Fatal vasculitis associated with ofloxacin

Joseph L Pace, Paul Gatt

University Department of Dermatology, Paul Boffa Hospital, Floriana, Malta
Joseph L Pace, FRCP, consultant
Paul Gatt, MD, senior house officer

Correspondence to: Dr Pace.

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Vasculitis is an adverse effect of numerous drugs. We report on a man who developed vasculitis and died after taking ofloxacin for a chest infection.

Case report

A 75 year old man was treated with bumetanide and spironolactone for cardiac failure. Two weeks later he was given ofloxacin 200 mg twice daily for five days for apparent bronchitis. Several haemorrhagic bullae and palpable purpuric rash developed on the feet and hands (figure). He was mildly jaundiced, and his liver was palpable 2 cm below the costal margin. Full blood count, differential white cell count, and results of coagulation studies were normal. A test for antinuclear factor yielded negative results. Microscopy of urine showed numerous red cells, and analysis showed a trace of protein. The plasma concentration of urea was 56.4 mmol/l, creatinine 400 mmol/l, and bilirubin 43 mmol/l; γ -glutamyltransferase activity was 65 U/l and alanine transferase activity 56 U/l.

Twenty four hours later massive melaena with haematuria occurred. Haemorrhages were evident on the palate. Gastroscopy showed a bleeding prepyloric ulcer and nodular haemorrhagic lesions similar to those that had developed in the skin. Temporary improvement occurred with intensive care, but the patient died after a second massive gastrointestinal haemorrhage a few days later.

Haemorrhagic bullae on erythematous base

At necropsy extensive haemorrhages were seen in the mediastinum, pericardium, gastrointestinal tract, renal pyramids, and bladder. A haemorrhagic duodenal ulcer had penetrated into the pancreas. Histological examination of the skin lesions showed changes compatible with vasculitis.

Comment

Numerous drugs may cause vasculitis,¹ and systemic disease may be fatal.² Ofloxacin is a new fluorinated quinolone antibiotic drug. Adverse reactions have usually related to the gastrointestinal tract (nausea and diarrhoea) and the central nervous system (headache and restlessness). Rashes have been rare and transient, occurring in seven of 1965 patients in the first studies. Four cases of vasculitis were found during postmarketing surveillance,³ but in several others (14 cases) ofloxacin was not considered to be the main factor (Hoechst AG, personal communication). In the absence of previous symptoms of gastrointestinal disease doctors should bear in mind that acute drug induced gastric ulceration with vasculitis may have occurred⁴ and that systemic vasculitis may present with gastrointestinal bleeding. Uraemia may also aggravate the tendency to bleeding.

It is often difficult to establish whether drugs and reactions were related in fatal cases. This patient's rash, which was identical with that described by the drug's manufacturers, developed immediately after the drug was given (most drug induced rashes start within seven days). Bumetanide and spironolactone had been given three weeks earlier, and only two unconfirmed reports¹ have associated them with vasculitis. A closely related quinolone, ciprofloxacin, has caused vasculitis and abnormal hepatorenal function.⁵ Finally, the half life of ofloxacin is greatly increased in renal insufficiency, and its accumulation could lead to Arthus type hypersensitivity reactions such as certain types of vasculitis. Ofloxacin was probably an important factor in this case. We suggest that because of this the drug should be used only when other, better known agents are ineffective.

- 1 Bruinsma W, ed. Vascular reactions. In: *A guide to drug eruptions*. 4th ed. Oosthuizen, The Netherlands: De Zwaluw, 1987:67.
- 2 Schonhofer PS, Groticke J. Fatal necrotising vasculitis associated with nifedipine. *Lancet* 1985;ii:221.
- 3 Jungst G, Mohr R. Side effects of ofloxacin in clinical trials and postmarketing surveillance. *Drugs* 1987;34 (suppl 1):144-9.
- 4 Pain AK. Acute gastric ulceration associated with drug therapy. *Br Med J* 1967;ii:634.
- 5 Choe U, Rothschild BM, Laitman L. Ciprofloxacin-induced vasculitis. *N Engl J Med* 1989;320:257-8.

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Problems in setting standards for hospital referrals: experience with warts

M O Roland, M Dixon

Cambridge University School of Clinical Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ
M O Roland, DM, director of studies in general practice
M Dixon, BA, research assistant

Correspondence to: Dr Roland.

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After the publication of an article entitled "Dermatologists should not be concerned in routine treatment of warts"¹ we sent a questionnaire to dermatologists to determine whether this was a generally accepted view. We report our results, which show some of the difficulties in defining standards for hospital referrals.

Methods and results

We sent a questionnaire to 144 randomly selected consultant dermatologists in England and Wales; 131

replies were received (92%). Once general practitioners were sure about the diagnosis of warts 46 dermatologists agreed that they should be able to refer any patient they wanted; 43 that they should be able to refer patients with multiple warts; 33 that they should be able to refer patients with single plantar warts; and 93 that they should be able to refer patients with warts resistant to three months' topical treatment. Fifty six, 52, 59, and 17 respectively, however, disagreed that general practitioners should be able to refer under these conditions. Although several dermatologists did not fill in this part of the questionnaire, only three replied "don't know" to these questions. A similar divergence of views was seen in the response to a general question about the appropriateness of a hospital based service for treating warts (table).

Widely ranging views were expressed in additional comments or letters, several of which were very detailed. Some consultants argued that warts were far from trivial and that wart clinics offer a valuable