UNDER RECOGNIZED ENTITY: CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY WITH LUPUS

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ABSTRACT

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired, autoimmune peripheral neuropathy. It has an insidious disease progression resulting in a debilitating illness. It is a well known neurological disorder. The causative factors are elucidating and it is generally considered idiopathic. However, its' associations with various systemic disorders is well established albeit under recognized, especially with lupus as evident by few of the case reports/ series published in the recent past. The aim of this report is to highlight this neglected but important aspect of clinical neurology in common practice.

Key words: Chronic inflammatory demyelinating polyneuropathy: lupus; Intravenous immunoglobulin; pulse therapy; plasma exchange; steroids; immunosuppressant.

INTRODUCTION

While chronic inflammatory demyelinating polyneuropathy (CIDP) has been exclusively studied, the tempo-spatial relationship between CIDP and connective tissue diseases especially systemic lupus erythematosis (SLE) is still an active research subject emphasizing the importance of its identification as a possible cause of CIDP. SLE is a multisystemic, autoimmune disease that can affect the peripheral nervous system[1,2]. The term "CIDP with lupus" has been used in the category of "CIDP with systemic diseases" but only a handful of case reports/ series have been published so far [2,3]. By this report, we aim to share our own experience of a patient of CIDP with lupus in order to highlight this neglected but important aspect of clinical neurology in common practice.

CASE PRESENTATION

A 17 years old girl presented to us with numbness and progressive weakness of both the arms and legs for the last 6 months in January 2011. She had generalized edema for the last 2 months as well. Her motor power in upper limbs was 2/5 while that in the lower was 1/5 with absent reflexes and flexor plantar responses. She had microscopic hematuria and proteinuria with low C3 and C4. In the light of she having urinary findings with hypocomplimentemia, her ANA and anti-dsDNA were done, both of which turned out to be positive. Rest of the autoimmune work-up was negative. (Table 1) Nerve conduction studies (NCS) revealed markedly prolonged distal latencies with markedly reduced velocities and amplitudes of both the median motor nerves. There was no response in both peroneal and tibial nerves. Median and ulnar nerves did not show any F wave responses. The sensory median and ulnar nerves also showed no responses. NCS was clearly suggestive of demyelinating polyneuropathy and electromyography was therefore not conducted. (Table 2)CSF showed albuminocytological dissociation. Considering insidious onset and gradual progression of symmetrical proximal and distal weakness and sensory dysfunction of all extremities over a course of more than 8 weeks; clinically absent tendon reflexes in all extremities and NCS showing motor distal latency prolongation ≥ 50% above upper limit of normal in two nerves plus reduction of motor conduction velocity ≥ 30% below lower limit of normal in two nerves; with all the exclusion criteria fulfilled; the patient was labeled as CIDP. (Table 2) Autoimmune workup confirmed SLE with lupus nephritis. (Table 1)
Table 1: Lab parameters of our patient shown serially with time

Year	Lab parameters	Value	Inference
Jan. 2011	ANA	13.31 IU/l (normal < 1.5 IU/l)	+ve
	ESR	56 mm/ 1sthr (normal < 20 mm)	High
	Anti ds DNA	72 IU/l (normal < 20 IU/ml)	+ve
	C3 level	0.69 g/l (normal 0.83-1.93-g/l)	Low
	C4 level	0.07 g/l (normal 0.15-0.57 g/l)	Low
	Anti Sm	0.0 g/l	-ve
	Anti-RNP	0.0 g/l	-ve
	Anti SSA	0.0 g/l	-ve
	Anti SSB	0.0 g/l	-ve
	Anti Jo 1	0.0 g/l	-ve
	Anti Sc 70	0.0 g/l	-ve
	c-ANCA	0.0 g/l	-ve
	p-ANCA	0.0 g/l	-ve
	Anti GBM	0.0 g/l	-ve
	AMA	0.0 g/l	-ve
	ASMA	0.0 g/l	-ve
	Proteinuria	3.12 g/l (normal < 0.3 g/l)	Nephrotic range
	WBC	7900/ ul	Normal
	Hb	12.2g/dl	Normal
	Platelets	214000/ul	Normal
	Bilirubin	0.30 mg/dl	Normal
	ALT	17 U/l	Normal
	Alkaline phosphatase	39 U/l	Normal
	Urea	20 mg/dl	Normal
	Creatinine	0.30 mg/dl	Normal
	U/S abdomen	-	Ascitis + pleural effusion
Jun. 2011	ANA	9.12 IU/l	+ve
	Anti ds DNA	61.6 IU/l	+ve
	ESR	36 mm/ 1sthr	High
	C3 level	0.29 g/l	Low
	C4 level	0.13 g/l	Low
	Proteinuria	1.56 g/l	Subnephrotic range
	Urea	20 mg/dl	Normal
	Creatinine	0.30 mg/dl	Normal
	U/S abdomen	-	Unremarkable study
Jun. 2014	ANA	10.30 IU/l	+ve
	Anti ds DNA	54.8 IU/l	+ve
	Proteinuria	Nil	-ve

Table 1: Lab parameters of our patient shown serially with time: starting from January 2011 to June 2014.
Table 2: Nerve conduction studies of our patient revealing features of CIDP in 2011

NCS of June 2011											
Motor Nerves											
Site	NR	Onset (ms)	N. onset (ms)	O-P (mV)	N.Amp (mV)	Neg. Dur (ms)	Segment Name	Delta-O (ms)	Dist (cm)	Vel (m/s^2)	N. Vel (m/s^2)
Right Median (APB)											
Wrist	-	8.98	< 4.2	0.88	> 5.0	6.72	Elbow-Wrist	11.17	25	22.38	> 50.0
Elbow	-	20.16		0.22		8.20					
Right Ulnar (ADM)											
Wrist	-	5.55	< 4.2	1.80	> 3.0	7.66	B Elbow-Wrist	6.02	24	39.87	> 53.0
B Elbow	-	11.56		1.47		9.45					
Right Peroneal (EDB)											
Ankle	NR	-	< 5.5	-	> 2.5	-	-	-	-	-	> 40
B Fib	NR	-		-		-					
P-TA	NR	-		-		-					
Right Tibial (AHB)											
Ankle	NR	-	< 6.0	-	> 3.0	-	-	-	-	-	> 41
Knee	NR	-		-		-					
Left Tibial (AHB)											
Ankle	NR	-	< 6.0	-	> 3.0	-	-	-	-	-	> 41
Knee	NR	-		-		-					
Left Median (APB)											
Wrist	-	10.55	< 4.2	0.31	> 5.0	6.41	Elbow-Wrist	12.03	24	19.95	> 50.0
Elbow	-	22.58		0.18		7.27					
Sensory Nerves											
Site	NR	Peak (ms)	N. Peak (ms)	PT-Amp (μV)	N. Amp (μV)	-	Segment Name	Delta-P (ms)	Dist (cm)	Vel (m/s^2)	N. Vel (m/s^2)
Right Median Anti (2nd digit)											
Wrist	NR	-	< 3.7	-	>15.0	-	-	-	-	-	> 39
Right Ulnar Anti (5th digit)	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 50
Left Median Anti (2nd digit)											
Wrist	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 39
Left Ulnar Anti (5th digit)											
Wrist	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 50

Table 2: Nerve conduction studies in 2011: NR = No response; N.= Normal; Amp = Amplitude; Neg. = Negative; Dur. = Duration; O = Onset; P = Peak; Dist = distance; Vel = Velocity; APB = Abductor PolicisBrevis; ADM = Abductor DigitiMinimi; EDB = Extensor DigitorumBrevis; AHB = Abductor HallucisBrevis.

Thus, consolidated diagnosis was that of CIDP with lupus. She was given 1g methylprednisolone for 3 days. Her limb power gradually improved and proteinuria markedly decreased until she was able to walk without any functional disability as estimated using modified Rankin Scale (mRS) over a period of 4 weeks. She was discharged on maintenance dose of oral prednisone (1mg/kg/day) and 500 mg of cyclosporine three times daily. On follow-up visits after 3 months, the patient showed well controlled lupus with no renal or neurological impairment. Dose of prednisone was tapered down to 10 mg per day and cyclosporin continued with well controlled symptoms for both CIDP and SLE on 3 monthly follow-ups. After 30 months from initial diagnosis, the patient again presented with progressive weakness and numbness of all four limbs for the last 45 days, following a lower respiratory type infection. Her motor power in upper limbs was 4/5 while that in the lower was 2/5 with absent reflexes and flexor plantar responses. She, however, did not show any symptoms, signs or lab abnormalities suggesting renal compromise this time. (Table 1) Repeat NCS showed markedly prolonged distal latencies with reduced voltage and markedly reduced velocities in both median nerves and ulnar nerves. Peroneal and tibial nerves showed no response and median and ulnar nerves did not show any F wave responses. There was a conduction block from right median motor nerve; an electrophysiological hallmark of acquired demyelination. The sensory median and ulnar nerves also showed no responses. (Table 3) CSF showed albuminocytological dissociation. Her plasma exchange was done (200-250 ml/kg) with gradual improvement of symptoms until she was able to walk without support. She was discharged and put on maintenance dose of prednisone 1mg/kg/day plus 1g methyprednisolone once monthly. On routine follow-ups, patient showed marked recovery with resolution of neurological symptoms and regain of full functional status over the next 6 months.

Table 3: Nerve conduction studies of our patient revealing features of CIDP in 2014

NCS of April 2014												
Motor Nerves												
Site	NR	Onset (ms)	N. onset (ms)	O-P (mV)	N.Amp(mV)	Neg. Dur(ms)	Segment Name	Delta-O (ms)	Dist (cm)	Vel (m/s^2)	N. Vel(m/s^2)	
Right Median (APB)												
Wrist	-	9.38	< 4.2	1.90	> 5.0	7.73	Elbow-Wrist	8.28	20.5	24.76	> 50.0	
Elbow	-	17.66		0.85		7.73						
Right Ulnar (ADM)												
Wrist	-	3.67	< 4.2	4.04	> 3.0	7.89	B Elbow-Wrist	7.27	22	30.26	> 53.0	
B Elbow	-	10.94		3.27		9.38						
Right Peroneal (EDB)												
Ankle	NR	-	< 5.5	-	> 2.5	-	-	-	-	-	> 40	
B Fib	NR	-		-		-						
P-TA	NR	-		-		-						
Right Tibial (AHB)												
Ankle	NR	-	< 6.0	-	> 3.0	-	-	-	-	-	> 41	
Knee	NR	-		-		-						
Left Median (APB)												
Wrist	-	8.52	< 4.2	1.82	> 5.0	4.53	Elbow-Wrist	7.89	20.5	25.98	> 50.0	
Elbow	-	16.41		1.69		5.47						
Left Ulnar (ADM)												
Wrist	-	5.23	< 4.2	4.42	> 3.0	6.56	B Elbow-Wrist	7.89	22.5	28.52	> 53.0	
B Elbow	-	13.13		4.16		7.19						
Sensory Nerves												
	NR	Peak (ms)	N. Peak (ms)	PT-Amp (μV)	N. Amp (μV)	-	Segment Name	Delta-P (ms)	Dist (cm)	Vel (m/s^2)	N. Vel (m/s^2)	
Right Median Anti (2nd digit)												
Wrist	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 39	
Right Ulnar Anti (5th digit)	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 50	
Left Median Anti (2nd digit)												
Wrist	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 39	
Left Ulnar Anti (5th digit)												
Wrist	NR	-	< 3.7	-	> 15.0	-	-	-	-	-	> 50	

Table 3: Nerve conduction studies in 2014: NR = No response; N.= Normal; Amp = Amplitude; Neg. = Negative; Dur. = Duration; O = Onset; P = Peak; Dist = distance; Vel= Velocity; APB = Abductor PolicisBrevis; ADM = Abductor DigitiMinimi; EDB = Extensor DigitorumBrevis; AHB = Abductor HallucisBrevis.

DISCUSSION

Chronic inflammatory demyelinating polyneuropathy is an acquired immune-mediated inflammatory disorder of the peripheral nervous system. CIDP is at times considered the chronic subset of acute inflammatory demyelinating polyneuropathy (AIDP), most common form of which is GuillainBarré syndrome (GBS). [4, 5, 6] CIDP is under-recognized and under-treated due to its heterogeneous presentation (both clinical and electrophysiological) and the limitations of clinical, serologic, and electrophysiologic diagnostic criteria. [15] While difficult to diagnose earlier in its course, timely treatment is important in preventing irreversible axonal loss and improving functional recovery. [7, 8, 9] The pathologic hallmark of the disease is loss of the myelin sheath of peripheral nerves. [3,6] As a result of immune action, affected nerves demyelinate and fail to respond or respond only weakly to stimuli causing numbness, tingling, pain, progressive muscle weakness and loss of deep tendon reflexes. Weakness in CIDP is both proximal and distal; a hallmark of acquired demyelinating polyneuropathy. Cranial nerve and bulbar involvement occurs in 10-20% of patients only. Sometimes, CIDP presents with back pain and rarely with symptoms of lumbar canal stenosis and caudaequina syndrome suggestive of nerve root hypertrophy and requires neurosurgical intervention. Autonomic involvement in CIDP is generally mild and limited. Impaired bowel and bladder control usually are not the presenting symptoms and rather appear late in severe cases. [4, 8, 9, 10] Most patients with CIDP exhibit a slowly progressive course, but a relapsing-remitting course, relapsing/ recurrent AIDP like episodes exist in at least one-third of patients. Such an observation is more common in younger patients. The accession of early treatment for CIDP has made the temporal progression of the disease more difficult to characterize and categorize, since remissions may be related to therapy rather than to the natural course of the disease. This is why it's almost always impossible for neurophysicians to differentiate between the two on first visit. [7, 8] The treatment of CIDP requires a systemic approach including the prevention of further demyelination and recovery of functional disability using exercise, occupational and physical therapy. In general, it includes an induction phase, long term management plan and supportive care. [9, 10] It is only in recent past that physicians have been able to appreciate association of the disease with lupus.The combination can present either way; diagnosed SLE followed or complicated by CIDP or vice versa. That is why it is extremely important for physicians to be aware of this association as general weakness due to multisystem involvement in SLE as a part of chronic ailment is often blamed to be the cause behind motor weakness whereas the real problem lies undiagnosed. This is said so because it is a potentially treatable disease that can greatly improve the quality of life for such patients and reduce morbidity associated with functional disability. [9, 10] As such cases can pose difficulty in diagnosis at times, whenever in doubt, physicians should have a low threshold of suspicion and timely refer such cases for specialist care.

CONCLUSIONS

Successful management of CIDP with lupus requires high degree of suspicion to correctly diagnose and thereafter manage such cases. This may at times require the expertise of a trained neurologist and therefore physicians should not hesitate to timely refer such cases for specialist care.

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