‘Pulse’ methylprednisolone and cyclophosphamide therapy in idiopathic rapidly progressive glomerulonephritis

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Summary

The clinical report of a 31-year-old man who developed acute renal failure due to idiopathic rapidly progressive glomerulonephritis is presented.

Intravenous pulse methylprednisolone therapy in combination with cyclophosphamide resulted in marked improvement in renal function. The literature dealing with pulse therapy is reviewed.

Introduction

Rapidly progressive glomerulonephritis (RPGN) is characterized by crescent formation with proteinuria, oliguria and rapid deterioration in renal function. Most of the patients die within weeks or need dialysis (Bierne et al., 1977). Many therapeutic modalities have been attempted in RPGN but the effect on the disease course was not encouraging (Briggs et al., 1979). Bolton and Couser (1979) reported recently that therapy with intravenous ‘pulse’ methylprednisolone causes favourable improvement in renal function.

The present authors wish to report on another patient with RPGN whose renal function improved dramatically after therapy with i.v. ‘pulse’ methylprednisolone in combination with cyclophosphamide.

Case report

A 31-year-old man was admitted to another hospital with a one-week history of chills, fever and malaise. There was no history of renal disease, recent pharyngitis, diabetes mellitus, arthritis or exposure to known nephrotoxic agents. The physical findings were non-specific. Urine analysis showed protein 2+, numerous red and white blood cells and red cell casts per high power field. Blood urea 6 mmol/l; serum creatinine concentration 100 μmol/l. Other laboratory results were negative. In the next 3 weeks renal function deteriorated rapidly to oliguria and he was transferred to Hadassah University Hospital. On admission he was a pale, ill-looking patient, the temperature was 37.1°C, pulse 98/m, BP 180/115 mmHg. Physical findings and urine analysis gave results similar to those described previously. ESR 140 mm/hr; Hb 6·8 g/dl; WBC and thrombocyte count were normal. Urea was 42 mmol/l, plasma creatinine 2254 μmol/l. Total protein was 77·9 g/l; albumin 28 g/l; globulin 51 g/l. Complement determinations (C₃ and total haemolytic complement) were normal. Serological studies including measurement of ASO titre and detection of antinuclear antibody, rheumatoid factor and cryoglobulins were negative. The electrocardiogram and chest X-ray examination were normal. There were no other distinct abnormalities of blood chemistries. Abnormalities found in electrolyte and acid-base studies were related to the degree of renal functional impairment.

Circulating anti-glomerular basement membrane antibodies were not demonstrated. On arrival the patient started haemodialysis, and an open kidney biopsy was performed. Light microscopic examination of the kidney biopsy specimen showed over 50 glomeruli, all involved by epithelial proliferation and a polymorphonuclear infiltrate with crescent formation, diffuse fibrosis in the interstitium and no glomerular sclerosis (Fig. 1). Immunofluorescence showed linear glomerular deposition of IgG, (Fig. 2). No electron-dense deposits were found in capillary walls or mesangium.

The histological and immunofluorescence picture was compatible with the diagnosis of RPGN type I. Treatment was begun with ‘pulse’ intravenous administration of one g methylprednisolone sodium succinate given daily for 3 days followed by oral prednisone 60 mg/day with subsequent tapering and...
cyclophosphamide 200 mg/day i.v. for 5 days, followed by 100 mg/day orally for one month. Over the next days there was a striking and dramatic improvement in renal function and the patient who initially required haemodialysis regained sufficient renal function to discontinue this (Fig. 3).

During a follow-up period of 8 months the patient has remained well with a creatinine clearance of 30 ml/min.

**Discussion**

Rapidly progressive glomerulonephritis is a well-defined clinical entity. It may occur as an idiopathic form (Bierne et al., 1977), as well as in some systemic disease (Spargo, Ordonez and Ringus, 1977).

The most consistent histopathological finding is the presence of glomerular crescents resulting from proliferation of the extra-capillary epithelial cell of Bowman's capsule (Heptinstall, 1974). Three distinct immunofluorescent patterns are known: Diffuse linear deposits of antibody directed against the glomerular basement membrane—type I; diffuse granular deposits of immune complexes accompanied by C3 in the glomeruli—type II; and crescents with

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**Fig. 1.** Circumferential cellular crescent and compressed glomerular tuft (Silver methenamin ×100).

**Fig. 2.** Immunofluorescence. Strong linear pattern of IgG in glomerular tuft.
sparse or no immune deposits (Glassock and Bennett, 1976)—type III.

Although there are few reports of spontaneous recovery (Maxwell et al., 1979), the clinical course is characterized by rapid deterioration of renal function so that most of the patients die within weeks, or need dialysis. Little benefit has been gained from various therapeutic modalities, including anticoagulants, cytotoxic agents and steroid therapy alone (Briggs et al., 1979). Plasmapheresis and immunosuppression have been used with apparent beneficial effect in Goodpasture’s syndrome (Lockwood et al., 1977).

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![Graph](image)

**Fig. 3.** Summary of the clinical course. ○ ○ [Cr]p = Plasma creatinine; Ccr = creatinine clearance; □ = prednisone; ■ = cyclophosphamide.

Cole et al. (1976) suggested that a therapeutic approach similar to that employed by Bell (Bell et al., 1971) for transplant rejection might be efficacious in severe glomerulonephritis. They described the beneficial effect of ‘pulse’ methylprednisolone in 4 out of 5 children with RPGN. O’Neill, Etheridge and Bloomer (1979) found benefit in 4 out of 10 patients with renal failure due to idiopathic rapidly progressive glomerulonephritis. The improvement in renal function appeared to be directly related to ‘pulse’ methylprednisolone administration.

Recently, Bolton and Couser (1979) noted improvement in renal function in 7 of 9 patients from one to 4 weeks after ‘pulse’ therapy. The addition of cyclophosphamide to the pulse therapy was suggested by its use as the main immunosuppressant by Lockwood et al. (1977) and by other reports of its usefulness in many forms of glomerulonephritis (Ibels et al., 1975) and vasculitis (Fauci, 1979).

This experience suggests that the administration of ‘pulse’ methylprednisolone in combination with cyclophosphamide may produce a dramatic improvement in a certain group of patients with idiopathic RPGN, and supports other similar experience in the literature. Although it is recognized that spontaneous remission may have occurred simultaneously with the initiation of therapy, the temporal relationship among therapy and recovery cannot be ignored.

The authors hope that controlled studies will confirm their expectations of the benefit of ‘pulse’ methylprednisolone and cyclophosphamide therapy in idiopathic RPGN, if started early in the course of the disease.

References


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