Naproxen-associated vasculitis

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Summary: Three cases of digital vasculitis attributable to naproxen ingestion are reported. The vasculitic changes were reversed by withdrawal of the drug. These three cases emphasize the need to consider drug sensitivity as a cause of unexplained digital vascular lesions.

Introduction

Naproxen is a non-steroidal anti-inflammatory drug used commonly in the treatment of arthritis. Reports of naproxen-associated cutaneous vasculitis, nephritis and paralytic ileus are noted in the literature.\(^1\)\(^-\)\(^3\) The three cases in this report highlight the importance of vigilance in prescribing naproxen especially in the elderly.

Case 1

A 72 year old man presented with increasing pain in both hands. He had developed multiple superficial necrotic lesions on all his fingers 2 weeks previously. He had intermittent gouty arthritis associated with chronic renal failure and had been taking naproxen 500 mg twice daily for 2 years as and when necessary. Prior to the onset of his latest symptoms, he had taken the drug for about 4 weeks. An aortic aneurysm was repaired one year earlier, and he was known to have ischaemic heart disease and mild heart failure. There was no history of cold exposure and there were no transient ischaemic attacks. On examination, the thumbs and fingers of both hands appeared ischaemic with exquisitely tender pulps. The radial pulses were present.

Investigations showed ESR 14 mm/hour, haemoglobin 10.7 g/dl, blood urea 28 mmol/l, electrolytes and liver functions tests were normal. Echocardiogram was normal. An arch aortogram showed no pathology other than narrowing of the ulnar artery in the left forearm. In the absence of any obvious organic cause for these symptoms, drug sensitivity was suspected and naproxen was stopped. His fingers improved dramatically and he has had no further problems since.

Case 2

A 60 year old man presented with a recent history of painful toes on both feet. In the past, he had suffered from Raynaud’s disease and underwent bilateral cervical and lumbar sympathectomies 20 years ago. He had been hypertensive for 3 years and on nifedipine 10 mg twice daily. He had also suffered from Stokes–Adam’s attacks and had had a pacemaker implanted. There had been a transient cerebral ischaemic episode 3 months ago. He had developed a painful stiff neck and had been taking naproxen 500 mg twice daily prior to onset of symptoms. Three weeks later he developed painful ischaemic-looking lesions on the toes of both feet. All pulses were palpable with normal Doppler pressures except dorsalis pedis on the left side. There were no carotid bruits and he had no neurological deficits. Investigations including full blood count, ESR, urea and electrolytes, chest X-ray and echocardiogram were normal.

He was already taking soluble aspirin 150 mg daily and he was started on anticoagulants in case the lesions were embolic. Our experience with the previous case prompted us to withdraw the naproxen. He quickly showed signs of improvement and 3 weeks later the lesions on the toes had completely disappeared.

Case 3

A 79 year old man presented with a 3 week history of painful toes. His symptoms initially developed over 24 hours. His past history was one of severe arthritis of the spine and he had been taking naproxen 500 mg twice daily for 8 months. On examination, his right big toe, and his left second and third toes appeared severely ischaemic and cyanosed. He had a superficial necrosis on the left second toe. All his pulses were present.

Investigations showed ESR 13 mm/hour, nor-
mal blood count, blood urea and electrolytes, and liver function tests. Naproxen treatment was stopped, and within 48 hours he was virtually pain free and the necrotic lesions completely healed 3 weeks later.

**Discussion**

We describe three patients who developed acute digital ischaemia associated with naproxen. It is presumed this was caused by local vasculitis although no histology was available. To our knowledge, there are three isolated reports of cutaneous vasculitis secondary to naproxen ingestion.\(^1\)\(^2\) Nephritis and paralytic ileus have also been reported following administration of naproxen and it seems likely that these are also due to vasculitis.\(^3\) There are approximately 20 cases of vasculitic lesions possibly related to naproxen ingestion reported to Syntex Company (UK). In our three cases, the changes were reversed by withdrawal of the drug. Vascular disease and arthritis may well co-exist in patients presenting to vascular clinics and one must therefore determine if the treatment of one is contributing to or causing symptoms of the other. These three cases emphasize the need to consider drug sensitivity as a cause of unexplained digital vascular lesions particularly in patients on treatment with naproxen.

**References**