A 52 Year Old Female with Abdominal Pain and Diagnosed with Chronic Inflammatory Demyelinating Polyradiculopathy: A Case Report*

Kimberly S. Yu, MD

ABSTRACT

Chronic inflammatory demyelinating polyneuropathy (CIDP) is often misdiagnosed due to its presentation as it can mimic different kinds of peripheral neuropathies. CIDP is a rare immune-mediated neurologic disorder that can be associated with systemic lupus erythematosus, HIV, diabetes mellitus or thyroid disorders. For this paper, it aims to present a 52-year-old female whose chief complaint was abdominal and radicular pains. A series of diagnostics pointed to diagnose the patient with CIDP associated with diabetic polyneuropathy with a provisional diagnosis of SLE. CIDP is said to be an uncommon manifestation of SLE and Diabetes Mellitus. This paper aimed to discuss the approach and management in patients with CIDP and different forms that can mimic CIDP.

Key words: Chronic inflammatory demyelinating polyradiculopathy, peripheral neuropathy

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare immune-mediated neurologic disorder that targets the peripheral nerves and nerve roots which can cause progressive weakness and sensory loss, usually seen in adults aged 40 to 60 years old. The classic presentation of CIDP is described as a gradual to chronic progression of symmetric, proximal, distal weakness lasting for 8 weeks or more along with clinical manifestations of diminished or absent deep tendon reflexes, some may also present with atypical manifestations such as purely sensory or purely motor asymmetric presentations. It has been associated with several diseases such as systemic lupus erythematosus, HIV, diabetes mellitus and thyroid disease. CIDP is said to be rare and has an incidence of 1.6 in every 100,000/year and a prevalence of 8.9 in every 100,000/year; CIDP may also be present in 9% to 26% of patients who have diabetes mellitus, Charcot-Marie Tooth disease, or monoclonal gammopathy (Laughlin, et al., 2009).

The objective of the report was to present a case of a 52 year old female diagnosed with chronic inflammatory demyelinating polyradiculopathy with associated DM polyneuropathy and possible SLE.

THE CASE

This is a case of a 52 year old female who presented with a 4 month history of spontaneous, intermittent, excruciating, spastic epigastric pain not related to food intake. Patient was previously diagnosed to have diabetes 6 years ago and was controlled on metformin, diet and exercise although there was a recent increase in FBS and HbA1c during this time. She is also hypertensive, and obese, a chronic smoker and an occasional alcoholic beverage drinker. The patient was initially admitted due to abdominal pain and was initially diagnosed with acute calculous cholecystitis and underwent laparoscopic cholecystectomy. Post cholecystectomy, there was

* From the Department of Internal Medicine

still persistence of the intermittent spastic abdominal pain. DM gastroparesis, autoimmune vasculitis, pancreatic malignancy, small intestinal obstruction or volvulus were among the differential diagnoses but extensive work ups proved otherwise; all this time she was constantly treated as acid peptic disease.

During her subsequent admissions, still with spastic abdominal pain and was diagnosed and treated as having acute gastritis with Helicobacter pylori infection. She was also diagnosed to have pulmonary tuberculosis by chest CT scan and GeneXpert and was started on treatment. At around this time, she started complaining of thoracic (T8 to T9) and lower extremities radicular pains; on physical exam there was minimal weakness of distal lower extremities noted to have absent deep tendon reflexes and objective sensory loss. An Electromyography – Nerve Conduction Velocity test was done which revealed an abnormal study showing moderate symmetrical sensorimotor axonal polyneuropathy affecting the upper and lower extremities; which may be seen in toxic-metabolic conditions (e.g. Diabetes Mellitus), Vasculitis, or autoimmune diseases; and an evidence for an active chronic lumbosacral radiculopathy affecting the bilateral L5/S1 nerve roots, she was then started on pregabalin, duloxetine, eperisone, norgesic, tramadol, fentanyl patch, and rescue doses of oxycodone.

She still complains of epigastric pain and radicular pains, with a finding of a possible hepatic and celiac arteritis on Abdominal MRI, the patient was worked up for Connective Tissue Disease with concomitant vasculitic neuropathy as a cause of her persistent abdominal and radicular pains. Her ANA was positive at 1:160, but the other lupus antibodies were negative hence, autoimmune vasculitis with polyneuropathy was entertained; she was given pulse therapy of methylprednisolone 500mg/day for 3 days. This afforded minimal relief, and aggravated the epigastric pains, causing her to take her prednisone irregularly, there was also worsening of the lower extremity and thoracic radicular pains.

After 2 months a repeat EMG was done and showed almost the same finding but concomitant CIDP was entertained and a repeat ANA was positive at 1:320, but the rest of the lupus panel were again negative. As a treatment for CIDP, she was started on IVIg 2g/kg/day infusion for 5 days, and prednisone 20 mg/tab was continued and overlapped with increasing doses of mycophenolate mofetil. She was also referred to rehabilitation medicine for physical therapy. Review of the history also revealed that as early as 2017, she had several episodes of right lumbar (L2) radiculopathy, thoracic radical pains and was treated as zoster sine herpete with distal paresthesia and was started on pregabalin 100mg/tab 2x a day.

After 2 weeks from her initial IVIg infusion, there was a significant resolution of epigastric and lower extremity pains and her medication doses were lowered, opioids were then used sparingly. A third EMG-NCV was done 2 weeks after the confirmed CID polyradiculoneuropathy process with few denervation changes suggesting axonal involvement as well. On physical examination, her distal lower extremities were weak but with improved strength 4/5, still with positive Rhomberg's test, and absent Deep Tendon Reflexes, has no vibration sense on the left knee and both ankles.

With significant improvement in her abdominal and radicular pains after the 1st IVIg infusion, she agreed to continue with her CIDP treatment of 2 more cycles of IVIg infusion at 2g/kg/day for 5 days every 4 weeks for 3 months; then 1g/kg/day for 5 days every 3 to 6 months thereafter as her clinical condition warrants. Prednisone was eventually tapered and stopped and she was maintained on mycophenolate mofetil 1.5g/day. Her pains and somehow her distal leg weakness improved, but areflexia and loss of pain, position and vibration sense was still apparent. On her 2nd cycle of IVIg infusion (2 g/kg/day), still with complaints of radicular pains and stated to be more tolerable, has no complain of abdominal pain. On physical examination, the upper extremities were unremarkable but then her lower extremities were weak; right more than the left; still has absent deep tendon reflexes, has no vibration sense on the left knee and bilateral medial malleolus, bilateral ankles has limited dorsiflexion and plantarflexion, no joint pains or rashes were noted.

During her 3rd cycle of IVIg Infusion (2 g/kg/day), still with radicular pain, has less attacks and has a more tolerable pain, she had a complete undisplaced fracture of the left 5th metatarsal and lateral malleolus. With the same PE findings as the previous admission, with pain limited by motion of the left ankle.

DISCUSSION

Chronic Inflammatory Demyelinating Polyradiculopathy (CIDP) is a rare immune-mediated neurologic disease, that has been associated

with several diseases such as systemic lupus erythematosus, HIV, and diabetes mellitus (Gorson, et al., 2000). CIDP is often seen in adults aged 40 to 60 years old and rarely seen in children, classic presentation of CIDP is described as a gradual to chronic progression of symmetric, proximal, distal weakness lasting for 8 weeks. Some may also present with atypical manifestations such as purely sensory or purely motor asymmetric presentations.

The clinical presentation of CIDP is slow and progressive, with symmetric weakness of the proximal and distal muscles, nerve signals are often altered and can have an impaired sensory and motor function. In some cases, CIDP presents with fatigue, burning pain, weak muscles, absent or reduced deep tendon reflexes and an abnormal gait. CIDP is often mistaken or misdiagnosed due to the presence or overlaps with diabetic polyneuropathy clinically and electrophysiologically. In comparison to diabetic polyneuropathy, which is the most common microvascular complication of diabetes mellitus that can affect almost 50% of patients that are diagnosed with type 1 and type 2 diabetes mellitus suffers from peripheral neuropathy, which can also present with symmetric, progressive sensorimotor neuropathy with proximal and distal weakness of muscles due to the impaired vasodilation activity that can lead to ischemia and neuropathy (Zeng, et al., 2017). In cases of CIDP with underlying causes such as toxic, metabolic or immune mediated, there is also a presentation of weak distal lower limbs may be seen with an impaired pinprick sensation, describes as a glove or stocking distribution, absent or reduced deep tendon reflexes and an impaired position sense (Abraham, et al., 2017). SLE neuropathy on the other hand presents with an asymmetric and lower extremity involvement, most specifically affecting the peroneal and sural nerve (Florica, et al., 2011).

There are several variants of CIDP, in a study by Suanprasert & Hanchaiphiboolkul last 2017, they have described 4 variants of CIDP: 1) classic CIDP which presents with proximal and distal neuropathy and weakness; 2) multifocal motor neuropathy which presents with an asymmetric neuropathy and a pure motor weakness; 3) multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy which presents with an asymmetric neuropathy with both sensory loss and motor weakness and lastly, 4) distal acquired demyelinating symmetric (DADS) neuropathy which presents with symmetric distal sensory loss and motor weakness.

Chronic inflammatory demyelinating polyneuropathy is said to occur in 2 distinctive pathophysiologies: 1) Macrophage-Induced Demyelination, termed as the classical pathophysiology of CIDP in which the demyelinating process is a result from phagocytosis of myelin by macrophages. This mechanism is found in different variants of CIDP which are the typical, atypical, MADSAM, DADS and in pure sensory CIDP. 2) Nodo-Paranodopathy caused by IgG4 Autoantibodies, this mechanism is an emerging concept as a pathophysiology of CIDP in which it suggests that IgG4 autoantibodies (anti-neurofascin 155 and anti-contactin 1) against components present at the nodes of Ranvier and paranodal junctions in between the myelin terminal loops and axolemma, which explains why some CIDP variants are unresponsive to Intravenous immunoglobulin (IVIg) treatment. The Nodo Paranodopathy concept may be present in patients diagnosed with typical CIDP and DADS (Koike & Katsuno, 2020). In comparison to diabetic polyneuropathy, it is commonly seen in long standing diabetics, autonomic neuropathy, lumbosacral radiculopathy which presents with asymmetric pain that can progress to lower extremity weakness and muscle atrophy; and distal symmetric sensorimotor polyneuropathy, the most common diabetic neuropathy which present with paresthesia and numbness.

In correlation to diabetes mellitus, CIDP can occur in 16.9% on both type 1 and type 2 diabetic patients and 1.8% are classified as idiopathic CIDP. Diabetic patients are prone to have an 11 times higher occurrence for CIDP. There are 2 mechanisms proposed on how DM-CIDP occurs due to nerve ischemia and metabolic derangement of nerve, in which these patients also respond to IVIg and steroids. In comparison to DM polyneuropathy, controlling the diabetes is the ideal goal of treatment as nerves are already damaged by the said disease (Sharma, 2002).

According to the study of Gable, there is a high rate of 47% in misdiagnosing patients with CIDP in the US alone. Individuals that are misdiagnosed are the ones with underlying diseases such as motor neuron disease, small fiber neuropathy, diabetic neuropathy, systemic lupus erythematosus, inclusion body myositis, anti-MAG (Myelin Associated Glycoprotein) peripheral neuropathy, multifocal motor neuropathy, or fibromyalgia. Based on the 2010 European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS), the

diagnostic criteria for CIDP must have a clinical and electrophysiologic finding to confirm the diagnosis of CIDP; focusing on electrophysiologic or clinical findings alone often leads to an inaccurate diagnosis of CIDP. The diagnostic criteria is usually 81% to 99% sensitive and 61 to 97% specific, in which it can provide a better diagnosing outcome compared to other diagnostic criteria for CIDP. (Table 1)

Table 1. Diagnostic criteria for CIDP based on the EFNS/PNS (2010)

TABLE. SUMMARY OF EUROPEAN FEDERATION OF NEUROLOGICAL SOCIETIES/PERIPHERAL NERVE SOCIETY DIAGNOSTIC CRITERIA (2010) FOR CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)		
	Typical	**Atypical**
Clinical criteria	Chronically progressive, stepwise or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities that developed over ≥2 months with absent or reduced tendon reflexes in all extremities	Predominantly distal (distal acquired demyelinating symmetric [DADS])
		Asymmetric (multifocal acquired demyelinating sensory and motor neuropathy [MADSAM], Lewis-Sumner syndrome)
		Focal (involving brachial or lumbosacral plexus or ≥1 nerves in 1 limb)
		Pure motor
		Pure sensory
	NOT caused by *Borrelia* infection (Lyme disease), diphtheria, drug, or toxin Nonhereditary Without prominent sphincter disturbance Not meeting criteria for multifocal motor neuropathy, IgM with high titer antiMAG antibodies, POEMS syndrome, osteosclerotic myeloma, diabetic or nondiabetic lumbosacral radiculoplexus neuropathy, lymphoma, amyloidosis	
Electrophysiologic criteria	**Definite:** includes at least 1 of the following:	
	Prolonged motor distal latency ≥50% above upper limit of normal (ULN) in 2 nerves (not including median neuropathy at wrist from carpal tunnel syndrome), or	
	Reduced motor conduction velocity ≥30% below lower limit of normal (LLN) in 2 nerves, or	
	Prolonged F-wave latency ≥30% above ULN in 2 nerves (≥50% if amplitude of distal negative peak compound muscle action potential (CMAP) <80% below LLN, or	
	Absent F-waves in 2 nerves if these nerves have distal negative peak CMAP amplitudes ≥20% of LLN + ≥1 other demyelinating parameter is seen in ≥1 other nerve, or	
	Partial motor conduction block ≥50% amplitude reduction of proximal negative peak CMAP relative to distal, if distal negative peak CMAP ≥ 20% of LLN in 2 nerves, or may be present in only 1 nerve if a different demyelinating parameter is seen in ≥1 other nerve(s), or	
	Abnormal temporal dispersion (>30% duration increase between the proximal and distal negative peak CMAP) in ≥2 nerves, or	
	Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in ≥1 nerve (median ≥6.6 ms, ulnar ≥6.7 ms, peroneal ≥7.6 ms, tibial ≥8.8 ms) + ≥1 other demyelinating parameter in ≥1 other nerve	
	Probable: ≥30% amplitude reduction in proximal negative peak CMAP relative to distal, excluding the posterior tibial nerve, if distal negative peak CMAP ≥ 20% of LLN, in 2 nerves; may be present in only 1 nerve if a different demyelinating parameter is seen in ≥1 other nerve(s)	
	Possible: any of the electrophysiologic criteria for definite CIDP, but in 1 nerve only	
Supportive tests	Elevated CSF protein with leukocyte count <10/mm^3	
	MRI gadolinium enhancement and/or hypertrophy of cauda equina, lumbosacral or cervical nerve roots, or the brachial or lumbosacral plexuses	
	Abnormal sensory nerve conduction study (NCS) in at least 1 nerve: a. Normal sural with abnormal median (excluding median neuropathy at wrist from carpal tunnel syndrome) or radial sensory nerve action potential (SNAP) amplitudes; or, b. sensory conduction velocity <80% of LLN (<70% if SNAP amplitude <80% of LLN); or, c. delayed somatosensory evoked potentials without central nervous system involvement	
	Evidence of demyelination /remyelination by nerve biopsy with electron microscopy or teased fibre analysis	
For diagnosis, clinical criteria (typical and atypical) and either possible, probable, or definite findings of CIDP by electrophysiologic criteria are recommended. Refer to EFNS/PNS criteria (2010) for detailed recommendations and use of supportive data in diagnosis.		

Laboratory results for CIDP with underlying SLE, typically present with an increased CSF protein, an elevated ANA titer, a decreased C4 complement, an Electromyography and Nerve Conduction Velocity test that reveals a conduction block, prolonged distal motor latency, slowed conduction velocity, and an absent or delayed F wave is seen. For CIDP in diabetic patients, it may also present with an elevated CSF protein and demyelinating features on nerve conduction tests same as the typical CIDP. Currently, there is no established diagnostic criteria for CIDP in diabetic patients but it is important to identify CIDP as it is treatable and many patients respond to treatment as compared to diabetic neuropathy.

CIPD patients usually respond to a loading dose of IVIg 2 g/kg/day infusion for 5 days and often repeat infusions of either 0.5 g/kg/day 2 to 5 days every 2 weeks, 1 g/kg/day for 2 to 5 days every 3 weeks, or 2 g/kg/day for 5 days every month, for a total of 2 or 3 months. IVIg must then be tapered down or discontinued and must be determined if continuous use is still needed (Donofrio, et al., 2009). IVIg has proven to be a safe and more effective treatment compared to steroids (60mg/day to be tapered to 10mg/day) in a short-term prospective randomized controlled trial for CIDP; especially for those with pure motor CIDP (Abraham, et al., 2017). In some cases of CIDP, wherein patients do not respond well to IVIg and steroids, immunosuppressants such as cyclophosphamide or mycophenolate together with corticosteroids are used and often recommended to patients who have neuropsychiatric lupus erythematosus. There was significant improvement seen where there is an increased proximal muscle power for those who were treated with oral cyclophosphamide and corticosteroids and did not respond well with IVIg (Jasmin, et al., 2012).

The patient in this case fulfilled a typical clinical criteria for CIDP and with probable underlying SLE, wherein there were absent deep tendon reflexes, and a supportive test which fulfills an elevated CSF Protein of 57.8 mg/dL (1.28x elevated), a decreased C4 complement at 10.50 mg/dL (0.66x decreased), a positive ANA titer at 1:320 and her Electromyography – Nerve Conduction Velocity also showed the other signs of demyelinating neuropathy like wave dispersion, prolonged distal latency and slow conduction velocity of tested nerves, an absent F wave on the distal lower extremity on her nerve conduction test. Patient was initially started on methylprednisolone pulse therapy but was not responsive to the medication. A loading dose of IVIg infusion of 2g/kg/day for 5 days was started, patient tolerated the procedure and stated that the spastic abdominal pain and radicular pain was lesser and tolerable. She was maintained in prednisone 20mg/tab once a day during the succeeding days prior to another session of IVIg infusion. Patient completed 3 cycles of IVIg at 2g/kg/day for 5 days, maintained on prednisone for 1 month tapered to 10mg/tab for 2 weeks then to 5mg/tab for 2 weeks and overlapped with mycophenolate mofetil 500mg/tab once a day for 1 week and increased to twice a day continuously.

CONCLUSION

Reported here is a case of CIDP with concomitant diabetes mellitus and possible systemic lupus erythematosus, which initially presented with spastic abdominal pain and radicular pain. The diagnosis of CIDP was initially delayed until diagnostics were highly suggestive of an autoimmune CIDP. There is a need for diagnostic vigilance as there is no proven diagnostic test to highly prove the diagnosis of CIDP, it is highly dependent on physical examination, neurologic evaluation, Electromyography – Nerve Conduction Velocity test, lumbar puncture and nerve biopsy. Early diagnosis and treatment of CIDP and its underlying cause is beneficial to patients. CIDP is treatable and responds to IVIg and steroids as well as compared to those suffering from diabetic polyneuropathy. Identification and reporting of this case can benefit physicians to establish a diagnosis and treatment in order to prevent progression of the disease.

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