Case report

Leucopenia and thrombocytopenia possibly associated with lamotrigine use in a patient

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ABSTRACT – Haematological side effects are rather exceptional with lamotrigine. We report the case of a 25-year-old woman with epilepsy who developed combined leucopenia and thrombocytopenia eight weeks after starting lamotrigine. Within weeks after lamotrigine was discontinued, all of the haematopoietic abnormalities had disappeared. To our knowledge, this is the first report of combined leucopenia and thrombocytopenia associated with lamotrigine treatment suggesting, in our patient, a causal reaction.

Key words: lamotrigine, epilepsy, leucopenia, thrombocytopenia

Lamotrigine (LTG; Lamictal®), a wide-spectrum antiepileptic drug (AED), is derived from the dihydrofolate reductase inhibitor class of compounds and is thought to act mainly through blocking the influx of sodium ions, thereby reducing excess glutamate release and stabilizing neuronal membranes (Leach et al. 1986). Lamotrigine is effective as monotherapy in both newly diagnosed adults with either partial or mixed seizure disorders and newly diagnosed children with absence seizures (French et al. 2004, I). It is also effective as an adjunctive treatment of refractory partial seizures and idiopathic generalized epilepsy in adults and children, as well as in the treatment of Lennox-Gastaut syndrome (French et al. 2004, II). It is eliminated mainly by hepatic metabolism to the glucuronide conjugate (Brodie 1992). Clearance of the drug is slightly lower in patients with Gilbert's syndrome, who have decreased uridine diphosphate glutamyl transferase activity (Peck 1991). LTG is well tolerated in children and adults (Arzimanoglou et al. 2001). The most frequent adverse events include somnolence, rash and episodes of transitory diplopia. It can very occasionally cause minimal haematological side effects, including agranulocytosis, neutropenia, thrombocytopenia and asymptomatic disseminated intravascular coagulation (DIC) (Nicholson et al. 1995, De Camargo and Bode 1999, Facul et al. 1997, Mackay et al. 1997, Wong et al. 2001). We report a female patient who developed leucopenia and thrombocytopenia after receiving LTG for partial seizures.
Case study
A 25-year-old woman was started on LTG (25 mg, p.o., twice daily) because of simple, partial seizures. Her neurological examination and cranial MRI were normal; EEG showed left temporal focal abnormalities. LTG continued to be increased by 50 mg every two weeks up to 200 mg daily, because of progressively difficult-to-control, simple, partial seizures. Four weeks after starting LTG, she was clinically well and free of seizures. Laboratory studies revealed a platelet (PLT) count of 342 x 10^9/L and a white blood cell (WBC) count of 5.5 x 10^9/L with a normal differential. Four weeks later, at her routine follow-up, laboratory studies demonstrated a PLT count of 29 x 10^9/L and a WBC count of 1.7 x 10^9/L (neutrophils 0.8 x 10^9/L); her serum LTG concentration was 1.6 mg/L before taking LTG and 2.4 mg/L after 6 hours. Other laboratory values including hepatic, renal and thyroid function tests, antibody titers against rubella, toxoplasmosis, CMV, HSV, EBV, HCV, HIV and HBV, as well as the VDRL test, were unremarkable and she was asymptomatic. A particular drug might bind to the membrane of circulating platelets, where it could then act as a hapten to trigger antibody formation (Levine 2004). However, in our patient, antiplatelet and platelet-associated antibodies were not detected.

In conclusion, there have been a few sporadic reports of isolated neutropenia or thrombocytopenia associated with the use of LTG over the past 10 or more years, however, this is the first report of combined leucopenia and thrombocytopenia associated with LTG treatment.

References


