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**Gold, nitritoid reactions and angiotensin-converting enzyme inhibitors**

Sir, Vasomotor or nitritoid reactions are well-recognized reactions occurring in approximately 5% of patients treated with gold [1]. Patients may experience facial flushing, nausea, vomiting, hypotension or syncope. Serious sequelae have been reported, including myocardial infarction (MI) [2]. The reactions are most commonly associated with gold sodium aurothiomalate (myocrisin) but have been reported with oral gold (auranofin) [3]. The reactions are
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, nicorandil 20 mg od, amlodipine 10 mg od, clodipogrel 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 angrina and hypertension. His other medication included perindopril 6 mg od, amlodipine 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 bradykinin levels. Angioedema has been reported in patients who are taking ACE-I, which may also be a result of increased 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.

The authors have declared no conflicts of interest.

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Systemic sclerosis, morphea and breast cancer

SIR, systemic sclerosis (SSc) and localized scleroderma (LS) are generally considered to be different entities. Raynaud’s phenomenon, sclerodactyly, internal organ involvement and scleroderma-specific autoantibodies are usually not observed in LS. Nevertheless, there have been occasional reports of SSc and LS occurring together or LS evolving into SSc [1], suggesting a link.