Letter to the Editors

Glimepiride-induced vasculitis: a case report

Chaker Ben Salem, Houssein Hmouda & Kamel Bouraoui
Department of Clinical Pharmacology, Faculty of Medicine of
Sousse, Sousse, Tunisia

Glimepiride is the most recently introduced sulphonylurea agent. It is generally well tolerated. Cutaneous adverse reactions attributed to glimepiride are rare and include rash, pruritus, photosensitivity and lichenoid eruption [1]. We report here a case of leukocytoclastic vasculitis (LV) associated with glimepiride.

A 72-year-old woman had a 4-year history of hypertension treated by captopril 25 mg daily and a 2-year history of Type 2 diabetes mellitus that was initially treated with diet, then with glimepiride 1 mg day⁻¹. Six weeks after starting glimepiride, the patient noticed the onset of a nonpruritic eruption on her legs and was seen by a dermatologist of our university hospital. Physical examination revealed a temperature of 37 °C and palpable erythematous papules on both lower limbs. The eruption also involved the upper extremities and the trunk (Figure 1). There were no physical signs suggesting clinical evidence of connective tissue or other systemic disease. A skin biopsy showed leukocytoclastic vasculitis. Neutrophils and eosinophils were present in the inflammatory infiltrate. Direct immunofluorescence was negative. Laboratory tests revealed the following: haemoglobin 13 g dl⁻¹, total white blood cell count $11 \times 10^3 \text{ mm}^{-3}$ and platelets $244 \times 10^3 \text{ mm}^{-3}$. Prothrombin time and partial thromboplastin time were normal, as were C-reactive protein and results of kidney and liver function tests. Other causes of LV were ruled out, with negative results for antinuclear antibodies, antineutrophil cytoplasmic antibodies, cryoglobulins, rheumatoid factor and hepatitis B and C serology. Serum protein electrophoresis and serum concentrations of C3 and C4 were normal. Immunoglobulin levels were normal, except for IgE level, which was slightly elevated. Urinalysis was negative for haematuria and proteinuria. Viral investigations showed previous infection with cytomegalovirus and

Figure 1

Purpuric and erythematous eruption in extremities and trunk

Epstein–Barr virus. Drug-induced vasculitis was suspected and glimepiride was stopped. All lesions resolved spontaneously within 1 week and the patient had no further episodes of skin eruption over a follow-up period of 3 months. Her glycaemia was well controlled by diet alone and glimepiride was not re-administered.

According to the Naranjo probability scale, glimepiride-induced vasculitis was probable [2]. In our review of the literature and according to data from a MEDLINE search, we have not identified any previous report of glimepiride-induced LV.

Medications from many different pharmacological classes are incriminated in the development of LV. The diagnosis of drug-induced vasculitis is based on exclusion of known causes of vasculitis, the patient's drug exposure and improvement of the symptoms when the suspected drug is withdrawn. The exact pathogenic mechanism of drug-induced vasculitis is unknown, but it seems to be a type III hypersensitivity reaction.

The formation of circulating immune complexes leads to vascular wall damage. Vasculitic lesions can also be mediated by other immunopathological mechanisms such as allergic vasculitis, antibody-mediated vasculitis and T-cell-mediated hypersensitivity vasculitis [3]. Hypersensitivity reactions, including skin reactions, due to sulphonylureas can occur in the first 6–8 weeks after starting therapy. Prior reports of LV have implicated oral hypoglycaemic agents [4, 5]. However, we have found no prior reports of LV related to glimepiride. Considering the wide use of glimepiride, clinicians should be vigilant for the possibility of leukocytoclastic vasculitis occurring during its use.

References

- 1 Noakes R. Lichenoid drug eruption as a result of the recently released sulfonylurea glimepiride. *Australas J Dermatol* 2003; 44: 302–3.
- 2 Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30: 239–45.
- 3 Carlson JA, Cavaliere LF, Grant-Kels JM. Cutaneous vasculitis: diagnosis and management. *Clin Dermatol* 2006; 24: 414–29.
- 4 Ben Salem C, Hmouda H, Slim R, Denguezli M, Belajouza C, Bouraoui K. Rare case of metformin-induced leukocytoclastic vasculitis. *Ann Pharmacother* 2006; 40: 1685–7.
- 5 Dickey W, Handley J. Purpura, leukocytoclastic vasculitis, and glibenclamide. *BMJ* 1986; 293: 823–4.

Received

16 November 2006

Accepted

4 December 2006

Published OnlineEarly

23 February 2007

Correspondence

Chaker Ben Salem, Department of Clinical Pharmacology, Faculty of Medicine of Sousse, Avenue Mohamed Karoui, Sousse 4002, Tunisia.
E-mail: chaker_doc@yahoo.fr