usually occurring, within a few minutes of drug administration and most within the first year of treatment, although late reactions have been reported rarely [4]. We report two cases of nitritoid reactions occurring in patients with rheumatoid arthritis (RA) who have been treated with intramuscular myocrisin for over 20 yr. Both patients had been started on an angiotensin-converting enzyme inhibitor (ACE-I) in the previous year and we suggest there may be a link between the two.

The first case is a 63-yr-old male who was diagnosed with RA in 1984. He had stable joint disease on myocrisin 50 mg monthly since diagnosis. He had a past medical history of ischaemic heart disease (IHD) including previous MI and coronary artery bypass graft. His other medications included ramipril 10 mg once daily (od), isosorbide mononitrate 120 mg od, aspirin 75 mg od, atorvastatin 20 mg od, atenolol 50 mg od, nicardil 20 mg od, amiodipine 10 mg od, clopidogrel 75 mg od and prednisolone 5 mg od. On the 22 August 2002, 10 min after his myocrisin injection, he became unwell, complaining of nausea and angina and was found to be hypotensive with a blood pressure (BP) of 94/60 mmHg. He settled with symptomatic treatment within a few hours. His ECG showed no acute changes and an MI screen was negative. It was concluded that he had had a vasovagal episode secondary to the myocrisin injection, exaggerated by atenolol. The myocrisin was discontinued. On reviewing his medical records, it was noted that he had been started on ramipril on 10 May 2001.

The second case is a 74-yr-old male with RA since 1982. He had been on intramuscular myocrisin 50 mg monthly since, with stable joint disease. He had a past medical history of angina and hypertension. His other medication included perindopril 6 mg od, amiodipine 10 mg od, aspirin 75 mg od, simvastatin 20 mg od, omeprazole 20 mg od and celebrex 100 mg bd. He attended for his myocrisin on the 18 October 2004. Twenty minutes after injection he lost consciousness whilst driving his car. He was admitted, uninjured, to the accident and emergency department were an MI screen was negative. It was concluded that he had had a vasovagal episode secondary to known IHD. A month later he attended for his next myocrisin injection, which was given after careful consideration with a view to observing him post-injection for an hour. Ten minutes following the injection he became unwell with severe chest pain. He remained conscious but was hypotensive with a BP of 80/40 mmHg and a heart rate of 40 beats/min. He was treated with oxygen and intravenous fluids. Investigation revealed a normal ECG and cardiac enzymes. Within the hour he had recovered. Review of his notes in light of the first case also confirmed that perindopril was a recent alteration to his drug regimen. He was started on perindopril in December 2003 at a dose of 2 mg. This was increased to 4 mg in January 2004 and to 6 mg in May 2004.

Both patients had several risk factors for ischaemic events but in both cases the events seem closely linked to the myocrisin injection. Both have previously been well controlled on myocrisin with no side-effects in over 20 yr. Why should they develop problems now? An interaction with the ACE-I may be a possibility.

A link between late-occurring nitritoid reactions in four patients recently started on an ACE-I was first reported in 1989 by Healey and Backes [6]. There have been several other case reports since, including a case of anaphylaxis in a 49-yr-old female on myocrisin (16 months’ duration) and lisinopril (12 months’ duration) who developed cardiac arrest after injection. She was successfully resuscitated with adrenaline and hydrocortisone [7, 8]. One audit found two cases out of eight nitritoid reactions occurring 1–4 weeks after starting an ACE-I. One patient had been on myocrisin for 13 yr and one 2 yr (second course of myocrisin). These patients were managed by changing the myocrisin to gold sodium aurothioglucose (ATG) with no further problems [5].

An ACE-I may unmask drug hypersensitivity reactions possibly by potentiating kinins. ACE-I prevent the breakdown of bradykinins, thereby exposing patients to higher circulating bradykinin. It is also of interest that the onset of angioedema may be delayed for months or years after starting an ACE-I [9].

Both our patients were on low doses of myocrisin monthly for over 20 yr and developed nitritoid reactions between 10 and 15 months after the initiation of an ACE-I. We feel the need to highlight this potential interaction, as although gold is being less commonly used ACE-I are being increasingly used in the treatment of IHD and hypertension. Many of our rheumatoid patients on myocrisin may be the elderly who have been on this drug for several years and are more likely to have co-morbidities requiring treatment with an ACE-I. Considerable time lag between initiation of an ACE-I and precipitation of nitritoid reaction, which can be fatal in some instances, calls for increased vigilance with this combination of drugs.

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between these disorders. We therefore describe a woman with SSc who developed typical lesions of generalized morphea. A year later, invasive ductal carcinoma of breast was diagnosed. We discuss the rare coexistence of systemic sclerosis and morphea, and the possible implications of breast cancer.

A 47-yr-old woman from North Wales presented in February 2003 with a 10-month history of Raynaud’s phenomenon, arthralgia and mild heartburn. There was no other relevant past or family history, and no reported exposure to chemicals or toxins. On examination, the significant findings were sclerodactyly, a positive ‘prayer sign’ and abnormal nail fold capillaroscopy with capillary dropout. There was no clinical internal organ involvement; haematology, biochemistry, chest X-ray, pulmonary function tests and 2D echocardiogram results were normal. The ANA was positive at 1:160, in a nucleolar pattern. Limited cutaneous SSc was diagnosed.

In June 2003, she developed progressively enlarging intensely pruritic, hyperpigmented lesions on the back of both knees, the posterior aspect of both thighs and the outer aspect of the upper arms bilaterally. Examination showed extensive, confluent, hyperpigmented, indurated lesions with a violaceous, erythematous border typical of generalized morphea. The surrounding skin was normal and there was no extension of sclerodactyly or any other clinical development. Methotrexate 15 mg once a week was started.

In June 2004, she reported a lump in the upper outer quadrant of left breast, present for 3 months. The patient had undergone pan-hysterectomy in 1994 and was on hormone replacement therapy (HRT). Histology confirmed an invasive ductal carcinoma of the breast. HRT was discontinued. Left mastectomy with axillary clearance surgery was followed by adjuvant chemotherapy with epirubicin for 3 months, then anastrozole 1 mg daily. By October 2004, there was a marked improvement in the morphoea. Induration of the skin and subcutaneous tissue had receded with epirubicin for 3 months, then anastrozole 1 mg daily. By October 2004, there was a marked improvement in the morphoea. Induration of the skin and subcutaneous tissue had receded completely with only residual hyperpigmentation. Arthralgia and sclerodactyly remained unchanged. Methotrexate was continued.

Although considered to be rare, coexistence of SSc and LS has been reported in the past. Soma et al. [2] reported that 6.7% of 135 SSc patients at presentation had additional lesions of LS. Mizutani et al. [3] described recurrent morphea lesions over 6 yr in a patient with SSc. Conversely, Rosenberg et al. [4] reported a positive ANA in 63% of children with LS. The scleroderma specific anticientromere antibody was detected in three of 25 patients with LS in another study [5]. Maricq [6] reported two of 27 LS patients with Raynaud’s and fully established SSc.

SSc, but not LS, has been associated with approximately a two-fold increase in malignancy, the greatest risk being for lung cancer [7]. The results have been non-uniform and inconclusive for breast cancer. As reviewed in [7], a large population-based Australian study reported an insignificant increase whereas a Swedish study found no increase in breast cancer in SSc. Furthermore, a USA study reported no increase in breast or lung cancer but rather a non-significant decrease in risk of both. Although by itself not associated with increased risk of malignancy, LS may occur following radiotherapy for breast or other cancers.

The mechanisms explaining a relationship between SSc and cancer are unknown. A multitude of factors such as exposure to environmental agents, prior genetic damage, immunosuppressive therapy or paraneoplastic phenomenon have been implicated as potential common links between the two conditions [8]. Breast cancer in our patient developed within 2 yr of the onset of scleroderma. She had symptoms of breast cancer before methotrexate therapy was instituted and had never received radiotherapy. It is likely that the 10 yr of HRT was a contributing risk factor. HRT, however, is associated with an increased risk of lobular but not ductal carcinoma [9]. It remains unexplained why the morphea improved dramatically within months of treating the breast cancer. While this may have been in response to cancer chemotherapy, another possibility was the eradication of the breast tumour per se since the morphea in this setting was unusual and may have represented a paraneoplastic syndrome.

In summary, this case highlights the interesting association between SSc and LS. Such cases, although rare, might provide important clues to the pathogenesis of scleroderma. Development of breast cancer in such a rare clinical situation points to the possibility of common links between the three conditions.

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Devic’s syndrome in systemic lupus erythematosus and probable antiphospholipid syndrome

Sir, Dr Ferreira and colleagues [1] have given an excellent description of a lupus patient with Devic’s syndrome (neuromyelitis optica, NMO) but it seems that a fundamental issue of this case has not been answered. Was this patient suffering from NMO with inflammatory demyelinating disease targeting the optic nerves and spinal cord as described, or a genuine case of multiple sclerosis (MS) instead?

It is of paramount importance to make a clear distinction between these two entities; this is of interest not only academically but also because of the markedly disparate clinical outcomes and therapeutic strategies [2–4]. In the largest retrospective comparative study of 30 NMO and 50 MS patients, it has been shown that NMO usually carries a much graver prognosis [2]. Furthermore, NMO and MS differ substantially in treatment,