention recommend treatment with full-dose i.v. unfractionated heparin or with s.c. LMWH vs no anticoagulation in patients with NBTE and systemic or pulmonary emboli [6]. The indications and appropriate timing for surgery in non-infective endocarditis have not been formally studied and should be based on an individualized decision. Severe valvular dysfunction and recurrent embolic events despite anticoagulation are clear surgical

References
indications and in clear contrast to bacterial endocarditis; valve repair rather than replacement may be possible in selected cases [7].

To conclude, we would like to emphasize that although extremely rare, NBTE with embolization and stroke can occur in SSc. It should be suspected in SSc patients with stroke, especially when bihemispheric lesions are present, when valve insufficiencies are discovered and in case of recurrent emboli.

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**Fig. 1** Neuroimaging of index and recurrent cerebral ischaemia

Diffusion weighted imaging showing multiple hyperintense areas corresponding to ischemic infarcts in both hemispheres the first day after the symptom onset (A-B). Two weeks later repeated imaging revealed an increase in ischemic lesions predominantly in the right hemisphere (C-D).
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