The efficacy of an individual treatment schedule in patients with vasculitis

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Abstract

The aim of the study was to determine the efficacy of an individual treatment schedule in patients with systemic vasculitis. Clinical, laboratory, morphological and immunological data before and after treatment were followed in 18 patients: eight with microscopic polyangiitis, two with Wegener’s granulomatosis, four with leukocytoclastic vasculitis and four with necrotizing/crescentic glomerulonephritis. Patients received individual treatment for 14.89±13.9 months according to the disease activity. Methylprednisolone pulse therapy (PT) was given to 16 patients, mean 1.94±0.4 PT/patient, followed by a slowly tapered oral dose (0.7–1 mg/kg). Cyclophosphamide PT was received by 15 patients, mean 3.13±0.9/patient in doses of 8–10 mg/kg, followed by an oral dose of 1 mg/kg for 9.17±1.9 months. Four additional patients were treated with cyclosporin A for 3 months. Plasmapheresis was provided in seven patients. Two patients were treated with azathioprine and one patient with mycophenolate mofetil. There were no significant changes in serum creatinine and creatinine clearance during the observation period. Proteinuria and haematuria improved after treatment. Kidney function improved or became stable in 66.67% of patients. No patient required haemodialysis. Haematuria was no longer observed at the end of the study in nine of 11 patients. Thirteen patients (72.22%) had clinical remission. Relapses occurred in five patients. Kidney re-biopsies showed a decrease in morphological changes in 57.2%. In conclusion, individual treatment is more flexible and controls the disease activity better.

Keywords: disease activity; immunosuppression; kidney function; treatment; vasculitis

Introduction

The term ‘vasculitides’ encompasses a heterogeneous group of inflammatory disorders which may affect the kidney by damaging its blood supply.


The most convincing current classification is that based on the size of the vessels involved, on the prevalent organ involved and on the characteristics of the perivascular infiltrates (granulomatous or non-granulomatous) [4]. There is evidence for an increasing incidence of primary renal vasculitis [5,6].

Systemic vasculitis can be difficult to recognize because of the many disease types and the conditions that can mimic it. Early identification and initiation of treatment (often empirical) are important to avoid severe morbidity [7]. It is known that disease severity may vary considerably in patients with different vasculitides. There is general consensus that the most valid therapeutic strategy in vasculitis consists of combined administration of steroids and cyclophosphamide [8,9].

The following aspects of the strategy are still controversial: the utility of i.v. pulses of methylprednisolone at the start of the treatment; the utility of substituting cyclic i.v. pulses for daily oral administration of cyclophosphamide; the duration of the induction treatment with the two drugs and the subsequent maintenance therapy; the utility of adding plasma exchange for the most severe cases;
and the potential beneficial effect of high-dose i.v. immunoglobulin [10].

There are few other drugs that can be considered, especially in patients with antineutrophil cytoplasmic autoantibody (ANCA)-positive vasculitis. One of them is cyclosporin, but few data are available on its efficacy. Mycophenolate mofetil has been used to treat patients with a variety of immune-mediated nephritides including systemic lupus erythematosus (SLE), other proliferative glomerulonephritides and ANCA vasculitis. Other alternative drugs or therapies were azathioprine, deoxyxpergulain, methotrexate, leflunomide, monoclonal antibodies (anti-CD4 or anti-CD18), anti-thymocyte globulin, anti-tumour necrosis factor (TNF) antibody therapy, l-tryptophan immunoabsorption, myeloperoxidase-bound immunosorbent columns and immunoablation with autologous bone marrow stem cell transplantation [11].

Subjects and methods

To determine the efficacy of individual treatment strategies, we studied 18 patients with vasculitis (mean age 41.55±15.5 years, four females and 14 males). Eight patients suffered from microscopic polyangiitis, two from Wegener’s granulomatosis, four from leukocytoclastic vasculitis and four from necrotizing/crescentic glomerulonephritis. The period of observation was 4.7±3.27 years (from 1 to 12 years). At the onset of the disease and at the end of the observation period, the following parameters were examined: serum creatinine, creatinine clearance, serum albumin, urine sediment, proteinuria and immunological tests.

Renal involvement was established with a kidney biopsy in all patients, and in seven of them the biopsy was repeated. Ten patients underwent a skin–muscle biopsy.

The decision on the treatment strategy was based on the stage of the disease and individual clinical, morphological, laboratory and immunological data. The duration of the treatment was 14.89±13.9 months (from 6 to 42 months).

Fifteen patients received initial pulse therapy (PT) with methylprednisolone and cyclophosphamide. Ten patients received more than one PT with methylprednisolone, mean 2.9±1.3 PT per patient, followed by a slowly tapered oral dose of 0.8–1 mg/kg. Nine of them received additional ‘subpulses’ with 250 mg of methylprednisolone i.v on three consecutive days. Ten patients were treated with more than one PT with cyclophosphamide, mean 2.7±0.8 PT per patient, followed by an oral dose of 0.7–0.8 mg/kg for 4–15 months. Two patients were treated with a combination of corticoids, cyclophosphamide and azathioprine.

Because of non-response to that therapy, four patients switched to cyclosporin A (3 mg/kg for 3 months) and one to mycophenolate for 3 months. Eleven patients received heparin for 24±3.1 days. Seven patients underwent plasma exchange in addition to the immunosuppressive treatment. Patients received symptomatic therapy when necessary.

The results are expressed as the mean ± SD. The mean values were compared by t-test, and P < 0.05 was considered significant.

Results

During the observation period, we observed a stable serum creatinine (from 228.9±177.8 to 237.9±149.6 μmol/l), creatinine clearance (from 40.8±20.8 to 46.22±31.8 ml/min/1.72 m²), and a non-significant improvement in serum albumin (from 36.67±7.45 to 38.55±7.44 mmol/l).

Fifteen patients suffered from chronic renal failure, 14 of them mild to moderate and one with severe renal insufficiency at the onset of the disease. At the end of the observation period, serum creatinine decreased in seven (46.66%), increased in six (40%) and was stable in two (13.3%) of the patients. No patient required haemodialysis treatment.

Of 11 patients who had haematuria, nine were without it at the end (81.8%) of the observation period.

Proteinuria decreased significantly by the end of the study from 3.95±2.9 to 1.54±1.32 g/day (P < 0.01). Eight patients showed a nephrotic range proteinuria at the beginning, and their number decreased by 37.5% at the end of the study period.

During the study, six patients (33.33%) had relapses of the disease.

ANCAs were positive in two patients at the beginning and were negative at the end of the study.

Repeated kidney biopsies showed a decrease in morphological changes in four out of seven (57.14%) patients.

Discussion

Treatment has changed the outcome of vasculitis, and there must be a balance between the dangers of the disease and those of the treatment [10,11]. Most studies discuss early and rapidly introduced immunosuppressive treatment that controls the disease activity effectively [12]. The individual treatment strategy described herein was flexible and was selected according to each patient’s disease activity, type of morphological changes and indication, and eventually contraindication, of the applied drug. The results from that therapy showed improvement in morphological changes in 54.17%, in kidney function in 38.9%, and in proteinuria in 61.1% of the patients. Relapses occurred in 33.3% of patients, and 33% showed decreased kidney function; however, no one required haemodialysis treatment.

We suggest that such individual flexible therapy is efficient for vasculitis and is associated with limited adverse effects.

Conclusion

The systemic vasculitides are a group of rare inflammatory conditions resulting in inflammation and necrosis of blood vessel walls. Renal involvement carries a poor prognosis and high mortality. A variety
of treatments have been employed, but their role is still being elucidated.

Therapy with cyclophosphamide and corticoids continues to be the treatment of choice. There are still different opinions on the duration, mode of application and dosage of those drugs. The efficacy of other drugs and the role of plasmapheresis are controversial. For this reason, we select individual treatment schedules according to clinical, morphological, laboratory and immunological data of each vasculitis patient. Our study suggests that such individual therapy is beneficial for different forms of vasculitis. This schedule controls the activity of the disease, stabilizes kidney function, partly decreases morphological changes and reduces adverse effects of the therapy.

References