

CASE REPORT

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# Use of cyclophosphamide for treatment of fulminant CIDP in the rehabilitation setting

Hamilton Chen

## ABSTRACT

**Introduction:** We present a patient with fulminant chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) refractory to conventional interventions successfully treated with cyclophosphamide. **Case Report:** 54-year-old male with history of GBS presented to a tertiary care center with bilateral upper and lower extremity weakness, double vision, decreased sensation with bowel movements and micturition, dysphagia, CHF with hypotension, and dyspnea. On examination he demonstrated generalized weakness, areflexia and diminished sensation in bilateral lower extremities. The patient underwent workup, and his laboratory and electrodiagnostic presentation were consistent with CIDP. After he had no response to conventional immunosuppressive treatment, the decision was made to administer cyclophosphamide. The patient demonstrated progressive improvement in his symptoms within one week. He was transferred to the rehabilitation unit and received two additional dosages of cyclophosphamide. He was discharged at an independent level. **Conclusion:** CIDP is an autoimmune disease driven by an immune response involving T cell activation. It is estimated that 20% of CIDP patients do not respond to the conventional treatments of

prednisone, IVIG, and plasma exchange. Cyclophosphamide is an alkylating agent that prevents cell division by cross-linking DNA strands and decreasing DNA synthesis. Previous cases have shown that pulse cyclophosphamide and high dose cyclophosphamide are effective for treating select patients with refractory CIDP, but has never been reported for treatment in patients with fulminant CIDP. Our patient tolerated the medication with few complications. Cyclophosphamide is an option for treatment for fulminant CIDP when conventional immunosuppressive treatment is not effective in the acute and rehabilitation setting

**Keywords:** CIDP, Cyclophosphamide, Rehabilitation, IVIG

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## INTRODUCTION

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an autoimmune disease that is driven by an immune response involving T cell activation resulting in segmental demyelination [1, 2]. Due to the autoimmune nature of the illness, clinical trials have demonstrated few effective treatments. Randomized trials have shown the efficacy of prednisone in treatment of CIDP. IVIG has been used

successfully in four randomized placebo-controlled trials [3–6]. Plasma exchange has also been shown to be effective [7–9]. Often, these studies have shown the treatments to offer only a temporal benefit. In addition, it is estimated that up to 20% of CIDP patients do not respond to the conventional treatments [10].

For the reasons mentioned above, immunosuppressive therapies have long been instituted in small clinical trials and case reports. Good et al. demonstrated that pulse cyclophosphamide administered over a period of six months is effective for treating CIDP [11]. Brannagan et al. demonstrated that high dose cyclophosphamide can also be used to treat patients with chronic CIDP refractory to conventional treatment [12]. We present a patient with fulminant CIDP with symptoms of cardiomyopathy and respiratory failure refractory to conventional measures successfully treated with cyclophosphamide in the hospital setting and subsequently in acute rehabilitation setting.

## CASE REPORT

A 54-year-old male was transferred from an outside hospital with complaints of bilateral upper and lower extremity weakness. The patient's symptoms started five months prior to transfer, when he initially had complaints of flu-like symptoms: headache, sinus pain, yellow discharge, and cough. Two weeks after the flu-like symptoms resolved, he began experiencing bilateral lower extremity paresthesias that spread to his bilateral upper extremities. The symptoms of paresthesias evolved into frank numbness, and eventually became associated with motor weakness. The motor weakness started in the lower extremities, and progressed to involve the upper extremities. At this time, the patient presented to an outside hospital, where he was diagnosed with presumed Guillain-Barre syndrome and administered five doses of IVIG. After he was given the medication, the weakness/numbness resolved completely.

The patient was well until four months later, when his bilateral upper extremity and lower extremity paresthesias and numbness recurred. He returned to the outside hospital where he was once again administered IVIG, with minimal relief of symptoms. The patient was then transferred to our facility for further management.

On presentation, the patient was in significant distress. In addition to weakness and paresthesias, he had a myriad of other symptoms: double vision, decreased sensation with bowel movements and micturation, dysphagia, CHF with hypotension, and dyspnea on exertion. On examination, he was alert and oriented. Pupils were reactive 4–2 mm bilaterally; cranial nerves II–XII were intact. Motor exam showed 4/5 strength in biceps, triceps, brachioradialis and hand intrinsic bilaterally. Lower extremity motor exam revealed a generalized 2/5 strength in bilateral hips, knees and dorsiflexion and plantarflexion of ankles.

Weakness was slightly worse proximally in each limb. Reflex exam demonstrated areflexia in brachioradialis, biceps, triceps, patella and achilles bilaterally. Sensory exam elicited decreased sensation to light touch in bilateral lower extremities below the L2 level.

Results from lumbar tap are demonstrated in Table 1. The patient had elevated protein in the CSF. Initial nerve conduction studies are shown in Table 2. The patient had greater than 50% prolonged distal motor and sensory latency in median, ulnar and tibial nerves, meeting the electrodiagnostic criteria for EFNS/PNS for typical CIDP [13].

Biopsy of the left sural nerve showed evidence of mild to moderate demyelination on the biopsy. The peroneus longus muscle was also biopsied and demonstrated demyelination and severely atrophied muscle fibers.

The patient's CIDP symptoms progressed requiring intubation early during hospitalization. Regular clinical examination revealed worsening weakness despite frequent courses of IVIG, prednisone and plasma exchanges. Mechanical ventilation was unable to be weaned off over the course of one month and the patient required a tracheostomy for airway management. A repeat nerve conduction study performed one month after the first nerve conduction study showed worsening of distal motor latency in median, ulnar and tibial nerves, as well as reduced amplitudes and conduction velocity in the median, ulnar, and tibial nerves. Results are shown in Table 3.

With no response to conventional treatment after being symptomatic for over two months, the decision was made to administer cyclophosphamide. The patient was initially treated with cyclophosphamide 1800 mg over 60 minutes and he showed progressive improvement within one week. His initial symptoms of double vision, decreased sensation with bowel movements and micturation, dysphagia and respiratory failure improved. His cardiomyopathy symptoms improved with titration of medication and diuresis. He was successfully weaned off the ventilator and transferred to the acute rehabilitation unit for aggressive physical therapy.

Upon transfer to the rehabilitation unit, patient's initial evaluation by physical therapy and occupational therapy for ADLs and mobility are shown in Table 4. During his course of rehabilitation, he received two additional dosages of cyclophosphamide of 1800 mg over 60 minutes. After one month of intense physical and occupational therapy, he demonstrated significant improvement in his symptoms and eventually had his

Table 1: CSF laboratory values.

Lab	Value	Normal
Glucose (mg/dL)	65	50–80
Protein (mg/dL)	52	15–45
WBC	2	0–3
RBC	3	0

Table 2: First motor nerve conduction study.

Site	Onset Latency (ms)	Norm Onset Latency (ms)	Amplitude (mV)	Norm Amplitude (mV)	Segments	Distance (cm)	Velocity (m/s)	Norm Velocity (m/s)
R Median-APB								
Wrist	7.7	<4.4	6.0	>4.9	Wrist-APB	7		
Elbow	11.7		5.8		Elbow-Wrist	21.5	53.1	>45
R Ulnar-ADM								
Wrist	4.8	<4.2	11.5	>4.9	Wrist-ADM	7		
B. Elbow	8.8		11.3		B. Elbow-Wrist	21.5	54.4	>49
A. Elbow	11.3		11.0		A. Elbow-B. Elbow	10	40.8	>49
R Common Peroneal-EDB								
Ankle	12.0	<6.5	2.9		Ankle-EDB	9		
Fibular Head	18.1		2.6		Fib Head-Ankle	28.5	47.1	>45
Knee	20.1		2.6		Knee-Fib Head	10	48.8	>45
R Tibial (Knee) AH								
Ankle	6.4	<5.8	6.5		Ankle-AH	9		
Knee	15.8		6.7		Knee-Ankle	39.5	42.2	>41

Abbreviations: R – Right; APB – Abductor Pollicis Brevis ; ADM – Abductor Digiti Minimi ; EDB – Extensor Digitorum Brevis ; AH – Abductor Hallucis

tracheostomy decannulated. The patient was discharged home at an independent level.

Cyclophosphamide was relatively well tolerated by our patient. Side effects after administration included: neutropenia, urinary tract infection, and nausea.

## DISCUSSION

Immunosuppressants have long been used for treatment of refractory CIDP, but randomized controlled trials have only been reported for azathioprine and methotrexate. Azathioprine (2 mg/kg) showed no benefit for treatment of CIDP when added to prednisone in 14 CIDP patients for nine months [14, 15]. No significant benefit was observed when methotrexate 15 mg daily for 24 weeks was compared with placebo in 62 patients treated with IVIG or corticosteroid [16].

Cyclophosphamide is an alkylating agent that prevents cell division by cross-linking DNA strands and decreasing DNA synthesis, which leads to cell death. It is not active against pluripotent stem cells due to high aldehyde dehydrogenase levels in these cells, but is active against B and T cells. It is a relatively well

tolerated chemotherapy drug. Some commonly reported side effects include: alopecia, nausea, headache, lightheadedness, rash, anemia, leukopenia and hemorrhagic cystitis [14]. Previous studies have shown that pulse cyclophosphamide administered over a period of six months is effective for treating refractory CIDP [11]. High dose cyclophosphamide has also been used successfully [12]. However, the treatments in these studies were administered to select population of patients without fulminant symptoms affecting multiple organ systems. Fulminant CIDP symptoms including cardiomyopathy and respiratory failure requiring tracheostomy, have, to our knowledge, never been reported to be successfully treated with cyclophosphamide. In addition, cyclophosphamide has never been reported for use in the inpatient acute rehabilitation setting with concurrent physiotherapy.

## CONCLUSION

As a relatively well tolerated chemotherapy drug, cyclophosphamide can be administered safely for treatment of fulminant CIDP when patients are refractory to conventional immunosuppressive treatment

Table 3: Repeat motor nerve conduction study – one month follow up study.

Site	Onset Latency (ms)	Norm Onset Latency (ms)	Amplitude (mV)	Norm Amplitude (mV)	Segments	Distance (cm)	Velocity (m/s)	Norm Velocity (m/s)
R Median-APB								
Wrist	10.0	<4.4	2.1	>4.9	Wrist-APB	7		
Elbow	15.8		1.9		Elbow-Wrist	20	34.8	>45
L Median-APB								
Wrist	9.6	<4.4	3.4	>4.9	Wrist-APB	7		
Elbow	13.1		3.0		Elbow-Wrist	20	57.1	>45
R Ulnar-ADM								
Wrist	4.8	<4.2	11.5	>4.9	Wrist-ADM	7		
B. Elbow	8.8		11.3		B. Elbow-Wrist	21.5	54.4	>49
A. Elbow	11.3		11.0		A.Elbow-B.Elbow	10	40.8	>49
R Ulnar-ADM								
Wrist	6.9	<4.2	6.8	>4.9	Wrist-ADM	7		
B. Elbow	11.9		6.3		B. Elbow-Wrist	22	44	>49
A. Elbow	15.0		5.9		A.Elbow-B.Elbow	10	32.8	>49
L Ulnar-ADM								
Wrist	5.6	<4.2	5.3	>4.9	Wrist-ADM	7		
B. Elbow	10.1		4.7		B. Elbow-Wrist	21.5	54.4	>49
A. Elbow	12.5		4.5		A.Elbow-B.Elbow	10	40.8	>49
R Tibial (Knee) AH								
Ankle	11.6	<5.8	2.1		Ankle-AH	9		
Knee	20.6		1.3		Knee-Ankle	38	42.2	
L Tibial (Knee) AH								
Ankle	11.3	<5.8	1.8		Ankle-AH	8		
Knee	21.6		1.4		Knee-Ankle	41	40.0	

Abbreviations: R – Right; APB – Abductor Pollicis Brevis ; ADM – Abductor Digiti Minimi ; EDB – Extensor Digitorum Brevis ; AH – Abductor Hallucis

Table 4: Therapy summary in acute rehabilitation.

	Admission	Discharge
Mobility	Mod/Max Assist	Independent
Transfers	Max Assist	Independent
Gait	Not Assessed	Modified Independent (Cane)
Eating/Grooming	Supervised	Independent
Upper Body Dressing	Total Assist	Independent
Lower Body Dressing	Total Assist	Independent
Toileting	Total Assist	Independent
Bathing	Total Assist	Independent

with IVIG, prednisone, and plasma exchange. It can be safely used in the subacute and rehabilitation setting with good functional outcomes.

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### Author Contributions

Hamilton Chen – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

### Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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