Sir,

Guillain-Barré syndrome (GBS) is a monophasic disease with time to nadir within 4 weeks. In chronic inflammatory demyelinating polyneuropathy (CIDP), the initial progression for more than 2 months is proceeded by a variable course—either relapsing-remitting, steadily progressive or monophasic. However, a significant number of patients with CIDP may experience an acute clinical onset with a nadir within first the 8 weeks itself with variable evolution. These patients classified as acute-onset CIDP (A-CIDP) constitute 16–20% of CIDP. Distinguishing acute inflammatory demyelinating polyneuropathy (AIDP) from A-CIDP is crucial because the treatment strategies and long-term prognosis are different. Unlike GBS, patients with CIDP require long-term immunosuppressive treatment including corticosteroids and even biologicals like rituximab.

Here, a young adult male patient presenting as short duration areflexic quadriparesis, and the diagnostic dilemma therein is discussed.

An 18-year-old boy presented with low back pain and symmetrical weakness of both lower followed by upper limbs for 11 days. The initial recurrent buckling of the knees was followed the next day by complete paralysis of both the lower limbs on awakening. The same day, he developed weakness of both upper limbs and by the third day, was quadriplegic with subsequent non-progression of symptoms. No sensory, autonomic, or cranial nerve dysfunction or loss of bladder and bowel control were there. No history of headache, vomiting, vertigo, dyspnea, or orthopnea was noted. Fifteen days before onset, he had a fever for 2 days not associated with cough, expectoration, pain abdomen, burning micturition, and diarrhea. No recent exposure to pesticides or ticks was noted.

The patient was conscious, alert, and without respiratory distress or orthostatic hypotension. Apart from grade II papilledema, the remaining cranial nerves were unremarkable. Generalized hypotonia and loss of muscle bulk were present. The power was proximally 2/5 Medical Research Council (MRC grade) in the upper limbs, 1/5 in the lower limbs, and 0/5 distally in all extremities with generalized areflexia and intact sensory examination. Neck rigidity and Kernig’s sign were present. Bilateral lancinating pain was elicited at 30° by straight leg raising. The initial diagnosis of meningitis with arachnoiditis versus GBS was considered.

The routine hematological parameters were normal. The serology for Hepatitis B, Hepatitis C, Human Immunodeficiency Virus-1/2, and Campylobacter jejuni was negative. The blood, urine, and stool cultures were negative. The cerebrospinal fluid (CSF) was abnormal (pressure 28 cm H₂O, turbid with coagulum, protein 5,900 mg/dL, sugar 68 mg/dL (corresponding blood sugar: 92 mg/dL), cell count 45 (all lymphocytes and no atypical cells)). The CSF aerobic culture, Mycobacterium culture, Lyme antibody, qualitative Polymerase chain reaction (PCR) for adenovirus, enterovirus, Ebstein Barr virus, Herpes h virus (HHV) 6, HHV 7, parvovirus B 19, Varicella zoster virus, Herpes simplex virus (HSV) 1, HSV 2, and fungal culture were negative. The nerve conduction study (NCS) [Table 1] suggested a severe degree of mildly asymmetrical (left > right), small and large fiber sensorimotor axonal polyradiculoneuropathy involving the lower limbs more than upper limbs. The serology was negative for ganglioside autoantibodies (GM 1, GM2, GM3, GD1a, GD1b, GT1b, and GQ1b by Mycobacterium Immunodot blot method). Contrast-enhanced Magnetic resonance imaging (MRI) whole-spine [Figure 1a–d] revealed enhancement of multiple nerve roots in the lower dorsal and cauda equina regions while MRI of the brain was normal. The patient did not give consent for a nerve biopsy.

As infections and malignancies were ruled out, and in view of various odd features against GBS, the possibility of A-CIDP was considered, pulse methylprednisolone for 5 days followed by maintenance oral prednisolone and later azathioprine was given. After a week, the CSF showed protein 120 mg/dL, sugar 86 mg/dL, and cell count 2 (all lymphocytes). There was a progressive clinical improvement and the patient

Figure 1: Sagittal (a), coronal (b), and axial (c) post-contrast T1
fat-suppressed images of lumbar spine reveal linear enhancement and thickening of the cauda equina nerve roots (thin white arrows). (d) The maximum intensity projection T1 post-contrast-enhanced images of the cervical spine show thickening and enhancement of the bilateral brachial plexus nerve roots and trunk (thick white arrow). (e) Post-contrast T1 sagittal lumbar spine and (f) T1 coronal imaging of the cervical spine on follow-up after 3 months show complete resolution of the thickening and enhancement of the cauda equina nerve root and brachial plexus, respectively.

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was ambulatory with 1-person support after 1 month with concomitant improvement in the NCS [Table 1b] and MRI studies [Figure 1e, f] at 3 months. At 18 months, the patient was ambulant with normal muscle power except minimal grip weakness and no relapses.

Contrary to the classical definition, atypical variants of CIDP have now been recognized demonstrating variation in clinical phenotypes, serological markers, and treatment response.\(^1\) This case highlights a now-accepted subtype, i.e., A-CIDP. Understandably, due to the significant overlap in time to nadir in GBS and A-CIDP, misdiagnosis in favor of GBS is bound to occur.\(^1\) The early diagnosis of A-CIDP is of paramount importance as it will prevent the ongoing irreversible nerve damage and inappropriate therapeutic strategies.\(^3\) The index case presented at 11 days after onset with time to nadir of only 3 days. This would probably indicate GBS as suggested by Ruts et al.\(^1\) who concluded that A-CIDP should be suspected only if the patient with GBS deteriorates >8 weeks after onset or has >3 treatment-related fluctuations (TRF).

However, high CSF protein up to 6 g/dL leading to the formation of coagulum, papilledema, and lack of cranial nerve or autonomic involvement were atypical features for GBS. These observations triggered the diagnosis of probable A-CIDP. Dionne et al.\(^3\) reviewed 30 AIDP and 15 A-CIDP from 1993 to 2007 and found that the history of antecedent infectious illness, facial, bulbar, respiratory muscles weakness, and autonomic dysfunctions are more common with AIDP than A-CIDP. In this case, also, there was no facial, bulbar, or respiratory muscle weakness, autonomic dysfunction, or need for ventilation despite severe quadripareisis. Antecedent febrile illness, which can be seen in 33% of A-CIPD, was observed.\(^3\)

Although CSF protein can be high in AIDP, it rarely exceeds 3 g/dL, unlike in this case, wherein it was 5,900 mg/dL.\(^3\) Drulovic et al.\(^4\) analyzed CSF of 16 patients of AIDP and CIDP each and found an equal incidence of mean elevated CSF proteins in both patient groups, reaching 1,100 and 1,150 mg/L, respectively, though, in CIDP, it could be beyond 2,000 mg/L.

The electrophysiological studies were also not commensurate with AIDP. Previously, NCS has not proven useful to distinguish A-CIDP from AIDP in the early stages.\(^3\) In our case, NCS revealed an axonal pattern of symmetrical polyradiculoneuropathy. As seen in Table 1, sural sparing seen in acute demyelinating polyneuropathies was not observed. This axonal pattern with a loss of distal sensory nerve action potentials may be seen in nodopathies and paranodopathies as has been postulated in the pathophysiology of CIDP. Conceptually, demyelination in CIDP may be at multiple sites, especially in nodes, paranodes, and juxtaparanodes leading to reversible conduction failure with damage to the nodal axolemma that recovers well compared to AIDP.\(^3\) The atypical axonal pattern in the electrophysiological findings may, therefore, well be explained by this mechanism.

Similarly, the ganglioside antibody panel was negative for GM1, GM2, GM3, GD1a, GD1b, GT1b, and GQ1b. This again reiterates the lack of antibodies against gangliosides and myelin-associated glycoproteins (MAG) in CIDP unlike GBS and may support our patient having A-CIDP due to nodopathy/paranodopathy.\(^3\) Exceptions occur in CIDP variants which may have autoantibodies to MAG (distal acquired-demyelinating polyneuropathy), GD 1b (chronic sensory ataxic neuropathy), and GD1b, GD3, GT1b, and GQ1b (chronic ataxic neuropathy,
ophthalmoplegia, IgM paraprotein, cold agglutinin, and antidisialosyl antibodies or Chronic Ataxic Neuropathy Ophthalmoplegia IgM paraprotein Cold Agglutinins Disialosyl antibodies (CANOMAD) syndrome.\[3\]

Again, the remarkable treatment response to steroids and immunomodulators supports A-CIDP. As the treatment strategy and prognosis for GBS, especially with TRF and A-CIDP, differ considerably, it is relevant to distinguish between them early in the course of the disease. Most patients with AIDP will respond to a single dose of gammaglobulin (IVIg) or plasmapheresis, with only a minor percentage (8–16%) presenting TRF and requiring a repeated IVIg course or plasma exchange, whereas A-CIDP patients require long-term maintenance treatment with steroids, IVIg, or plasma exchange with or without immunosuppressive agents.\[3]\)

Thus, this case highlights the challenges in differentiating GBS and A-CIDP. Acute flaccid quadriplegia with generalized areflexia without extraocular, facial, bulbar, respiratory weakness, and autonomic dysfunction but with very high CSF protein should raise the possibility of A-CIDP. A sensorimotor axonal pattern could be a new electrophysiologic variant of A-CIDP that would need further studies.

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Conflicts of interest
There are no conflicts of interest.

References

1. Ruts L, Drenthen J, Jacobs BC, van Doorn PA; Dutch GBS Study Group. Distinguishing acute-onset CIDP from fluctuating Guillain-Barré syndrome. A prospective study. Neurology 2010;74:1680-6.
2. Eftimov F, van Schaik I. Chronic inflammatory demyelinating polyradiculoneuropathy: Update on clinical features, phenotypes and treatment options. Curr Opin Neurol 2013;26:496-502.
3. Dionne A, Nicolle MW, Hahn AF. Clinical and electrophysiological parameters distinguishing acute-onset chronic inflammatory demyelinating polyneuropathy from acute inflammatory demyelinating polyneuropathy. Muscle Nerve 2010;41:202-7.
4. Drulovic J, Apostolski S, Stojašavljević N, Trikic R, Sokic D, Levic Z. Cerebrospinal fluid finding in patients of acute and chronic inflammatory demyelinating polyradiculoneuropathy. Srp Arh Celok Lek 1996;124:1-5.
5. Uncini A, Kuwabara S. Nodopathies of the peripheral nerve: An emerging concept. J Neurol Neurosurg Psychiatry 2015;86:1186-95.

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