Hypogammaglobulinaemia associated with long term, low dose steroid therapy

R.J.E. Lee¹ and A.C. Fay²

¹ Department of Medicine, The Queen's University of Belfast, and ² Department of Microbiology and Immunobiology, Royal Victoria Hospital, Belfast, UK.

Summary: Repeated pneumonia and hypogammaglobulinaemia was associated with long term low dose steroid therapy. Clinical improvement with restoration of antibody levels followed substitution of aerosol for oral therapy.

Introduction

It is known that systemic corticosteroid therapy can cause immunosuppression. This is predominantly due to inhibition of T-cell function, causing a reduction in the cell-mediated immune response. Conventional doses of steroids do not usually cause hypogammaglobulinaemia.

Case report

A 50 year old heterosexual car mechanic was admitted with an infective exacerbation of chronic wheezy bronchitis. He had been asthmatic since childhood, and for three years previously had been taking 7.5 mg enteric coated prednisone in addition to regular bronchodilator therapy. There had been a recent deterioration in his chest condition, with five admissions to hospital in the previous year because of infective exacerbations.

On this admission *Haemophilus influenzae* was cultured in the sputum. He was treated in the usual way, and his steroid dose was temporarily increased to 30 mg/day, tapering down to 5 mg/day over 4 weeks. Serum analysed 4 d after this increase showed a low normal protein at 65 g/l (normal 59–80 g/l) and a raised albumin 45 g/l (normal 31–43 g/l). The immunoglobulins were IgG 2.02 g/l (normal 5.0–16.0 g/l), IgA 1.52 g/l (normal 1.25–4.25 g/l) and IgM 0.74 g/l (normal 0.4–2.0 g/l).

There was no evidence of lymphoproliferative or other disease causing secondary antibody deficiency.

Further investigation of the patient's immune sys-

tem showed that his total lymphocyte count was normal ($1.98 \times 10^9/l$), as was the number of sIg⁺ cells ($0.13 \times 10^9/l$), OKT3⁺ cells ($1.29 \times 10^9/l$), OKT4⁺ cells ($0.79 \times 10^9/l$), OKT8⁺ cells ($0.65 \times 10^9/l$), and esterase⁺ cells ($0.73 \times 10^9/l$). The surface isotypes of the sIg⁺ cells showed a normal distribution. There was a normal response of his lymphocytes to PHA stimulation. These results are in keeping with a diagnosis either of late onset hypogammaglobulinaemia (Asherson & Webster, 1980), or a drug induced phenomenon (Ten Berge *et al.*, 1984). When the patient's peripheral B cells were used in a colony-forming assay by culturing in soft agar, the number of colonies produced was normal. This is in contrast to our experience with cases of true late onset hypogammaglobulinaemia, where the number of B cell colony-forming cells in the peripheral blood is dramatically reduced (Fay, unpublished data).

A second admission 4 weeks later was precipitated by acute respiratory infection. The patient was now on 5 mg prednisone daily. Immunoglobulins were again low – IgG 3.46 g/l, IgA 1.00 g/l and IgM 0.66 g/l.

Oral therapy was withdrawn and replaced with beclomethasone aerosol, two inhalations every 6 h. IgA returned to normal within 1 week and IgG by 2 weeks. Now, 6 months later, the immunoglobulins remain in the normal range. The patient's chest condition is stable, with one infective episode only during this time.

Discussion

Systemic corticosteroids cause lymphocytopenia and T cells are affected more than B cells (Fauci *et al.*, 1976). Interference with B cell function is rarely sufficient to cause a reduction in gammaglobulin levels

Correspondence: R.J.E.Lee, M.B., M.R.C.P., Department of Medicine, Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ, UK.
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(Lachman & Peters, 1982), although 'supra pharmacological' doses i.e. 96 mg prednisone for 3 or 5 d, will cause this (Butler & Rossen, 1973). The mechanisms involved are complex and controversial. Butler & Rossen suggested reduced synthesis and increased catabolism of antibody. More recently, Galanaud *et al.* (1983) have proposed that steroids potentiate prostaglandin-mediated inhibition of B cell function.

One explanation for the low antibody levels in this case might be that the patient was taking much larger

doses of steroid than he admitted. We believe the patient was genuine and cannot accept that theory.

Whatever the mechanism, the rapid return of the IgA and IgG levels to normal after withdrawal of oral steroid suggests a direct drug induced inhibition of antibody synthesis. This supports the view that this is a case of clinically important hypogammaglobulinaemia caused by long term low dose steroid therapy. Perhaps an increased awareness of this possibility will result in similar cases being found.

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