Reversible agranulocytosis due to meprobamate

S. Ward and J. Meecham

Arrowpark Hospital, Wirral, Merseyside, UK.

Summary: A 52 year old man admitted to hospital in a toxic state, was found to have agranulocytosis, which recovered when an analgesic containing meprobamate was stopped. The patient was known to have had similar symptoms 9 months previously when the drug was first used, thereby demonstrating an idiosyncratic reaction to meprobamate.

Introduction

Meprobamate is a constituent of a number of compound drugs listed in the British National Formulary and is used alone as a minor tranquillizer. Although standard texts on the side effects of drugs list agranulocytosis as an adverse reaction to meprobamate, no causal relationship has been established. We wish to report a case of reversible agranulocytosis following the use of meprobamate, where there is a clearly defined association.

Case history

A 52 year old South African male presented with a 10 day history of severe mouth ulceration, sore throat, pyrexia and general malaise. Two days before the onset of symptoms, the patient had been prescribed an analgesic drug containing meprobamate 300 mg, paracetamol 250 mg, caffeine 50 mg and codeine phosphate 5 mg. No other medication had been used in the preceding 6 weeks. Nine months previously the patient had experienced the same symptoms after taking the meprobamate compound. On that occasion the mouth ulceration and pyrexia resolved 7 days after stopping the tablets. The meprobamate compound had not been prescribed again until this admission.

On examination he looked unwell with temperature 38°C, cervical lymphadenopathy, and sinus tachycardia. There were no skin rashes or signs of bleeding. Widespread deep, inflamed and painful ulcers were present on the tongue, buccal mucosa, and pharynx. There were no other abnormal signs, in particular the spleen was not palpable. Initial investigations showed haemoglobin 14 g/l, white cell count $0.9 \times 10^9/l$. Differential: lymphocytes 90%, neutrophils nil, eosino-

phils nil, monocytes 10%. Sodium 140 mmol/l, potassium 4.0 mmol/l, urea 8.0 mmol/l, erythrocyte sedimentation rate 60 mm/h. Chest radiograph was normal.

The diagnosis of agranulocytosis with systemic infection was made, no obvious focus could be found and treatment was commenced with intravenous piperacillin, tobramycin and oral nystatin. The analgesic was stopped. Over the next 14 days, the patient improved with recovery of the white cell count and granulocyte series. Blood cultures, viral studies and rickettsial antibody screen with thick and thin film for malarial parasites did not isolate any infecting organism. Mouth and throat swabs grew *Candida* species. Bone marrow aspirate and biopsy carried out 24 hours after admission and 10 days after first taking the drug, showed an absence of mature neutrophil white cells, with occasional myelocytes only. All other cell lines appeared normal. The patient made a full recovery and was discharged home 10 days after admission.

Discussion

Agranulocytosis due to meprobamate has been reported on two occasions only. Curran & Barabas (1961) described a 56 year old woman with fatal agranulocytosis, but this patient was also taking imipramine and it was unclear which drug had been responsible. Nitscheiner (1967) reported a patient who developed fatal agranulocytosis with meprobamate but this was thought to be due to an allergic cross-reaction with procaine penicillin. Two other cases have been reported to the Committee on Safety of Medicines since 1965 but no details are available (Personal communication, 1984). Although there have been four episodes of agranulocytosis due to paracetamol or codeine phosphate reported to the Committee on Safety of Medicines since 1964, this patient had taken these two

Correspondence: S. Ward, M.B., M.R.C.P., Freeman Hospital, High Heaton, Newcastle upon Tyne 7, UK
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drugs without ill effect, on a number of occasions over the preceding year. The onset of an identical illness 9 months previously when the patient was first exposed to meprobamate and the recurrence of symptoms due

to agranulocytosis with re-exposure to the drug demonstrates an idiosyncratic reaction to meprobamate causing reversible agranulocytosis.

References

CURRAN, T.P. & BARABAS, E. (1961). Agranulocytosis after imipramine and meprobamate. *British Medical Journal*, **4**, 257.

NITSCHHEINER, H. (1967). Agranulocytosis as a result of a cross reaction following application of procaine penicillin and meprobamate. *Deutsche Gesundheitswesen*, **22**, 565.