

Fever, vasculitic rash, arthritis, pericarditis, and pericardial effusion after mesalazine

Drs A G LIM and K R HINE (Princess Royal Hospital, Haywards Heath, West Sussex RH16 4EX) write: A 30 year old man with an 11 year history of mild ulcerative colitis presented with a relapse. He had been treated with oral sulphasalazine in the past with no ill effect, but during a recent relapse he developed a vasculitic rash on his lower legs and painful swollen ankles after three weeks of sulphasalazine treatment. These symptoms had receded a couple of days after stopping sulphasalazine. We therefore gave him oral mesalazine (800 mg a day), rectal hydrocortisone (25 mg a day), and oral prednisolone (20 mg a day). Three weeks later both diarrhoea and rectal bleeding had subsided, but he developed a florid purpuric rash over his lower legs and was breathless and unable to walk because of painful swollen ankles. His temperature was 39°C and he had a loud pericardial rub.

A chest x ray film showed a globular cardiac outline. Electrocardiography showed sinus tachycardia with reduced QRS voltages. Echocardiography showed the presence of a pericardial effusion. Haemoglobin concentration was 112 g/l, white cell count $15.9 \times 10^9/l$, and platelet count $647 \times 10^9/l$. A blood film showed hypochromia, microcytosis, neutrophilia, and rouleaux. Erythrocyte sedimentation rate was 63 mm in the first hour. Serum globulin concentration was 40 g/l (normal range 18-36) and γ -glutamyltransferase concentration was 81 IU/l (7-49). The rest of the results from the biochemical screen were normal, as were his autoimmune profile, results from blood and urine cultures, and results of viral serology. Mesalazine induced hypersensitivity reaction was diagnosed and the drug was stopped. Oral prednisolone was also stopped and intravenous hydrocortisone 50 mg was given four times a day. After 48 hours the rash faded, the fever settled, and the ankle pain and swelling diminished. A week later he had fully recovered and the steroids were reduced. A repeat echocardiogram showed a small residual pericardial effusion.

To our knowledge, this is the first report of a combination of fever, vasculitic rash, arthritis, pericarditis, and pericardial effusion after treatment with mesalazine. It has similarities to previously reported cases of mesalazine associated pericarditis,¹ pericardial effusion,² Kawasaki-like syndrome,³ and lupus-like syndrome.⁴ The rapid onset of this patient's reactions to two different 5-aminosalicylic acid products and resolution of the reaction soon after stopping the

drugs suggests that they were due to the drugs and not the disease. Although the pathogenetic mechanisms are unclear, this case shows that serious drug hypersensitivity reactions previously attributed to sulphasalazine may also develop to aminosalicic acid preparations that do not contain sulphapyridine.

- 1 Habal FM, Greenberg GR. Treatment of ulcerative colitis with oral 5-aminosalicylic acid including patients with adverse reactions to sulfasalazine. *Am J Gastroenterol* 1990;83:15-9.
- 2 Jess H, Becker EW, Weber P. Pericardial effusion during treatment with 5-aminosalicylic acid in a patient with Crohn's disease. *Am J Gastroenterol* 1990;85:332-3.
- 3 Waanders H, Thompson J. Kawasaki-like syndrome after treatment with mesalazine. *Am J Gastroenterol* 1991;86:219-21.
- 4 Dent MT, Ganapathy S, Holdworth CD, Channer KC. Mesalazine induced lupus-like syndrome. *BMJ* 1992;305:159.

Is there a problem with long term use of sumatriptan in acute migraine?

Messrs M J OSBORNE, R C T AUSTIN, K J DAWSON, and Dr L LANGE (Royal Free Hospital, London NW3 2QG) write: We report a case of a migraine sufferer treated with sumatriptan who developed a dramatic increase in the frequency of migraine attacks with consequent dependence.

For 50 years a 62 year old man had suffered severe migraine attacks with vomiting and prostration, lasting for 24-36 hours and recurring about once a month. Previous medication had been unhelpful. One year before admission he started taking subcutaneous sumatriptan, which terminated his migraine attacks fully within 25 minutes. Two months before admission he realised that every morning he was waking with a mild headache which frequently progressed to a migraine needing sumatriptan. He converted to the oral form, which was as effective, although slower acting, and he progressed to taking a morning tablet to avoid a migraine. A home attempt at drug withdrawal resulted in a severe migraine terminated at four hours by sumatriptan.

On admission his sumatriptan was replaced with pizotifen and trifluoperazine. That evening he developed a severe migraine for which ergotamine and caffeine suppositories, pethidine, and metoclopramide gave only moderate relief. The next day diazepam was added and eventually the attack subsided. The sedatives were stopped and he suffered a further brief migraine, which resolved with ergotamine, caffeine, and diazepam; he was discharged with a small supply of diazepam. Subsequently his migraine attacks have been treated successfully with a combination of drugs not including sumatriptan.

Sumatriptan is seen as an advance in the treatment of acute migraine¹⁻⁴; previously only immediate side effects have been reported.¹ This case suggests that longer term use of sumatriptan may lead to a dependent state.

- 1 Sumatriptan: a new approach to migraine. *Drug and Therapeutics Bulletin* 1992;30:85-7.
- 2 Feniuk W, Humphrey PP, Perren MJ, Connor HE, Whalley ET. Rationale for the use of 5-HT₁-like agonists in the treatment of migraine. *J Neurol* 1991;238(suppl 1):S57-61.
- 3 The Subcutaneous Sumatriptan International Study Group. Treatment of migraine attacks with sumatriptan. *N Engl J Med* 1991;325:316-21.
- 4 Cady RK, Wendt JK, Kirchner JR, Sargent JD, Rothrock JF, Skaggs HJ. Treatment of acute migraine with subcutaneous sumatriptan. *JAMA* 1991;265:2831-5.
- 5 The Oral Sumatriptan Dose-Defining Study Group. Sumatriptan—an oral dose-defining study. *Eur Neurol* 1991;31:300-5.
- 6 The Multinational Oral Sumatriptan and Cafergot Comparative Study Group. A randomized, double-blind comparison of sumatriptan and Cafergot in the acute treatment of migraine. *Eur Neurol* 1991;31:314-22.

Myoclonus associated with propafenone

Drs T P CHUA, T FARRELL, and D P LIPKIN (Department of Cardiology, Royal Free Hospital, London NW3 2QG) write: We report a case of myoclonus in a patient who took propafenone for paroxysmal atrial fibrillation.

An 82 year old woman with a history of paroxysmal atrial fibrillation had been taking amiodarone for three years. Treatment was stopped because of pulmonary fibrosis. She was also taking a thiazide diuretic for hypertension and thyroxine for hypothyroidism. She started propafenone treatment (150 mg twice a day) and the dose was increased (150 mg three times a day), which controlled her paroxysmal atrial fibrillation. Two weeks later she complained of immobility. A consultant neurological opinion was sought. Her muscle tone, power, and reflexes were normal, but she had developed myoclonus affecting her arms and legs. She also had apraxia of gait. Her serum calcium and magnesium concentrations were 2.38 (normal reference range 2.1-2.6) and 0.79 (0.7-1.0) mmol/l respectively. Her erythrocyte sedimentation rate was 13 mm in the first hour. Computed tomography of the brain showed only minor changes. Electroencephalography was not performed. Propafenone treatment was stopped. Her gait improved and myoclonus resolved after three days. She was rechallenged with propafenone and again developed myoclonus and apraxia. The drug was stopped and she quickly improved. Her arrhythmia was managed with quinidine, and she was discharged.

Myoclonus is the sudden, involuntary jerking of a single muscle or a group of muscles. We know of only one other published report of myoclonus associated with propafenone treatment.² Adverse reaction to propafenone should be considered in patients developing myoclonus and gait abnormality during the course of treatment.

- 1 Dukes ID, Vaughan Williams EM. The multiple modes of action of propafenone. *Eur Heart J* 1984;5:115-25.
- 2 Devoize JL, Flammang D, Marcombes JL. Encéphalopathie myoclonique probablement due à la propafénone. *Presse Med* 1986;8:15.

Allopurinol interaction with cyclosporin

Drs M GORRIE, M BEAMAN, and A NICHOLLS and Miss P BACKWELL (Renal Unit, Royal Devon and Exeter Hospital, Exeter EX2 5DW) write: We report a potentially serious interaction between allopurinol and cyclosporin which has not previously been reported in the United Kingdom (Sandoz Pharmaceuticals, personal communication).

A 27 year old woman whose renal transplant had been stable for 11 years had received maintenance doses of cyclosporin since 1990. For 18 months the lowest concentrations of cyclosporin in whole blood had been consistently around 130 $\mu\text{g/l}$ with a constant dose of cyclosporin (175 mg twice daily). She was treated for gout and hyperuricaemia with allopurinol (200 mg daily); naproxen for five days to cover the introduction of allopurinol. At routine review two months later cyclosporin concentrations were 410 $\mu\text{g/l}$. Allopurinol was stopped and three weeks later cyclosporin concentrations were 160 $\mu\text{g/l}$.

Rechallenge with allopurinol alone (200 mg daily) resulted in a rise in cyclosporin concentrations to 245 $\mu\text{g/l}$ after 10 days and 339 $\mu\text{g/l}$ after two months. The dose of cyclosporin was then reduced. Her usual treatment remained unchanged: ranitidine 150 mg daily, ferrous sulphate 200 mg daily, enalapril 20 mg daily, frusemide 80 mg daily, atenolol 100 mg daily, prednisolone 10 mg daily, and slow release nifedipine 10 mg twice daily.

During this relatively short period of drug interaction her serum creatinine concentration remained unchanged, which contrasts with a previously reported case. The interaction may not be widely recognised for this reason.¹ Cyclosporin nephrotoxicity may occur with long term implications unless the dose is reduced.

- 1 Stevens SL, Goldman MH. Cyclosporine toxicity associated with allopurinol. *Southern Medical Journal* 1992;85:1265-6.