PERIPHERAL NERVE HYPER- EXCITABILITY

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ABSTRACT

We report a case of a 32 year old patient of peripheral nerve hyper excitability who presented with fasciculation in all four limbs, muscle aches and fatigue. Electromyography study showed spontaneous, continuous activity in the form of discharges with high frequency. His symptoms disappeared when plasma exchange was employed along with steroid administration.

Keywords: Fasciculations, Peripheral nerve hyper-excitability, Voltage gated potassium channels.

INTRODUCTION

Peripheral nerve hyper-excitability (PNH) is characterized by muscle twitching at rest that results from repetitive motor unit action potentials that have a peripheral origin. Its prevalence is <1/1000 000. The presenting features include muscle fasciculations, muscle aches, mucle wasting or hypertrophy. These may be accompanied by sensory manifestations such as paresthesias and numbness[1], autonomic dysfunction and central nervous system features like personality changes and insomnia. It can be categorized as a) acquired, b) paraneoplastic and c) hereditary[2]. Acquired form being the commonest is autoimmune mediated with antibodies directed against voltage gated potassium channels (VGKC). Its onset is between the age of 15-60 years and the male: female ratio is 2.0:1.0. Almost quarter of the cases are associated with paraneoplastic syndromes such as thymomas, small cell lung carcinomas and lymphomas. Other causes include drugs like lithium and oxaliplatin[3,4]. Prognosis is good in cases where autoimmunity is the cause and is determined by underlying cancer where PNH is linked with paraneoplastic syndrome.

CASE REPORT

A 32 year old man who was a sepoy in the Army presented with history of unusual, involuntary movements in all four limbs along with pain for last 1 month and was admitted to the medical ward. He was in a normal state of health when fasciculations began in both his lower limbs and progressively involved the upper limbs and finally his back. This was accompanied with generalized weakness, fatigue and crampy pain. There was prominent muscle twitching of the four limbs which was present even at rest. The facial, bulbar, respiratory and the tongue muscles were not involved. Occasionally, he felt burning dysaesthesia in both his feet without any complaint of numbness. No fever or skin rash was reported by the patient. He had no difficulty in falling asleep. There was no change in his sleep cycle or duration of sleep. Cough, hemoptysis and dyspnea were not reported. He had no previous history of neurological, neuromuscular disorder and arthritis. He was not taking any prior medications. He reported hyperhidriosis but there was no accompanying feeling of restlessness or palpitations. Central nervous system features such as confusion, delusions, hallucinations and vertigo were not present.

On physical examination pulse was 78 beats/minute, blood pressure was 110/70 mmHg, respiratory rate was 17 breaths/minute, temperature was 98°F.

On neurological examination, the higher mental functions and cranial nerves function were intact. Bulk and tone of muscles (apart from

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mild increase in stiffness of muscles) was normal on motor examination. Widespread involuntary movements such as fasciculations and twitches were present. Progressive increase in fasciculations lead to increased difficulty in performing voluntary tasks. There was slight reduction in power of muscles. Gait was normal. Sensations such as touch, pain, vibration and position sense were intact.

The cardiovascular, respiratory and gastro intestinal examination revealed no abnormality.

Nerve conduction studies were done using surface electrodes. Normal distal motor latency, compound muscle action potential and motor conduction velocity of common peroneal nerve, tibial nerve bilateral, median nerve, ulnar nerve right were done (figure).

Normal sensory latency, sensory nerve action potential, sensory nerve conduction velocity, sural nerve bilateral, median nerve, ulnar nerve right were conducted (table).

Electromyography (EMG) was done using concentric needle electrodes. Repeated discharges with doublets and triplets were observed without fibrillations, positive sharp waves (PSWs) and myotonia along with normal recruitment pattern gastrosoleus, anterior tibialis, abductor pollicis brevis, first dorsal interossei, brachioradialis bilateral.

The nerve fiber studies were suggestive of "continuous muscle fiber activity syndrome."

Table: Motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) data of the patient.

MNCV Data		**Lat**	**SD**	**Amp**	**SD**	**CV**	**SD**
R Median							
Pos 1	Rec pos	3.3		6.3			
Pos 2	Pos 1	7.9		5.6		52.2	
R Peroneal							
Pos 1	Rec pos	4.1		1.9			
Pos 2	Pos 1	10.7		2.0		48.5	
L Peroneal							
Pos 1	Rec pos	4.1		1.8			
Pos 2	Pos 1	10.8		2.0		47.8	
R Tabial							
Pos 1	Rec pos	4.7		7.1			
Pos 2	Pos 1	12.3		1.1		44.7	
L Tabial							
Pos 1	Rec pos	4.4		7.5			
Pos 2	Pos 1	12.5		0.9		42.0	

MNCV Data		**Lat**	**SD**	**Amp**	**SD**	**CV**	**SD**	**Amp%**	**SD**	**F-M:**	**SD**
R Ulnar											
Pos 1	Rec										
Pos 2	pos	3.0		7.0		57.1		-7			
	Pos 1	7.2		6.5							
SNCV Data		**/Lat**	**SD**	**Amp**	**SD**	**CV**	**SD**	**Amp%**	**SD**	**ˆLat**	**SD**
R Median											
Stim 1	Rec 1	2.2		33.8		59.1				3.3	
R Sural											
Stim 1	Rec 1	2.2		18.3		63.6				3.3	
R Sural											
Stim 1	Rec 1	2.7		20.3		51.9				3.5	
R Ulnar											
Stim 1	Rec 1	2.1		32.7		52.4				2.9	

Test for antibodies against voltage gated potassium ion channels (VGKC) was not performed due to its non availability.

Complete blood picture was within the reference range. The anti nuclear antibody (ANA) test, HBsAg and Anti HCV antibody test were negative. The routine blood analysis such as the liver function tests, thyroid profile, renal function tests, electrolyte levels muscle, serum CPK and blood glucose levels were within normal reference range.

The cerebrospinal fluid (CSF) routine examination revealed no abnormality. The radiological studies such as the Magnetic Resonance Imaging (MRI) of brain, plain Computed Tomography (CT) scan chest and ultrasound (USG) of abdomen and pelvis showed normal study ruling out any paraneoplastic syndrome.

In our case, we started with analgesics and sodium valproate. The patient was relieved of pain and discomfort but fasciculations continued.

Next steroids were started as they suppress the immune system of the body. Intravenous methyl prednisolone was administered for 5 days followed by prednisolone tablets.

A marked reduction in symptoms was observed when plasmapheresis (plasma exchange) was employed. After five sessions of plasmapheresis which were performed with an interval of two days each, the patient was completely free of symptoms.

DISCUSSION

PNH is characterized by generalized hyper excitability of motor nerves resulting in spontaneous and continuous muscle fibre activity[5]. PNH is not just a single disorder but is a response to peripheral nerve dysfunction as a result of various causes. Benign fasciculation syndrome is the mildest form and involves twitching of a muscle or its part. It usually lasts for days. Cramp fasciculation syndrome mani-fests as cramps, fasciculation and muscle stiff-ness. Myokymia refers to muscle activity which appears rippling in nature. It can be localized or diffused. Morvan's syndrome is an autoimmune process which manifests as a triad of peripheral nerve hyperexcitability, autonomic system features (sweating, lacrimation, constipation) and central nervous system features (insomnia, disorientation). Isaac syndrome involves continuously contracting or twitching muscles.

A case has been reported where a 55 year old man presented with widespread cramps and

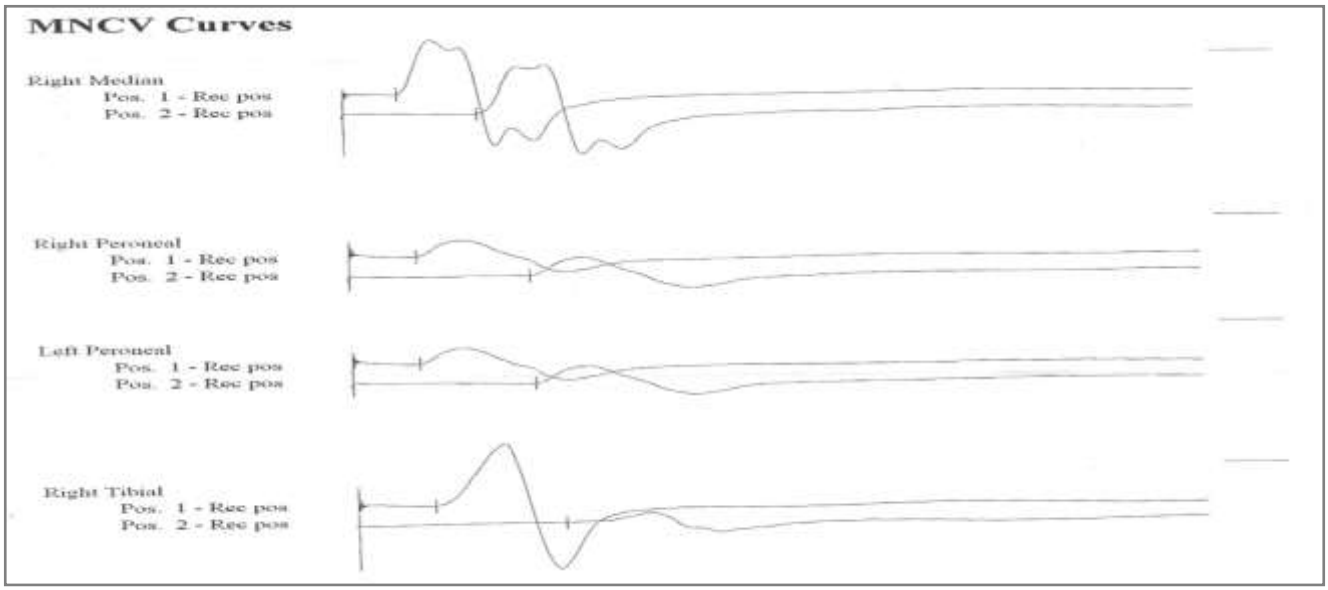

Figure: Motor nerve conduction velocity curves of the patient.

fasciculations during a six year period due to development of limited form of anterior horn cell degeneration[6]. Interestingly, a PNH associated KCNQ2 mutation has been described in a family with both PNH and neonatal seizures. This mutation can result in Idiopathic PNH[7].

Another case report has shown the effectiveness of Rituximab in treating a patient of Morvans syndrome and coexistent chronic inflammatory demyelinating polyradiculopathy (CIDP)[8]. This case showed that Rituximab can be used in cases of autoimmune neurological diseases refractory to other immunosuppressant therapy such as steroids and plasmapheresis.

Furthermore, phenotypic heterogeneity has been reported in voltage gated potassium channel (VGKC) associated disorder. In one such case, transient neurological disturbance was found in temporal and spatial distributions thus increasing the likelihood that such cases would be dismissed as functional disorders at first presentation[9].

In our patient, the cause of PNH was an autoimmune disease as he responded favorably to steroids and plasmapheresis. Intravenous immunoglobulins (IVIG) were not used because in autoimmune diseases it needs to be given in high doses (generally 1-2 g IVIG per kg body weight) over a five to six month period with a five day course in a month therefore making it cost ineffective.

A classification has been proposed that distinguishes immune mediated PNH (irrespective of whether VGKC antibodies are detected by standard assays) from non immune forms of PNH that includes toxins, anterior horn cell degeneration in motor neuron disease and genetic disorders[10]. We believe that this classification is relevant for disease etiology and management for all practical purposes.

CONCLUSION

Given the clinical symptoms of involuntary muscle activity in the form of fasciculations, muscle aches, cramps and muscle discomfort along with the findings of repeated discharges with doublets and triplets on electromyography and complete resolution of symptoms by steroids and plasmapheresis we believe our patient was a case of peripheral nerve hyperexcitability and in particular Isaac syndrome.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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