Acute-onset chronic inflammatory demyelinating polyneuropathy- a distinct entity mimicking Guillain-Barre syndrome

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Abstract:
We report a case of acute onset CIDP that illustrates the clinical features which differentiate it from classical presentation of GBS.

Keyword: Acute onset CIDP, GBS, TRF

The spectrum of immune mediated demyelinating polyneuropathy ranges from the acute variant, Guillain–Barre’s syndrome (GBS), to a chronic form, chronic inflammatory demyelinating polyneuropathy (CIDP) (1). CIDP differs from acute inflammatory demyelinating polyneuropathy (AIDP), by its temporal profile, course of disease and responsiveness to immunosuppressive agents like steroids. Antecedent events are recognized more in GBS (>70%) compared to CIDP (<30%) (2). IgG antibodies have been identified in GBS variants. No definitive antibodies have been identified in CIDP (3). Although CIDP is defined as a progressive or relapsing condition that develops over at least 2 months, up to 16% of CIDP patients may present acutely (4)(2). Such patients are usually initially diagnosed with AIDP, but later, as they either relapse or continue to progress beyond 2 months, they are then correctly diagnosed as having CIDP (5)(6). An early and accurate diagnosis has major prognostic and treatment implications. Unfortunately, the diagnosis can only be confirmed with certainty at follow-up, after a minimum of 2 months of clinical observation. Therefore, earlier indicators would be useful to guide treatment and prognostication. We report a case of acute onset CIDP that illustrates the clinical features which differentiate it from classical presentation of GBS.

Case report:
A 49 year old gentleman had presented with acute onset of tingling and numbness of both hands simultaneously and 2 days later similar symptoms in the distal lower limbs. The sensory symptoms progressed from distal to proximal in both upper and lower limbs. 10 days after onset of sensory symptoms he had a weakness of lower limbs (proximal greater than distal) and upper limbs (distal greater than proximal). He became profoundly weak within 2-3 days...
after onset of motor weakness and he required mild support to walk and for his activities of daily living (ADL’s). There was no history of cranial nerve dysfunction and respiratory muscle weakness. Examination revealed areflexia and Medical Research Council (MRC) grade power 3/5 in limbs and proprioceptive impairment. A clinical diagnosis of GBS was made elsewhere and treated with Intravenous Immunoglobulin (IVIG – 0.4 g/kg/day for 5 days). His motor weakness and sensory symptoms completely improved within 7-10 days. However after 10 days, he noticed acute onset of tingling and numbness of perioral region, distal upper and lower limbs along with weakness of both upper and lower limbs and bifacial weakness. He became profoundly weak within 3-4 days. There was no history of respiratory distress or bulbar weakness. Examination revealed bifacial weakness, areflexia, limbs weakness (MRC grade 2/5) and proprioceptive impairment. He was diagnosed elsewhere as GBS with “treatment related fluctuations (TRF)” and treated with IVIG (0.4 mg/kg/day for 5 days). His symptoms started improving with power in limbs MRC grade 3/5 and was advised to continue physiotherapy and occupational therapy. After 3 weeks, his symptoms began to worsen in the form of tingling and numbness in perioral, tongue, anterior aspect of chest and abdomen, upper and lower limbs along with weakness of upper and lower limbs. There was no history of double vision, bulbar weakness and respiratory distress. There was no history of postural giddiness, sweating abnormality, bladder and bowel dysfunction. There was no history of fever or diarrhea prior to onset of illness. There was no history of joint pains, rash, oral ulcers and dryness of eyes. There was history of dryness of mouth since 2 months. He had hypertension and diabetes mellitus since 5 years and was on regular medications. On physical examination, he was conscious and oriented. Vital signs were stable. He had trigeminal nerve involvement in the form of absent perioral and corneal sensations with jaw weakness. There was bifacial weakness of lower motor neuron (LMN) type. There was distal wasting of upper and lower limbs. Power in upper limbs was MRC 3/5 and lower limbs MRC 2/5 (both proximal and distal weakness). He had graded sensory loss to pain and temperature in upper and lower limbs along with sensory loss over midline trunk and face predominantly in the nasal and perioral area. Light touch, vibration, joint and position sensation were impaired in both upper and lower limbs distally. “Pseudoathetoid” movements were present in upper limbs. Superficial abdominal and deep tendon reflexes were absent. Bilateral plantar reflex was flexor. We were unable to assess gait as he was confined to bed due to significant proprioceptive sensory loss. Autonomic function tests showed significant sympathetic dysfunction. Results of routine hematological and urine tests, including liver and kidney function tests, thyroid function tests, and serum level of vitamin B12 and folate, were all normal. Serological tests for Human immunodeficiency virus (HIV), hepatitis B and C were negative. Autoimmune workup including ANA, ds DNA, anti SSA & SSB, ACE levels and anti onconeural antibodies were all negative. ESR was elevated and total complement levels was low. Nerve conduction studies showed absent sensory nerve action potentials (SNAPs) with reduced compound motor action potential (CMAPs) with prolonged distal latencies suggestive of sensory motor axonal and demyelinating polyneuropathy. Cerebrospinal fluid contained 2
lymphocytes /dl, protein level of 151 mg /dl. Serum immunoglobulin’s and serum electrophoresis were normal. Antiganglioside antibodies were negative. Right superficial peroneal nerve biopsy was done which showed mild nerve fiber loss. Right superficial peroneal brevis muscle with mild fiber atrophy. Skin biopsy with no specific lesion. Minor salivary gland biopsy showed grade 1 inflammation. His paraneoplastic workup including the whole body PET scan was negative for occult neoplasm. He was diagnosed to have acute-onset CIDP and IVIG (0.4/kg/day for 5 days) was administered. This was followed by pulse methyl prednisolone and pulse dose intravenous cyclophosphamide. He was started on physiotherapy and occupational therapy while he was in hospital. During the stay, his motor power improved to MRC grade 4+ and the numbness in the trigeminal distribution and limbs reduced by 80% within 4 weeks. Repeat conduction showed improvement in CMAPS with presence of conduction blocks. He was able to walk in the ward without any support with visual cues and carry out his activities. At eight week follow up, he was in full remission. Medications continued included tapering schedule of methyl prednisolone, monthly pulse cyclophosphamide and 6 weekly injections IVIG (0.4/g/kg).

Discussion:
Guillain-Barre’ syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP) are acquired immune-mediated neuropathies, sharing many symptoms and signs in the acute phase of disease. The time to reach maximum severity (nadir) and the subsequent course of the disease were used to differentiate between GBS and CIDP in the early phase of disease. By definition, the time to reach nadir in GBS is within 4 weeks; thereafter the course is monophasic(7) (8). According to the EFNS criteria for CIDP, initial progressive phase lasts at least 2 months (9). Thereafter the course may be relapsing-remitting, steadily progressive, or monophasic. However, not all patients fulfill all diagnostic criteria for either GBS or CIDP. It has been reported that 16% of patients with CIDP have rapidly progressive weakness, with a nadir within 8 weeks from onset of disease, which is followed by a chronic course. These patients are considered to have acute-onset CIDP (A-CIDP). On the other hand, 8%–16% of patients with GBS have 1 or more deterioration shortly after initial improvement or stabilization following plasma exchange or IV immunoglobulin (IVIG), described as treatment-related fluctuations (TRF). In clinical practice, it may be very difficult to distinguish a patient with GBS having a secondary deterioration after initial improvement or stabilization within the first weeks or months after onset of disease (GBS-TRF) from a patient having a second episode of weakness due to A-CIDP (10) (11)(12) (13)(14). TRF is defined as improvement in the GBS disability scale of at least one grade after completion of immunotherapy (immunoglobulin/plasmapheresis) followed by a worsening of the disability scale of at least one grade within the first 2 months after disease onset. The reasons proposed for TRF include wearing off of immunotherapy, ongoing immune activation, rebounding of antibodies and immune reactions on those epitopes. These patients probably have a prolonged immune response requiring a longer duration of treatment. It is important to distinguish GBS-TRF and A-CIDP in early phase of disease because prognosis and treatment strategies were different in both groups. A patient with GBS-TRF generally
requires a repeated IVIG course or plasma exchanges, whereas A-CIDP patients require long-term maintenance treatment with steroids, IVIG, or plasma exchange with or without immunosuppressive agents. The following features help to differentiate A-CIDP from GBS-TRF. A-CIDP should be considered when a patient thought to have GBS deteriorates again beyond 8 weeks from onset or when TRF occurs 3 times or more in patients with GBS (14). Prominent sensory signs can predict conversion to CIDP (1). Absence of cranial neuropathy, a preceding infectious illness, and respiratory failure predict to CIDP (4)(7)(5)(3).

In our case, the diagnosis of A-CIDP was considered, features which suggest A-CIDP were, initial clinical diagnosis of GBS which deteriorated beyond 8 weeks from onset, midline sensory symptoms, prominent sensory signs (impaired vibration sense, and impaired pinprick perception in a stocking and glove distribution), frequent treatment related fluctuations (3 times) and clinically significant autonomic instability and good response to steroids. In view of prominent midline sensory symptoms and sicca symptoms, neurological presentation of Sjogren’s and paraneoplastic syndromes was considered. However work up for the same was negative.

**Conclusion:**

Acute onset CIDP would be considered in patients with initial diagnosis of GBS if they have

1. Midline sensory symptoms
2. Prominent sensory signs
3. Frequent treatment related fluctuations (more than 3 times).

**Bibliography:**


