

106. Neutropenia Caused by Intravenous Immunoglobulins

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Background: Although neutropenias induced by intravenous immunoglobulins (IVIG) have been previously reported, this adverse effect is not mentioned in the SPC of these products. We have analysed reports of IVIG-induced neutropenia to the French Pharmacovigilance centres.

Methods: Cases of neutropenia defined by a neutrophil count $\leq 1,5$ G/l involving any IVIG were extracted from the French Pharmacovigilance database. Cases with other potential causes, clearly suspected co-medication or unknown outcome were excluded.

Results: Among the 34 of IVIG-associated neutropenia recorded between 1997 and 2006, 16 fulfilled our criteria. The female/male ratio was 2.2:1 and the mean age was 54.8 years (4 d - 80 y). The patients were treated for various conditions with a mean dose of 30 g per day and a mean cumulative dose of 132 g. Neutropenia was diagnosed from a systematic blood cell count performed 1 to 7 days (mean: 3.4 days) after the first infusion. The mean neutrophil count at diagnosis was 0.9 G/l (range: 0.28-1.5), and was less than 0.55 G/l in 4 patients or less than 1 G/l in 9. Five patients had moderate clinical symptoms including fever in 4, shivering in 2, local vein inflammation in 1 and hypotension in 1. Three patients also had a moderately decreased platelet count. Bone marrow aspiration performed in 2 patients was normal. Neutropenia resolved promptly (1-3 days in 5 patients) and spontaneously after treatment discontinuation in all patients. None of the patient experienced any infectious complications. In 10 patients, IVIG were subsequently readministered and 8 again experienced neutropenia without complications. In one patient, epinephrine 0.5 mg/m² produced demargination of granulocytes (> 50% increase).

Conclusion: The potential role of IVIG should be suspected in patients who develop asymptomatic neutropenia shortly after this treatment is started. IVIG-induced neutropenia are transient, resolved spontaneously, and are not associated with infectious complications. The more commonly suggested mechanisms are the presence of antineutrophil antibodies in some IVIG preparations, or an increase in leukocyte aggregation (pseudo-leucopenia) produced by IVIG. This last mechanism was suggested in one of our patient. Clinicians must be aware of this benign complication.