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**Isolated digital infarction associated with anticentromere antibody**

Sirs, The association between anticentromere antibody (ACA) and Raynaud’s disease and systemic sclerosis is well established. We report a case of digital gangrene with associated ACA but no other features of connective tissue disease.

An 87-yr-old female was admitted with a 2-week history of gradual blackening of her right ring fingertips and her left index and middle fingertips. Three months earlier she had noted her fingers turning white in cold weather but had not noted any other colour changes. Six weeks earlier she had been admitted elsewhere following a collapse. Examination at that time showed
dusky discoloration of the index, middle and ring fingers of her left hand along with the index and middle fingers of her right hand. During that admission she was treated for left ventricular failure and pneumonia. A myocardial infarction was excluded and an echocardiogram revealed a calcified mitral valve, a dilated left atrium and moderate left ventricular hypertrophy. She was discharged well on antibiotics, a proton pump inhibitor and a diuretic. Her medical history was otherwise unremarkable. Direct questioning revealed possible weight loss, without any dysphagia or abnormal bowel habit. She had never smoked and was teetotal. There was a family history of diabetes and ischaemic heart disease. On admission she was alert with dry gangrene over the left index and middle fingertips and the right ring fingertip (Fig. 1). No lesions were noted on her toes. There was no evidence of calcinosis, telangiectasia, scleroderma, arthropathy or of a skin rash. Radial, brachial and femoral pulses were of normal volume and rate. Blood pressure was 220/100 mmHg; no cardiac murmurs or carotid bruits were detected. Respiratory, abdominal and neurological examinations were unremarkable. The following initial investigations were all normal: full blood count, coagulation screen, glucose, bone profile, renal and liver function. Inflammatory markers were raised [erythrocyte sedimentation rate (ESR), 32 mm fall in 1 h; C-reactive protein (CRP), 20 mg/l (normal range < 5 mg/l)] and albumin was low at 27 g/l. Blood cultures were sterile and urinalysis was normal. ECG showed sinus rhythm with a left ventricular strain pattern, and a chest radiograph was normal. Initial management consisted of i.v. heparin and aspirin. Renal function deteriorated over 24 h but responded to i.v. fluid replacement. X-rays of the hands and cervical spine were normal. Abdominal ultrasonography examining the internal organs and abdominal aorta was normal. An arch aortogram showed no evidence of a stenosis in the right or left subclavian or brachial arteries. No source of emboli was identified on the echocardiogram. On the fourth day of admission, after a fall, a haematoma developed in the right upper arm which was followed 3 days later by a right-sided wrist drop (Fig. 2). The APPT ratio at that time was > 6.0 and anticoagulation was stopped. Fracture was excluded and conservative management was adopted. An ultrasound scan of the right upper arm revealed compression of the neurovascular bundle by the haematoma. Nerve conduction studies showed denervation in the radial and ulnar nerves but distinction between a mononeuritis multiplex and a single plexus lesion was not possible. Inflammatory markers continued to climb (ESR, 85 mm fall in 1 h; CRP, 128 mg/l). Antinuclear antibodies, rheumatoid factor, lupus anticoagulant, anticardiolipin antibodies, antithrombin III, proteins S and C, activated protein C resistance, complement (C3 and C4) and cryoglobulins were all normal or negative. The patient was weakly positive for antineutrophil cytoplasmic antibodies, which showed an atypical pattern. ACA tested by indirect immunofluorescence on HEP-2 cells was positive.

Further management included antibiotics for infected gangrene and nifedipine to improve circulation to the affected areas. Her condition remained stable until 5 weeks after admission, when new areas of discoloration developed on the index and middle fingers of the right hand and the ring finger of the left hand. The toes were normal but the wrist drop persisted. She was subsequently treated with six consecutive Ilprost infusions, with some improvement of the new lesions. She was discharged 5 months after admission after 3 months in a rehabilitation unit. She was readmitted 6 weeks later with pneumonia and unfortunately died.

ACA appears to identify a subset of systemic sclerosis patients who have less major organ involvement [1] but who are at increased risk of severe digital ischaemia [2]. There have been very few reports of patients with digital infarction and ACA who do not fulfil the criteria for either CREST syndrome (calcinosi, Raynaud’s phenomenon, oesophageal dysmotility sclerodactyly, telangiectasias) or systemic sclerosis according to the ACR criteria [3]. The few that are reported are nearly invariably seen in patients with pre-existing Raynaud’s phenomenon. A literature search to date revealed only one case of ACA associated with digital infarction in
the absence of Raynaud’s phenomenon or a connective tissue disease [4]. This was a 61-yr-old female smoker who suffered from a leg claudication syndrome and hypertension, who responded poorly to treatment. Our patient was previously asymptomatic, had never smoked and also responded poorly to treatment. Poor response to therapy and eventual amputation is a feature of the reported cases of ACA associated with digital ischaemia in patients with systemic sclerosis irrespective of the presence of Raynaud’s phenomenon, age and smoking habit [5]. Previous authors have suggested that there is a spectrum of clinical disease ranging from mild Raynaud’s phenomenon through to the CREST syndrome, and that ACA may serve as a marker for those patients likely to progress [6]. There is little evidence for a direct role of ACA in the pathogenesis of infarction, although Takahashi et al. [7] suggest that it may be toxic to endothelial cells. There are no longitudinal studies examining the prognostic significance of ACA in the absence of systemic sclerosis, but anecdotal evidence suggests that ACA may precede the onset of the CREST syndrome by many years [8]. The prevalence of ACA in female blood donors has been reported as 0.08% [9], whereas the reported prevalence in patients with idiopathic Raynaud’s syndrome is 31% [6]. Our case illustrates the need to test for ACA when investigating a patient with digital ischaemia as it may provide use information for the future management and prognosis.

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