

Childhood Chronic Inflammatory Demyelinating Polyneuropathy – A Report of Two Cases

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Abstract

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune disorder characterised by demyelination of nerve roots and nerves. CIDP is less common in children but it has a favourable outcome as compared to adults. The course may be monophasic and progressive or characterised by recurrent relapses. The characteristic clinical presentation is with both proximal and distal muscle weakness with areflexia. Steroids, immunoglobulin and plasmapheresis are the mainstay of treatment. Of all these modalities, steroids are more likely to induce long lasting remission.

In this article, we are reporting two children with CIDP – one with the monophasic and the other with the relapsing course, with a view to highlight the differences in presentation and the fact that it remains an under diagnosed condition due to its protean manifestations.

Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune mediated disorder, affecting the peripheral nervous system, whose pathogenesis is still poorly understood. It is an uncommon disease in children with a reported incidence of 0.5/1000001. In its classic form the characteristic features are progressive, proximal limb weakness, sensory involvement and areflexia with either a progressive or relapsing course. The other typical features are albumino – cytological dissociation in the cerebrospinal fluid, electrophysiological features of demyelination and nerve biopsy showing inflammation, demyelination, and remyelination. Various treatment modalities like intravenous immunoglobulin, steroids and plasmapheresis have been found to be effective in the management of CIDP. Though guidelines for the diagnosis and management of this condition have been developed, the wide spectrum of clinical presentations can make the diagnosis a major challenge for the clinician, more so as the outcomes depend on early treatment interventions. Two children with differing clinical presentations are being discussed in this article.

Clinical Presentation

Case 1

A previously healthy 10-year-old male child was admitted for the evaluation of progressive difficulty in ambulation of 3 months duration. The onset was with inability to put on his slippers which had gradually progressed to difficulty in walking to the extent that he had to be carried to the ward. He had paraesthesiae involving the lower limbs but no bowel or bladder involvement. The weakness had an ascending progression though the bulbar musculature was spared. There was no history of any antecedent infection, immunisation or toxin exposure. Neurologic examination revealed symmetric proximal

and distal muscle weakness of upper and lower limbs, distal muscle wasting, areflexia and flexor plantar response. There were no cranial nerve abnormalities and sensory modalities were intact. Gower's sign was positive and the child had a significant genu recurvatum indicating marked lower limb weakness.

This presentation of ascending weakness and areflexia made us suspect a chronic acquired demyelination. Cerebrospinal fluid (CSF) analysis revealed albumino – cytological dissociation, MRI of the brain and spinal cord was normal and nerve conduction velocity (NCV) revealed very prolonged distal latencies. Sural nerve biopsy was reported as normal. Based on the clinical picture and investigations a diagnosis of CIDP was made. Treatment was initiated with IV immunoglobulin (1g/kg X 2 days) following which there was no significant response. Subsequently, oral prednisolone was started, in the dose of 2 mg/ kg/ day for two months, which was then gradually tapered over four months. The boy showed a steady improvement in power while on prednisolone. The initial Modified Rankin score (MRS) of 5 gradually improved to a score of 2.

Case 2

A 3 ½ month old female infant presented with paucity of lower limb movements of 10 days duration. The mother noted a weak cry two days prior to presentation. There was no history of difficulty in feeding or nasal regurgitation. The infant had developed fever for two days prior to the onset of weakness. On examination, there was hypotonia, weakness of both upper and lower limbs with areflexia. The lower limbs were more involved than the upper. Gag reflex was weak and there was evidence of diaphragmatic paralysis. A clinical diagnosis of Guillian Barre syndrome (GBS) was made and investigations were carried out. CSF analysis revealed albumino – cytological dissociation following which IV immunoglobulin, 400 mg/ kg/ day over five days, was given. Investigations for infective etiologies were negative. MRI of the brain and spine were normal. There was a dramatic response to IV

immunoglobulin and the infant was discharged with improving power but with persisting areflexia. NCV showed severe sensory motor neuropathy of both upper and lower limbs.

Periodic follow up in the outpatient department revealed a residual weakness of the lower limbs while the upper limbs had recovered completely. The residual weakness was attributed to a recovering GBS.

She presented two months later with flaccid weakness (power 0/5) of both lower limbs with no diaphragmatic or upper limb involvement. CSF analysis this time showed very slight increase in

proteins with no cells. NCV was similar to the previous one. At this point, a diagnosis of CIDP was made in view of persisting signs for more than 8 weeks, worsening of power after an initial partial recovery and areflexia. The infant did not respond to IV immunoglobulin this time but showed a good response to oral steroids. Prednisolone was given for the initial two months at a dose of 2 mg/ kg/ day. The infant is currently on tapering doses of steroids.

The comparative clinical and electrophysiological features, of the two cases, are summarised in Table 1.

S. No	Characteristic	Case 1	Case 2
1	Gender	Male	Female
2	Age	11 years	3 ½ months
3	Onset of disease	Chronic (3 months)	Acute (10 days)
4	Time between symptom onset and maximum disability	12 weeks	2 weeks initially, with worsening at 8 weeks
5	Temporal course	Monophasic	Recurrent
6	Response to IV immunoglobulin	Partial	Good
7	Response to steroids	Good	Good
8	Muscle wasting	Yes, distal muscles	No
9	Sensory loss	No, paraesthesiae ⁺	Could not be assessed
10	NCV	Absent CMAP in both lower limbs. CMAP amplitude and conduction velocity is reduced in both upper limbs. Absent SNAP and non recordable F waves in all four limbs	Absent CMAP, absent SNAP with non recordable F wave in all 4 limbs
11	Modified Rankin score at onset	5	5
12	Modified Rankin score after treatment	2	2
13	Relapses	None so far	1

Table 1: Case characteristics.

Discussion

The clinical presentation of CIDP in children is very variable as it can be acute, mimicking Guillian Barre syndrome (GBS), or it can have a chronic, relapsing course. Though it is easy to make a retrospective diagnosis of CIDP after prolonged illness/relapses, diagnosis during the first episode, especially with an acute GBS kind of onset, may be challenging. The 1st case had a long duration of progressive disease thus making the diagnosis quite simple. Conversely the 2nd case presented like classical GBS, initially, with a rapid response to IV Ig. It was the subsequent worsening at 8 weeks that made the distinction obvious. Since CIDP, despite its potential for recurrences, has a favourable long term prognosis with initiation of steroid therapy, every attempt should be made to diagnose this condition early. The criteria to diagnose CIDP in an acute GBS like presentation is the documentation of neurological deterioration within 8 weeks (as was seen in the 2nd case) or if there have been 3 or more treatment related fluctuations [1-3].

CIDP and acute inflammatory demyelinating polyneuropathy (AIDP) have almost the same clinical presentation with varying duration but the line of management and ultimate outcome are entirely different. Since the time factor has a bearing on outcome, the International workshop has proposed to revise the diagnostic criteria for childhood CIDP to include patients with progressive weakness of over 4 weeks rather than the classical 8 weeks [4]. American Academy of Neurology (AAN) has very stringent criteria for the diagnosis with undue reliance on electro diagnostic studies, which in itself may be unpredictable in cases with axon loss or in pure sensory variant.

Pathological findings on nerve biopsy may not be specific to CIDP and can occur in several other disorders. The inconclusive nerve biopsy in our first case can probably be explained by the fact that the actual abnormality may exist in the proximal segments of the nerve/ root which may not be accessible to biopsy. However, nerve biopsy may still be useful in patients with inadequate proof of demyelination from other investigations and in whom vasculitis is suspected. Evidence of axonal loss in nerve biopsy predicts a worse prognosis,

though effective therapy can minimise axon loss. This invasive procedure was not done in the second case.

The principles of management of CIDP revolve around improvement of functional status as measured by the modified Rankin score and achievement of long term remission. These goals are achieved by immunotherapy with IV immunoglobulin or long term steroids. Plasmapheresis may show an initial improvement but long term remission rates are poor with this modality of treatment [5].

Best response to IV immunoglobulin occurs in infants and children with ongoing, generalised demyelination of recent onset. In such a setting this therapy induces remission in 90% of cases. In cases presenting late with established axon loss, IV immunoglobulin therapy has limited value. The 1st case presented quite late in the course of illness, with established muscle atrophy indicating axon loss, and hence did not improve with IV immunoglobulin therapy. In contrast, our 2nd case had presented much earlier in the disease course with a prompt response to IV immunoglobulin therapy at the onset. The lack of response to the 2nd course of IV immunoglobulin, in the same child, was probably the result of established axon loss by then.

The first child presented to us at 12 weeks after disease onset with severe disability (MR score 5). The response to oral prednisolone was remarkable with proximal power improving within 2 weeks from 2/5 to 4/5 though improvement of distal power from 0/5 to 2/5 took almost 6 months. This finding supports the observation that though the average time of improvement with oral steroid therapy is 2 months, maximal improvement is evident only after 6 months [6]. The 2nd child showed a marked initial recovery of proximal power from 1/5 to 3/5 within 2 weeks of oral steroids, though distal power still remains at 2/5 at 8 weeks of therapy. A slow taper over 6 months, with careful monitoring for steroid toxicity, is being planned to ensure maximal improvement of power and for prevention of relapse.

Despite the late initial presentation in the 1st case the remission is prolonged with no relapse for the past one year. In contrast, the infant presented very early and responded well to therapy but had an early relapse probably because relapses tend to occur more often in younger patients with CIDP [7]. To our knowledge, this infant is the youngest reported case with CIDP in the world.

Conclusion

Thus, we conclude that CIDP is more a clinical diagnosis. It is entertained even in the absence of electrophysiological/ pathological

criteria, as early initiation of therapy has a favourable outcome. GBS like initial presentation can distract the clinician from the diagnosis of CIDP and only the subsequent course or relapses can give a clear picture. Even with a late presentation, it is worth trying immunotherapy as it may still have a favourable outcome. The initial choice of therapy would be IV immunoglobulin. The addition of steroids is warranted in patients with either a poor response to IV immunoglobulin or in those with a relapsing course. Children with CIDP have a more favourable outcome as compared to adults. They are also more likely to present with the relapsing form of the disease but the number of relapses does not adversely affect the prognosis. The most promising fact is that the prognosis for remission of neurological deficits is good.

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