Case Report

Guillain–Barré syndrome as presenting feature in a patient with lupus nephritis, with complete resolution after cyclophosphamide treatment

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Introduction

Various neurological features have been reported in association with systemic lupus erythematosus (SLE). However, Guillain–Barré syndrome (GBS) as a presenting feature of SLE appears to be rare [1–3]. We report a patient presenting with GBS, in whom lupus nephritis was subsequently diagnosed. The GBS failed to respond to intravenous immunoglobulin treatment, but both GBS and lupus nephritis responded very favourably to intravenous pulses of cyclophosphamide and prednisone.

Case

A 20-year-old woman was referred to our hospital because of a 10-day history of progressive muscle weakness of arms and legs, paraesthesiae in both hands and feet, and diplopia. Her medical history was unremarkable. Physical examination on admission revealed a blood pressure of 150/110 mmHg and cardiac enlargement. Neurological examination showed a left abducens paresis, absent deep tendon reflexes, and severe symmetrical proximal muscle weakness. Laboratory examination revealed an erythrocyte sedimentation rate of 84 mm/h; C-reactive protein 71 mg/l; urea 12.3 mmol/l; creatinine 150 μmol/l; serum albumin 17 g/l; LDH 434 U/l; Coombs-positive haemolytic anaemia; but normal thrombocyte and leukocyte counts. Virological and bacteriological examination showed only a recent para-influenza infection, but no signs of a Campylobacter jejuni infection. Qualitative urine analysis revealed the presence of protein. Later, also an active urinary sediment was found (10–25 leucocytes, hyaline and coarse granular casts, 25–50 dysmorphic erythrocytes). The cerebrospinal fluid revealed a normal cell count, total protein, lactate, pyruvate and brain-specific proteins (neuron-specific enolase, myelin basic protein and S-100 protein). A slight IgM synthesis (0.4 mg/l) was found, but no synthesis of IgG or IgA. Oligoclonal immunoglobulin bands were absent.

On the chest X-ray, bilateral pleural effusion and cardiac enlargement were seen. The electrocardiogram displayed diffuse repolarization abnormalities. Echocardiography showed some pericardial effusion. The first electromyogram (EMG) (day 1) showed loss of F responses, and decreased amplitudes of sensory nerve action potentials and compound muscle action potentials in arms and legs. Because of the clinical picture of rapid progression of symmetric proximal limb weakness to total paralysis in 2 weeks, associated with areflexia, the diagnosis GBS, was made according to the Asbury criteria [4]. Retrospectively the patient also fulfilled the American College of Rheumatology (ACR) case definitions for GBS published in 1999 [5].

On day 1 treatment was started with intravenous immunoglobulin G (Gammagard, Baxter) 0.4 g/kg bodyweight per day, for 5 days. Muscle weakness rapidly progressed to a tetraparesis. On day 8, mechanical ventilation became necessary, due to respiratory failure.

Because of proteinuria with an active urinary sediment, additional investigations were performed, including autoimmune serology. This revealed a 3+ positive antinuclear antibody (ANA) test, anti-Sm and anti-RNP autoantibodies, but no anti-dsDNA, antineutrophil cytoplasmic antibodies (ANCA), or anticardiolipin autoantibodies, and slightly decreased C3 (620 mg/l) and C4 values (150 mg/l). On day 15 a bilateral peripheral facial paralysis and an exanthema on the face were noticed. Based on the presence of the
facial exanthema, pleural and pericardial effusion, proteinuria with cellular casts, autoimmune haemolytic anaemia, a positive ANA and the presence of anti-Sm auto-antibodies the diagnosis SLE with renal involvement was made, according to the ACR criteria [6,7].

A percutaneous kidney biopsy was performed, which showed glomeruli with mesangial and endocapillary proliferation and an influx of mononuclear cells. Focally, glomeruli showed crescent formation and splitting of the glomerular basement membrane. On immunofluorescence granular deposits of IgG, IgM, IgA, C1q and C3 were present in the mesangium and along the glomerular capillary walls. Electron microscopy revealed electron-dense deposits in the mesangium and glomerular capillary loops, both subendothelially and subepithelially. The biopsy findings were classified as a mesangiocapillary lupus nephritis with a membranous component (WHO class IV.C) with a NIH activity index of 10 and a chronicity index of 7 [8].

Because of this severe form of lupus nephritis the patient was treated from day 30 with intravenous pulses of cyclophosphamide (750 mg/m²) and high oral doses of prednisone (1 mg/kg body weight) [8]. Before this immunosuppressive treatment was started a second EMG was performed, which showed deterioration. In the first 6 months the patient was treated with monthly pulses of cyclophosphamide 750 mg/m², together with intravenous hydration and MESNA (2-mercaptopro-ethane-sulphonate) to reduce the urothelial toxicity of cyclophosphamide. In addition, prednisone 60 mg/day was given for 4 weeks and thereafter monthly tapered to a maintenance dose of 10 mg.

This treatment regimen was tolerated rather well. The peripheral facial paralysis disappeared and from day 45 muscle strength improved, first proximally, then also distally; On day 47 artificial respiration could be stopped and on day 65 the patient was transferred from the Intensive Care Unit to the neurological ward. By that time the proteinuria had decreased to 3.7 g/24 h and renal function had become normal. On day 74 she was transferred to a rehabilitation centre. Six months after the onset of the GBS the patient was in an excellent condition, muscle strength and tendon reflexes were normal without any physical restraints. Blood pressure was 130/70, while taking lisinopril 10 mg. Twenty-four-hour protein excretion was 0.12 g, ANA had become negative and the complement C3 and C4 levels were normal. The EMG had normalized, except for some F-wave dispersion. From then on the patient received cyclophosphamide pulses every 3 months for a total period of 18 months.

Discussion

The signs and symptoms in the present patient, fulfilled the Asbury criteria [4] and ACR case definitions [5] for the diagnosis of GBS. Approximately 1 month after the onset of neurological symptoms lupus nephritis was diagnosed. After initial unsuccessful GBS treatment with intravenous gammaglobulins, the patient was treated with cyclophosphamide pulses in combination with oral prednisone. This treatment regimen induced a complete resolution of the GBS and the renal and other lupus symptoms.

The prevalence of SLE in patients with GBS has been reported to be between 0.6 and 1.7% [9]. Because of the anecdotal nature of the reports on the combination of GBS and lupus nephritis, it is difficult to formulate an optimal therapeutic regimen for this combination. For the combination of GBS and lupus nephritis the efficacy of prednisone alone for treatment of the neuropathy is insufficient in about 50% of the cases [2], while for lupus nephritis the long-term effects are inferior [8]. The efficacy of intravenous immunoglobulin for GBS in lupus nephritis is controversial [2]. Plasma-exchange may have a beneficial effect on the neuropathy [1,3] but does not convert an additional effect for lupus nephritis [8]. After failure of the established GBS therapy, we decided to tailor the treatment to the presence of lupus nephritis by giving intravenous cyclophosphamide pulses together with high oral doses of prednisone. This approach is substantiated by the observation that in the majority of reported cases of GBS in lupus nephritis, exacerbations and remissions of lupus nephritis were paralleled by the neurological features [10].

Several observations in this patient suggest that GBS developed as a feature of lupus: the synchronicity of the clinical symptoms of GBS and lupus nephritis, the failure of standard GBS treatment, the positive effect of lupus treatment also on GBS, and the unusual complete remission of the predominantly axonal EMG abnormalities.

Therefore, the association of GBS with lupus seems to have implications for both treatment and prognosis. Prednisone and cyclophosphamide should be considered in patients with GBS as a feature of lupus. Furthermore, we propose that in patients with a GBS, not responding to intravenous gammaglobulins, lupus should be excluded.

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References


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