A 38-year-old female patient presented to the rheumatology clinic with a 3-week history of a painful fingertip ulcer. The pain was so severe that it was keeping her awake at night. For 20 years (since her teens) her hands had been turning white then purple in the cold weather, going red (with tingling) when rewarming. Her feet also felt cold. Her family doctor had told her that this was Raynaud’s phenomenon, which was very common. However, each winter her symptoms seemed to be worsening, and even a slight temperature change would bring on an attack. The previous winter she had had some finger ulcers which had, however, been less painful than the current one and which had healed spontaneously. Also of concern to her was that for 6 months the skin of her fingers had felt tight, and she had recently been experiencing some difficulty swallowing, with heartburn. There was no past medical history of note. She had smoked five cigarettes a day for 2 years. There was no history of chemical exposure nor of use of vibratory equipment.

**Question 1**

Which symptoms suggest that this is not primary (idiopathic) Raynaud’s phenomenon?

A. Onset of Raynaud’s phenomenon age 18 years.
B. The feet were affected as well as the hands.
C. Development of digital ulcers.
D. The skin of the fingers felt tight.
E. She was a smoker.

On examination she had a healing ulcer at the tip of the left middle finger (Fig. 35.1). The fingertip was extremely tender. She had mild skin thickening of the
fingers (sclerodactyly) but elsewhere the skin was normal. She had digital pitting of the right index and middle fingers. There were no other abnormal findings.

**Question 2**

What investigations would you perform?

A. Full blood count and erythrocyte sedimentation rate.
B. Angiography.
C. Testing for antinuclear antibody (ANA).
D. Testing for anticentromere antibody.
E. Nailfold capillaroscopy.

Full blood count and erythrocyte sedimentation rate (ESR) were normal. On immunological testing she was strongly antinuclear antibody (ANA) positive (titre 1/1000) and she was anticentromere antibody positive. Chest X-ray showed no cervical rib. Hand X-rays were normal. Nailfold microscopy was abnormal, showing widened, dilated loops with areas of avascularity (Fig. 35.2).

**Question 3**

What is the diagnosis?

A. Limited cutaneous systemic sclerosis (“CREST” syndrome).
B. Hyperviscosity state, for example secondary to malignancy.
C. Extrinsic vascular compression.
D. Atherosclerosis.
E. Buerger’s disease.
Question 4

Which of the following are true of systemic sclerosis (also termed “scleroderma”):

A. Digital pitting is a characteristic feature.
B. Males are more commonly affected than females.
C. The two subtypes – limited cutaneous and diffuse cutaneous – are separated on the basis of the extent of the skin involvement.
D. Raynaud’s phenomenon often precedes the diagnosis of limited cutaneous systemic sclerosis by many years.
E. Anticentromere antibody is a risk factor for severe digital ischaemia requiring amputation.

The diagnosis of limited cutaneous systemic sclerosis was explained to the patient. She was told that her Raynaud’s phenomenon and her upper gastrointestinal symptoms were most likely related, and that some checks of her cardiorespiratory function would be arranged on a routine basis.

Question 5

How would you have treated her Raynaud’s phenomenon had you seen her 6 months previously, when there was no digital ulceration?

A. Avoidance of cold exposure.
B. Low dose prednisolone.
C. Stop smoking.
D. Nifedipine (sustained release).
E. Biofeedback.

The patient was prescribed nifedipine (sustained release) and a course of flucloxacillin. When reviewed one week later, the fingertip had deteriorated and some of the tissue had become necrotic, with surrounding erythema.

**Question 6**

What would you do now?

A. Admit to hospital for intravenous prostanoid therapy.
B. Intravenous antibiotics.
C. Debridement of the ulcer.
D. Cervical sympathectomy.
E. Anticoagulation.

The patient was admitted for intravenous antibiotic therapy, intravenous prostanoid infusions, and a vascular opinion. The fingertip was debrided. The patient was discharged home 6 days later, with instructions to dress warmly, avoid cold exposure, and to seek medical advice early should any further ulcers develop.

**Commentary**

Raynaud’s phenomenon – episodic digital ischaemia usually in response to cold exposure or stress – can be either primary (idiopathic) or secondary to a number of different diseases/conditions, including connective tissue disease (most characteristically systemic sclerosis), external vascular compression (as with a cervical rib), vibration exposure, hyperviscosity, drug treatment (for example beta-blockers, ergotamine) and occupational chemical exposure. The terminology is confusing: primary Raynaud’s phenomenon was previously termed “Raynaud’s disease”, and secondary Raynaud’s phenomenon “Raynaud’s syndrome”. However, “primary Raynaud’s phenomenon” and “secondary Raynaud’s phenomenon” are now the preferred terms [1].

The pathophysiology of Raynaud’s phenomenon (either primary or secondary) is poorly understood. Raynaud’s phenomenon can occur because of abnormalities in vascular structure, vascular function, or the blood itself [2]. These are interdependent and may occur together, as in systemic sclerosis when structural vascular problems inevitably impair vascular function, and platelet and white blood cell activation, together with impaired fibrinolysis, are also thought to contribute to pathophysiology. It is generally accepted that primary Raynaud’s phenomenon is mainly vasospastic and does not progress to irreversible tissue damage. In contrast, Raynaud’s phenomenon secondary to connective tissue disease such as systemic sclerosis is associated with structural vascular abnormality, and patients often develop ulceration, scarring, and even gangrene necessitating amputation.
The vascular surgeon is likely to encounter patients with Raynaud’s phenomenon for two main reasons:

1. Diagnosis. Why does this patient have episodic digital ischaemia?
2. Treatment of a critically ischaemic digit, or of severe Raynaud’s phenomenon unresponsive to medical therapy.

The onset of primary Raynaud’s phenomenon is most commonly in the teens or twenties: onset in later years should always raise the suspicion of an underlying cause. Women are more commonly affected. For Raynaud’s phenomenon to be primary, there should be no clinical features of underlying connective tissue disease or other disease/disorder (including absence of digital pitting or sclerodactyly), there should be no digital ulceration or gangrene, the ESR should be normal, testing for ANA negative (titre <1/100) and the nailfold capillaries should be normal [1].

In the absence of any worrying features in the history and examination, the usual investigation screen therefore comprises a full blood count and ESR, testing for ANA, nailfold capillaroscopy and, if there is any question of a cervical rib, a chest or thoracic outlet X-ray. Anaemia and/or a high ESR may indicate an underlying connective tissue disease or other illness. However, a normal haemoglobin level and ESR (as in our patient) do not exclude a diagnosis of systemic sclerosis, in which the vascular abnormalities are primarily non-inflammatory [3]. In primary Raynaud’s phenomenon, the nailfold capillaries should be fairly regular “hair-pin” loops as opposed to the abnormal dilated loops, with areas of loop drop-out, that are characteristic of systemic sclerosis [4].

Other investigations are indicated by the history and examination. For example, if there is sclerodactyly (scleroderma of the fingers) and/or digital pitting (Fig. 35.3), which are both characteristic of systemic sclerosis, then anticentromere antibodies and antibodies to topoisomerase (anti-Scl-70 antibodies) should be looked for. These antibodies are highly specific for systemic sclerosis [5]. If there is any

Fig. 35.3. Digital pitting in a patient with systemic sclerosis.
question of a proximal vascular obstruction (absent peripheral pulses) then angiography should be considered, but in the majority of patients with systemic sclerosis and digital ischaemia this is not necessary. [Q2: A, C, D, E]

Systemic sclerosis, similarly to primary Raynaud’s phenomenon, is more common in women than in men. There are two main subtypes of systemic sclerosis – limited and diffuse cutaneous – defined on the basis of the extent of the skin involvement. In patients with limited cutaneous disease (previously termed CREST – calcinosis, Raynaud’s, oesophageal dysmotility, sclerodactyly, telangiectases), only the skin of the extremities and face is thickened, whereas in those with diffuse cutaneous disease there is proximal skin thickening, involving proximal limbs and/or trunk [6]. The patient described has clinical features typical of limited cutaneous disease: Raynaud’s phenomenon preceding the diagnosis of systemic sclerosis by a number of years, sclerodactyly, digital pitting, and upper gastrointestinal problems. [Q3: A] Patients with limited cutaneous disease typically have more severe digital vascular disease than patients with diffuse cutaneous disease, and antcen tromere antibody is predictive of severe digital ischaemia [7]. [Q4: A, C, D, E]

Treatment of Raynaud’s phenomenon is initially conservative – keeping warm, avoiding cold exposure, and refraining from smoking (smoking is a risk factor for severity of digital ischaemia in patients with systemic sclerosis [8]). If these measures do not suffice, then a vasodilator is prescribed, usually a calcium channel blocker [9, 10]. There is no role for steroid therapy in most patients with systemic sclerosis (and steroids are relatively contraindicated in patients with diffuse cutaneous disease). Biofeedback has gained considerable attention but was not found to be effective in a randomised trial of primary Raynaud’s phenomenon [11]. [Q5: A, C, D] If a patient has very severe digital ischaemia, with or without digital ulceration, then the patient should be admitted for intravenous prostanoids [12] and, if there is any question of infection, then intravenous antibiotics are also indicated.

The vascular surgeon is likely to be called to see a patient with severe Raynaud’s (often in the context of systemic sclerosis) because of either non-healing ulceration or because of very severe (sometimes critical) ischaemia. The reduced blood supply

Fig. 35.4. Digital pulp calcinosis in a patient with systemic sclerosis – there is a risk that this deposit will ulcerate.
impairs ulcer healing. Debridement often aids healing. However, a proportion of patients come to amputation. Some patients have calcinosis at the site of the ulceration, and so this may be a complicating factor (Fig. 35.4). Severe ischaemia often coexists with ulceration. Cervical sympathectomy is no longer advocated for upper limb Raynaud’s phenomenon. Recently digital sympathectomy has attracted interest for the treatment of severe digital ischaemia in patients with systemic sclerosis [10, 13]. Digital sympathectomy is unlikely to be indicated at this stage in our patient, unless things do not settle with intravenous prostanooids, antibiotics and debridement. At present there is no evidence base for anticoagulation in patients with systemic sclerosis and digital ischaemia and/or ulceration although the possibility of an underlying coagulopathy, for example antiphospholipid syndrome, should always considered in patients presenting with digital ischaemia. [Q6: A, B, C]

Finally, although the vascular abnormalities in systemic sclerosis are predominantly microvascular, an increased prevalence of large vessel disease in patients with systemic sclerosis has recently been reported [14]. Thus the possibility of a proximal obstruction should always be considered in patients with systemic sclerosis presenting with an ischaemic digit.

References