FEATURE

Medicinal mishap

Flecainide and neutropenia

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Case

A 73-year-old woman was admitted to hospital for investigation following a short episode of slurred speech which was diagnosed as a transient ischaemic attack. She had a history of paroxysmal atrial fibrillation, transient ischaemic attacks, essential hypertension, duodenal ulcer, chronic hepatitis B infection and acoustic neuroma.

Her drug history found that she had been switched from metoprolol to flecainide 50 mg twice a day for control of her atrial fibrillation three months previously. The only other drug she had been taking was omeprazole 20 mg twice a day for two years.

An incidental finding on admission was a white blood cell count of 2.5 x 10^9/L, with a neutrophil count of 0.61 x 10^9/L. Reactive lymphocytes were present. The remaining white cell differential was within normal ranges. Haemoglobin was normal, with a slightly raised mean cell volume. Platelet count was reduced at 127 x 10^9/L.

Liver function tests were mildly abnormal, consistent with chronic hepatitis B infection. Renal function was normal for age and testing for autoimmune and rheumatoid disorders, HIV and haematological malignancy was negative. C-reactive protein was 15 mg/L and erythrocyte sedimentation rate was 19 mm/hour.

On day two of admission, the neutrophil count dropped to 0.28 x 10^9/L. Flecainide was ceased on the same day. Five days after stopping flecainide, the neutrophil count had risen to 1.59 x 10^9/L. Omeprazole was continued throughout and metoprolol reinstated for rate control of her atrial fibrillation.

Comment

Flecainide is a class 1c antiarrhythmic drug indicated for use in supraventricular arrhythmias in patients without structural heart disease. It is not recommended for use in chronic atrial fibrillation.

Agranulocytosis is a rare but serious complication of antiarrhythmic drugs. It has previously been associated with procainamide, quinidine and flecainide. The mechanism by which agranulocytosis develops with flecainide is not clearly understood, however a putative mechanism involves the development of flecainide-specific IgG antibodies.[1,2]

This is the first case of flecainide-induced neutropenia reported to the Therapeutic Goods Administration in which no other drugs were suspected to have contributed.[3] There have been 32 cases reported to the Food and Drug Administration in the USA, with three-quarters of cases occurring within six months of starting flecainide.[4]

In this case the neutropenia could not be attributed to any other drug, concurrent disease or infection. Additionally, there was a plausible time relationship between starting flecainide and developing a neutropenia which resolved after the drug was stopped.

Conclusion

There was a probable causal association between flecainide and neutropenia. This is a rare adverse reaction associated with some antiarrhythmic drugs and this may be the first such report in Australia.

REFERENCES

1. Samlowski WE, Frame RN, Logue GL. Flecanide-induced immune neutropenia. Documentation of a hapten-mediated mechanism of cell destruction. Arch Intern Med 1987;147:383-4.
2. Starkebaum G, Kenyon CM, Simrell CR, Creamer JI, Rubin RL. Procainamide-induced agranulocytosis differs serologically and clinically from procainamide-induced lupus. Clin Immunol Immunopathol 1996;78:112-9.
3. Database of Adverse Event Notifications [database]. Canberra: Australian Government Department of Health and Ageing, Therapeutic Goods Administration. 2012. www.tga.gov.au/DAEN/daen-report.aspx [cited 2013 Jan 7]
4. Could flecainide acetate cause neutropenia, in real world? eHealthMe - Real world drug outcomes. 2012. www.ehealthme.com/ds/flecainide+acetate/neutropenia [cited 2013 Jan 7]