Leading Article

Dapsone in Henoch-Schönlein purpura – worth a trial

B.I. Hoffbrand

Whittington Hospital, London N19 3UA, UK

Dapsone and other sulphone drugs have been important therapeutic agents in dermatitis herpetiformis for over 40 years^{1,2} and have subsequently been used in a variety of dermatological conditions.³ Dapsone appears to be of especial value in diseases characterized by an accumulation of polymorphonuclear neutrophils notably with leucocytoclastic vasculitis, a feature of erythema elevatum diutinum,⁴ urticarial vasculitis^{5–7} and allergic vasculitis.^{8–10}

The most clearly delineated condition with prominent cutaneous leucocytoclastic vasculitis which presents to general physicians (and paediatricians) is Henoch-Schönlein purpura. In 1983 we presented what appear to be the first reported cases of Henoch-Schönlein purpura treated with dapsone to good effect.¹¹ Subsequently, Chamouard and colleagues¹² gave dapsone to a 69 year old man with leucocytoclastic vasculitis and gastrointestinal purpura with a rapid resolution of abdominal symptoms and the evidence of a protein-losing enteropathy.

In the past year we have seen two further patients with Henoch-Schönlein purpura who have responded dramatically to dapsone. The first, a 24 year old man, developed the characteristic skin lesions with abdominal pain, fever and arthritis following a sore throat. He was investigated in the department of rheumatology of a London teaching hospital and shown on skin biopsy to have leucocytoclastic vasculitis. The fever and, much later, the abdominal pain subsequently cleared but he had a total of 18 weeks off work. When we first saw him 7 months after the onset, he still had recurrent 'palpable purpura' involving his forearms as well as his legs, and painful swollen ankles. Within 24 hours of starting dapsone 100 mg/day the ankle pain cleared followed by the upper limb purpura a few days later. The dose was reduced over the next 2 months and then stopped. During this time and over the following 10 months there have been occasional sparse crops of purpura around the ankles associ-

ated with standing for long periods, without the need for further dapsone. The second patient was a 15 year old Taiwanese schoolboy, under the care of the paediatric department of the same hospital, with palpable purpura, arthralgia, vomiting and diarrhoea followed by recurrent abdominal pain. He had been away from school for 3 weeks. Within 3 hours of the first 50 mg tablet of dapsone the abdominal pain disappeared. There was no recurrence of purpura or rash with just one week of dapsone 50 mg/day. He returned to school the day after starting treatment.

The mechanism of action of dapsone in leucocytoclastic vasculitis is unknown. There is evidence that it has an antioxidant scavenger effect^{13,14} and may also suppress the generation of toxic free radicals in polymorphonuclear neutrophils.¹⁵ Actions in inhibiting prostaglandin PGD₂ production¹⁶ and the synthesis of IgG and IgA antibodies¹⁷ may also be relevant. The latter two properties of dapsone may be of particular importance for its use in Henoch-Schönlein purpura as a number of observations have been made which point to an immune dysregulation, primarily of IgA production, in this condition, whilst there are disturbances of prostaglandin metabolism in acute Henoch-Schönlein purpura which may contribute to the inflammatory process.¹⁸

There is general agreement that corticosteroids are of limited value in conditions characterized by leucocytoclastic vasculitis.^{10,19} Dapsone, on the other hand, appears to be effective and safe in relatively small doses. The evidence that dapsone may be of value in Henoch-Schönlein purpura is limited to the evidence presented here and does not include any pointers to a possible effect on associated glomerulonephritis. There is also no evidence that dapsone is curative or does other than reduce the inflammatory process and provide symptomatic relief. However, in a condition with no treatment of proven value,²⁰ there appears to be enough evidence to justify a trial of dapsone for symptom relief and for the possible life threatening complications of gut purpura and severe glomerulonephritis. The possibility that Henoch-Schönlein purpura is a systemic form of IgA nephropathy²¹

raises considerations (though certainly premature ones) of the use of dapsone in the latter disorder. As we suggested in 1983,¹¹ the proven value of dapsone in leucocytoclastic vasculitis should be more widely

appreciated in general medical practice and the place of dapsone in the treatment of Henoch-Schönlein purpura should be further assessed.

References

1. Esteves, J. & Brandao, F.N. Au sujet de l'action des sulfamides et des sulfones dans le maladie du Duhring. *Treb Soc Portuguesa Dermatol Venereol* 1950, **8**: 109.
2. Kruizinga, E.E. & Hamminga, H. Treatment of dermatitis herpetiformis with diaminodiphenylsulphone (DDS). *Dermatologica* 1953, **106**: 386–394.
3. Bernstein, J.E. & Lorincz, A.L. Sulfonamides and sulfones in dermatologic therapy. *Int J Dermatol* 1981, **20**: 81–88.
4. Katz, S.I., Gallin, J.I., Hertz, K.C., Fauci, A.S. & Cawley, T.J. Erythema elevatum diutinum: skin and systemic manifestations, immunologic studies and successful treatment with dapsone. *Medicine* 1977, **56**: 443–455.
5. Matthews, C.N.A., Saihan, E.M. & Warin, R.P. Urticaria-like lesions associated with systemic lupus erythematosus: response to dapsone. *Br J Dermatol* 1978, **99**: 455–457.
6. Highet, A.S. Urticarial vasculitis resembling systemic lupus erythematosus: efficacy of prednisolone and dapsone combined. *Br J Dermatol* 1980, **102**: 358–360.
7. Fortson, J.S., Zone, J.J., Hammond, M.E. & Groggel, G.C. Hypocomplementemic urticarial vasculitis syndrome responsive to dapsone. *J Am Acad Dermatol* 1986, **15**: 1137–1142.
8. Main, R.A. Allergic vasculitis (nodular dermal allergide of Gougerot). *Br J Dermatol* 1967, **79**: 68–69.
9. Wells, G.C. Allergic vasculitis (tri-symptom of Gougerot) treated with dapsone. *Proc R Soc Med* 1969, **62**: 665–666.
10. Fredenberg, M.F. & Malkinson, F.D. Sulfone therapy in the treatment of leukocytoclastic vasculitis. Report of three cases. *J Am Acad Dermatol* 1987, **16**: 772–778.
11. Ledermann, J.A. & Hoffbrand, B.I. Dapsone in allergic vasculitis: its use in Henoch-Schönlein disease following vaccination. *J R Soc Med* 1983, **76**: 613–614.
12. Chamouard, P., Baumann, R., Thomas, G. & Weill, J.P. Intérêt de la dapsone dans le traitement des manifestations digestives du purpura rhumatoïde de l'adulte. *Ann Med Interne* 1987, **138**: 599–600.
13. Niwa, Y., Sakane, T. & Miyachi, Y. Dissociation of the inhibitory effect of dapsone on the generation of oxygen intermediates in comparison with that of colchicine and various scavengers. *Biochem Pharmacol* 1984, **33**: 2355–2360.
14. Theron, A. & Anderson, R. Investigation of the protective effects of the antioxidants ascorbate, cysteine, and dapsone on the phagocyte-mediated oxidative inactivation of human alpha-1-protease inhibitor *in vivo*. *Clin Exp Immunol* 1982, **47**: 225–232.
15. Martin, W.J. II & Kachel, D.L. Reduction of neutrophil-mediated injury to pulmonary endothelial cells by dapsone. *Am Rev Respir Dis* 1985, **131**: 544–547.
16. Ruzica, T., Wasserman, S.I., Soter, N.A. *et al.* Inhibition of rat mast cell arachidonic acid cyclooxygenase by dapsone. *J Allergy Clin Immunol* 1983, **72**: 365–370.
17. Melsome, R., Harboe, M., Myrvang, B. *et al.* Immunoglobulin class specific antibodies to *M. leprae* in leprosy patients, including the intermediate group and healthy contacts as a step in development of methods for serodiagnosis of leprosy. *Clin Exp Immunol* 1982, **47**: 225–233.
18. Knight, J.F. The rheumatic poison: a survey of some published investigations of the immunopathogenesis of Henoch-Schönlein purpura. *Pediatr Nephrol* 1990, **4**: 533–541.
19. Smiley, J.D. & Moore, S.E. Immune-complex vasculitis: role of complement and IgG-Fc receptor functions. *Am J Med Sci* 1989, **298**: 267–277.
20. Fauci, A.S. The vasculitis syndromes. In: Wilson, J.D., Braunwald, E., Isselbacher, K.J. *et al.* (eds) *Harrison's Principles of Internal Medicine*. McGraw-Hill, New York, 1991, pp. 1456–1463.
21. Waldo, F.B. Is Henoch-Schönlein purpura the systemic form of IgA nephropathy? *Am J Kidney Dis* 1988, **12**: 373–377.