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Short communication

Acute-onset chronic inflammatory demyelinating polyneuropathy with focal segmental glomerulosclerosis

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ABSTRACT

Inflammatory neuropathies have been reported to occur in association with nephrotic syndrome. Their underlying immuno-pathogenic mechanisms remain unknown. A 50-year-old woman concurrently presented with acute-onset chronic inflammatory demyelinating polyneuropathy and nephrotic syndrome secondary to focal segmental glomerulosclerosis. Both neuropathy and proteinuria improved after plasma exchange and steroids. Literature review of cases of concurrent inflammatory neuropathies and nephrotic syndrome revealed similar neuro-renal presentations. This neuro-renal condition may be mediated by autoantibodies targeting myelin and podocytes.

1. Introduction

Inflammatory neuropathies, Guillain–Barré syndrome (GBS) or chronic inflammatory demyelinating polyneuropahty (CIDP) have been reported to occur in association with nephrotic syndrome. Their underlying glomerular pathologies include focal segmental glomerulosclerosis (FSGS) [1–8], membranous glomerulonephritis [9–18] and minimal change disease [19–22]. Here we describe a patient who synchronously developed acute-onset CIDP and FSGS, whose severe clinical manifestations were responsive to immunotherapy. The literature was reviewed for cases of nephrotic syndrome or proteinuria associated with GBS or CIDP [1–22]. This neuro-renal presentation raises pertinent questions regarding a common underlying immuno-pathogenic mechanism of inflammatory neuropathy associated with FSGS.

2. Case report

A 50-year-old woman with no antecedent infectious illness developed right-sided weakness, unsteady gait and numbness of her extremities over 5 days. Neurological examination was significant for mild right hemiparesis (Medical Research Council grade 4), right extensor plantar reflex, and generalized hyporreflexia with decreased pinprick sensation in a glove-and-stocking distribution. Blood pressure was 210/130 mmHg. Computed tomography revealed a small non-specific hypodensity in the left corona radiata, and aspirin was started for an initial diagnosis of stroke. However, subsequent magnetic resonance imaging of the brain did not reveal any corresponding restricted diffusion to suggest an ischemic infarct to account for her presenting symptoms.

Over the course of 2 weeks, her weakness rapidly progressed to involve all 4 limbs, affecting the proximal muscle groups more than distal. Deep tendon reflexes were diffusely absent. She was dysphagic and developed urinary retention. Median sensory nerve conductions were bilaterally absent while the amplitudes of sural potentials remained preserved (Fig. 1, Table 1). Cerebrospinal fluid (CSF) examination revealed mildly elevated protein (0.5 g/L, normal range 0.1-0.4) with normal white cell count (3/μl). Laboratory tests, including electrolytes, urea, creatinine, anti-nuclear antibody, anti-double stranded DNA, anti-extractable nuclear antigens, anti-neutrophil cytoplasmic antibodies and complement levels, were normal. Serum and urine protein electrophoresis did not reveal abnormal bands to suggest underlying gammopathy. Work-up for hypertension revealed nephrotic-range proteinuria (6.11 g/24 h; normal, <0.3) and hypoalbuminaemia (serum albumin was 24 g/L; normal, 38-48). As her clinical evolution was consistent with GBS, she received 6 cycles of plasma exchange over 12 days, which arrested her neurologic deterioration.

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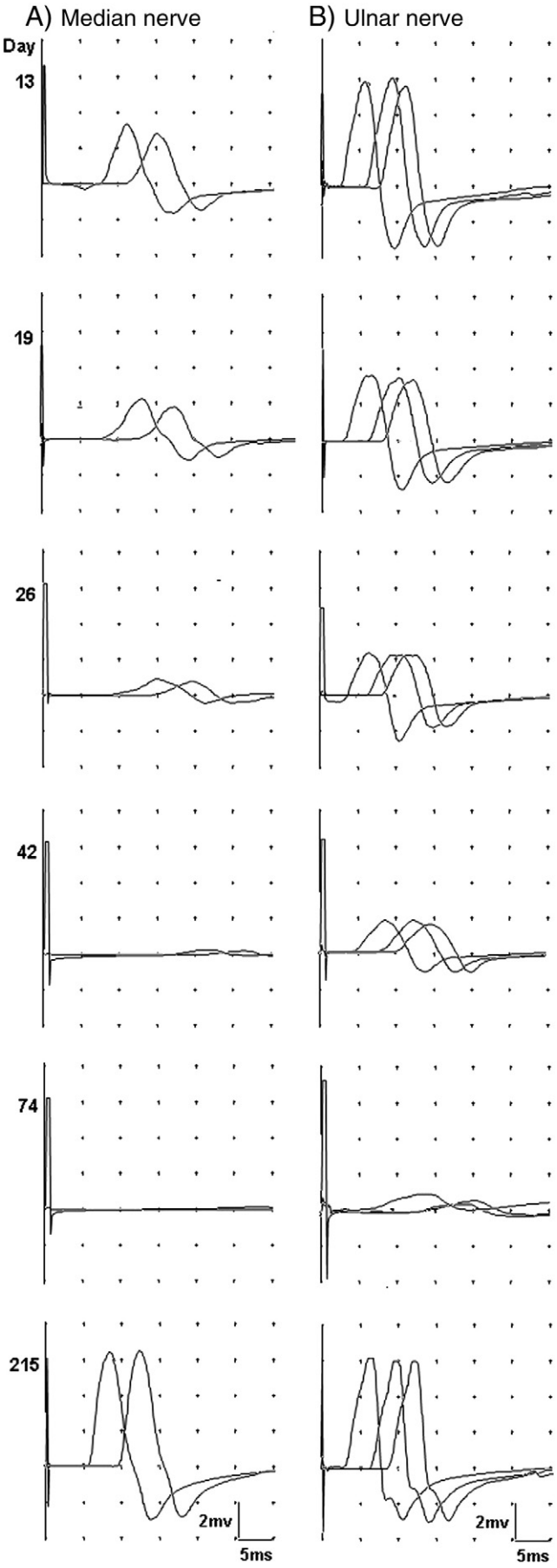

A fortnight after completing plasma exchange, she developed progressive muscle weakness (Medical Research Council grade 1 throughout) with ascending numbness involving her trunk. Repeat CSF evaluation revealed 8 white blood cells/μL (7 lymphocytes) and protein level of 2 g/L. Proteinuria had worsened to 8.53 g/24 h. Three weeks later, she developed type 2 respiratory failure and required mechanical ventilator support. She received further 5 cycles of plasma exchange. Serial nerve conduction study showed evolution of her neuropathy with progressive lengthening of distal motor latencies (Fig. 1). The renal biopsy showed 4 glomeruli with segmental sclerosis (Fig. 2A), out of a total of 28 glomeruli. The other glomeruli were within normal limits by light microscopy. The immunofluorescence pattern was negative. Electron microscopy confirmed the absence of immune complex deposits, and showed diffuse podocyte foot process effacement (Fig. 2B). The features were those of focal segmental glomerulosclerosis. High-dose prednisolone (1 mg/kg) was commenced for concurrent diagnoses of acute-onset CIDP and FSGS.

Mild improvement of her distal upper limb strength was seen by the 4th cycle of her second round of plasma exchange. At her last assessment, 4 months after plasma exchange and on tailing doses of prednisolone, her strength was almost back to normal, and she was able to ambulate without aids. The final nerve conduction study done on day 215 showed good recovery in latencies and amplitudes of nerve potentials. There was concomitant improvement of proteinuria to 0.24 g/day.

3. Discussion

Our patient was initially diagnosed with stroke when she first presented with hemiparesis. However, her rapidly deteriorating weakness within 2 weeks of presentation, accompanied by arreflexia and paresthesias, led to a diagnosis of GBS. Bilateral symmetric involvement is usually seen in GBS and CIDP. As in the case of this patient, weakness may sometimes be asymmetric initially but typically progresses to become generalized [23], although at times, significantly asymmetric presentation in GBS persists during the disease course [24,25]. With progression, our patient eventually had a clinical phenotype of "typical CIDP" [26]. An immune-mediated inflammatory neuropathic process was further supported by demyelination and abnormal median sensory responses (with sural sparing) noted on the serial nerve conduction studies [26]. Plasma exchange initiated at the time of GBS diagnosis led to a temporary interlude of neurologic stabilization before our patient neurologically worsened again. Subsequent deterioration at the plateau phase of illness could be due to GBS treatment-related fluctuations with evolution to respiratory failure. However, the continued neurologic deterioration (up to 9 weeks after initial presentation) revealed a chronic, relapsing disease that extended beyond 8 weeks, leading to a revision of her diagnosis to acute-onset CIDP [27–29]. Notwithstanding that CIDP is classically defined by a clinical evolution of more than 2 months, previous studies have reported that a proportion of patients with CIDP may present acutely [27–31], and severe weakness was observed in 31% of patients with acute-onset CIDP [29]. Ventilatory failure requiring mechanical ventilation is rare in CIDP, but has been reported in up to 9% of patients with CIDP [32]. Among patients with acute-onset CIDP, there is a trend towards a lower proportion that develops respiratory weakness compared to patients with GBS. (20% vs 53%, $p = 0.054$) [29] To our knowledge, we are the first to report this association in a patient who presented early with asymmetric weakness, and whose clinical course suggested acute-onset CIDP.

Coincident with her neurologic condition, our patient presented with poorly controlled hypertension, which ultimately led to a diagnosis of nephrotic syndrome secondary to FSGS. An association between inflammatory neuropathies and nephrotic syndrome had previously

Fig. 1. Progressive lengthening of distal latencies and reduction of amplitudes of the left median and ulnar compound motor action potentials with subsequent recovery seen in serial nerve conduction studies.