Reversible electrophysiological abnormalities in acute secondary hyperkalemic paralysis

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Abstract

Hyperkalemia manifests clinically with acute neuromuscular paralysis, which can simulate Guillain Barré syndrome (GBS) and other causes of acute flaccid paralysis. Primary hyperkalemic paralysis occurs from genetic defects in the sodium channel, and secondary hyperkalemic paralysis (SHP) from diverse causes including renal dysfunction, potassium retaining drugs, Addison's disease, etc. Clinical characteristics of SHP have been addressed in a number of publications. However, electrophysiological evaluations of these patients during neuromuscular paralysis are infrequently reported and have demonstrated features of demyelination. The clinical features and electrophysiological abnormalities in secondary hyperkalemia mimic GBS, and pose diagnostic challenges. We report the findings of nerve conduction studies in a middle-aged man who was admitted with rapidly reversible acute quadriplegia resulting from secondary hyperkalemic paralysis.

Key Words

Conduction block, hyperkalemia, nerve conduction studies, secondary hyperkalemic paralysis

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Introduction

Hyperkalemia is an uncommon cause of reversible acute flaccid paralysis. Primary hyperkalemic periodic paralysis (PHPP) is an inherited sodium channel disorder. Potentially lethal secondary hyperkalemic paralysis (SHP) and cardiac arrhythmias result from renal failure, Addison's disease, potassium sparing diuretics, potassium supplements and dietary excess.[1-10] While SHP was earlier considered to be of myogenic origin, there is accruing evidence that altered nerve excitability contributes significantly to the weakness.[7,8,11,12] SHP mimics clinical presentation of Guillain Barré syndrome (GBS) with rapidly evolving motor-dominant symmetrical quadriparesis.[5,6,8] Earlier publications reporting nerve conductions in SHP revealed features of demyelination.[3,5,6,8] We report the case history and electrodiagnostic studies in a middle-aged diabetic man who presented with acute secondary hyperkalemic paralysis.

Access this article online	
Quick Response Code:	**Website:** www.annalsofian.org
	DOI: 10.4103/0972-2327.104354

Case Report

A 57-year-old man presented in April 2011 with rapidly evolving quadriparesis of 4 hours that started proximally in both lower limbs progressing to quadriparesis making him bedbound. He had well-controlled diabetes for 15 years. Mild renal impairment was noted 3 months ago. Two months before admission, he developed progressive distal paresthesiae in the feet and hands.

Examination revealed a middle-aged man with normal pulse, blood pressure and respiration without edema or thickened nerves. Chest, abdomen and cardiac examination were normal. He was awake, alert and oriented with normal language functions. He had generalized hypotonia with atrophy of intrinsic muscles of hands and feet. He had quadriparesis with distal more than proximal weakness [Table 1]. There was graded distally dominant symmetrical sensory impairment involving touch, pain and vibration up to the knees and wrist. Muscle stretch reflexes were absent.

Motor nerve conduction studies (NCS) revealed increased latencies, segmental reduction of conduction velocities and partial conduction blocks [Table 2, Figure 1a] with absent sensory nerve action potentials (SNAP) in bilateral sural, right median and ulnar nerves. F-waves were delayed in the right median nerve [Figure 2a] and absent in the other nerves. He was diagnosed to have acute demyelinating polyneuropathy. Distal

symmetric amyotrophy and sensory loss were considered to be due to probable diabetic neuropathy.

Serum biochemistry revealed hyperglycemia (222 mg/dL) with elevated glycated hemoglobin (10.6%) and severe azotemia (urea 249 mg/dL, creatinine 13.2 mg/dL) with marked hyperkalemia (9.9 mEq/L). Serum creatinine kinase, calcium and magnesium were normal. Electrocardiogram revealed sinus rhythm with broad QRS complexes and tall T waves [Figure 3]. He had dimorphic anemia (hemoglobin 8.2 gm/dL) with bone marrow revealing early megaloblastic changes. Urgent hemodialysis was started in view of severe hyperkalemia and azotemia. There was rapid reversal of quadriparesis during dialysis, except for partial improvement in hand and foot muscles with reduction of serum potassium to 4.5 mEq/L. Sensory deficits remained unchanged. Cerebrospinal fluid revealed 5 lymphocytes/mm³ and 56 mg/dL protein.

Nerve conductions repeated on the third day revealed significant improvements [Table 2; Figures 1b and 2b]. Small amplitude sural SNAP could be recorded (right 0.6 µV and left 0.8 µv) with reduced conduction velocity of 28.5 m/s (right) and 27.6 m/s (left), whereas SNAPs continued to be absent in the median and ulnar nerves. Concentric needle electromyography (CNEMG) revealed fibrillations and positive sharp waves in the hand and leg muscles with increased duration and amplitude of motor unit potentials.

He has been on maintenance hemodialysis since then and has had no further episodes of hyperkalemia or worsening of weakness. Oral anticoagulation was started for deep venous thrombosis which precluded the planned nerve biopsy to elucidate the nerve pathology.

Discussion

Hyperkalemia is often clinically silent, being detected by laboratory investigations, and is an uncommon cause for acute flaccid paralysis. Hyperkalemic paralysis is divided into primary and secondary forms. PHPP has an autosomal-dominant inheritance pattern, and occurs due to mutations in the sodium channel gene in chromosome 17. Episodes of PHPP usually begin in the first decade of life, often precipitated by fasting or rest after exercise, unlike in hypokalemic periodic paralysis. Affected individuals have multiple brief episodes of paralysis due to episodes of hyperkalemia.[13,14]

SHP occurs in acute and chronic renal dysfunction, Addison's disease, rhabdomyolysis, excessive ingestion of potassium and drugs (angiotensin converting enzyme inhibitors, potassium sparing diuretics, non-steroidal anti-inflammatory drugs, cotrimoxazole, etc.).[1-10] SHP usually occurs with severe hyperkalemia, often with cardiac conduction and rhythm abnormalities. A recent review identified 73 patients of SHP with male predominance (55:18) and age ranging from 15 to 82 years. While the clinical presentation was dominated by muscle weakness, 26% had sensory symptoms and 11% had

Table 1: Muscle power by MRC grading at admission and after dialysis (*except hand muscles wherein degree of weakness is mentioned)

	At admission	After dialysis
Neck	4	5
Shoulder	4	5
Elbow	4	5
Wrist	4	4+
Fingers	3	4+
Hand muscles*	Moderate	Mild
Hip	3	5
Knee	1	5
Ankle (DF)	1	4
Ankle (PF)	3	4
Toes	1	3

DF = Dorsiflexion, PF = Plantar flexion
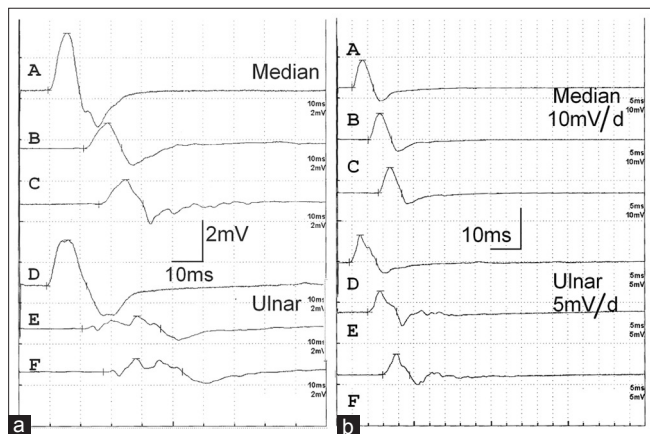
Figure 1: Motor nerve conduction studies in right median and ulnar nerves stimulated at wrist (A, D), elbow (B, E) and arm (C, F). At admission, distal latencies are prolonged with reduction of CMAP amplitude and duration on proximal stimulation (1a) which improved after dialysis (1b)
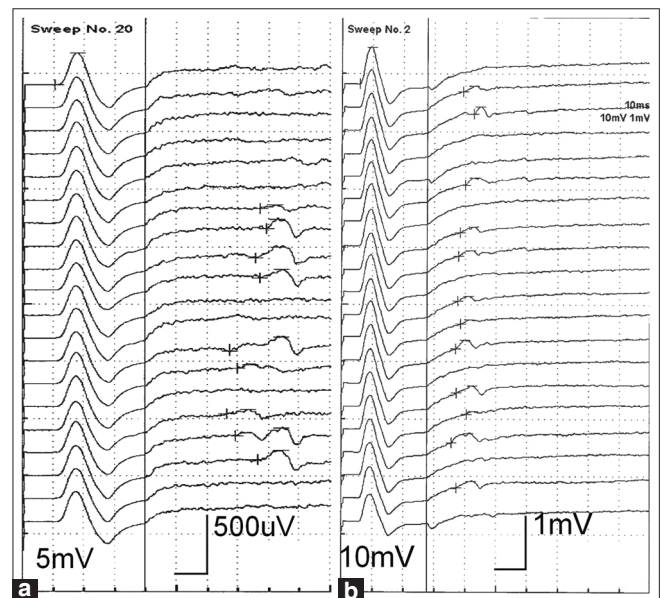
Figure 2: The F-wave studies in right median nerve at admission (a) and on day 3 after clinical improvement (b) revealing increased latencies of M and F response in the first study which improved after correction of hyperkalemia. Timescale 10ms/d.

sensory deficits at presentation. Eight patients succumbed to the consequences of hyperkalemia during admission and an additional eight died later due to other causes. Renal impairment was the most common cause, followed by Addison's disease and medications.[10]

Our patient had acute flaccid paralysis due to hyperkalemia occurring from end-stage renal disease resulting from long-
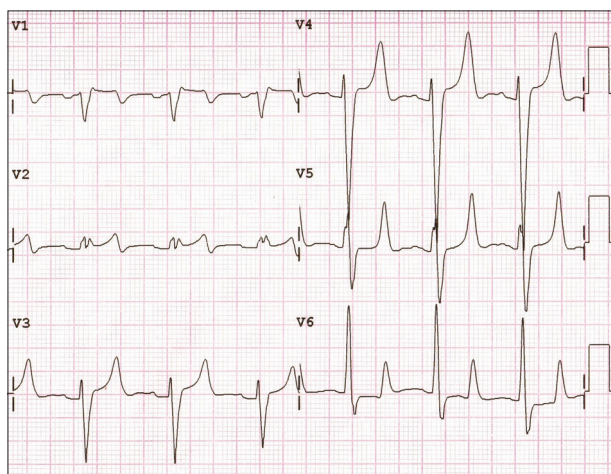
Figure 3: The electrocardiogram at admission revealing broad QRS complexes with tall peaked T waves

standing diabetes mellitus. Neurological recovery following dialysis was good but for residual distal sensory loss and distal weakness, which had probably resulted from diabetes mellitus and chronic renal disease. Muscle weakness in SHP usually occurs with high serum potassium levels. Half the patients had serum potassium above 9 mEq/L and three-fourth had serum potassium exceeding 8 mEq/L.[10] A possibility of acute demyelinating neuropathy/GBS was considered based on clinical and electrophysiological abnormalities in them initially.[3,5,6,8] However, presence of severe hyperkalemia and electrocardiographic changes provided clues to the etiology of the acute flaccid paralysis. In addition, the weakness improved rapidly with correction of hyperkalemia by hemodialysis.

Clinical Neurophysiological Investigations in SHP
Clinical neurophysiological data have been infrequently documented in SHP. Among the seven publications on electrophysiological evaluations in SHP, two patients had NCS, two had electromyography (EMG) and three had both EMG and NCS. EMG in a young fisherman with acute renal failure and hyperkalemia resulting from sea snake bite revealed small amplitude motor unit potentials (MUPs) with increase in polyphasic potentials.[1] A middle aged man with secondary Addison's disease was admitted with recurrent episodes of hyperkalemic quadriparesis and stiff muscles. Quadriparesis improved with hyperkalemia correction. Peroneal NCS after recovery revealed mild reduction of the conduction velocity with increased distal motor latency (DML). EMG was abnormal,

Table 2: Motor nerve conduction data at admission (Day 1) and after clinical improvement (Day 3). Latencies are in milliseconds, amplitudes in millivolts and velocities in meters per second

Nerve	Parameter	Site/segment	Normative data	Day 1	Day 3
Rt. median	Latency	Wrist	<4.2	9.60	4.95
	Amplitude	Wrist	>4.0	2.80	6.70
		Elbow		1.24	6.30
		Mid arm		1.20	6.30
	Velocity	Elbow–wrist	>48.0	18.70	38.50
		Mid arm–elbow		21.60	42.40
	F wave	Wrist	<31.0	66.40	35.70
Rt. ulnar	Latency	Wrist	<3.4	9.10	4.10
	Amplitude	Wrist	>3.8	2.26	3.40
		Below elbow		0.61	2.60
		Mid arm		0.62	2.50
	Velocity	Below elbow–wrist	>49.0	20.40	36.40
		Mid arm–belowelbow		16.70	29.00
Rt. common peroneal	Amplitude	Ankle	>2.0	0.00	0.00
Lt. common peroneal	Latency	Ankle	<5.5	10.50	7.40
	Amplitude	Ankle	>2.0	0.04	0.10
		Fibular neck		0.03	0.06
	Velocity	Fibular neck–ankle	>40.0	12.20	17.20
Rt. posterior tibial	Latency	Ankle	<5.8	10.90	4.50
	Amplitude	Ankle	>4.0	0.16	1.29
		Popliteal fossa		0.09	1.05
	Velocity	Popliteal fossa–ankle	>40.0	14.90	29.40
Lt. posterior tibial	Latency	Ankle	<5.8	12.60	4.85
	Amplitude	Ankle	>4.0	0.55	2.37
		Popliteal fossa		0.09	1.81
	Velocity	Popliteal fossa–ankle	>40.0	12.90	32.80

ND = Normative data, Lt = Left, Rt = Right

revealing runs of high-frequency biphasic and positive waves along with normal looking MUPs. Neuromuscular symptoms abated with diphenylhydantoin and oral corticosteroids.[2]

A young man with ruptured urinary bladder following drunken brawl was admitted with severe quadriplegia, hyperkalemia and azotemia. Median nerve was unexcitable at admission, while slow conduction velocity with increased DML was noted 3 hours after admission, when he partially recovered with pharmacotherapy and hemodialysis. Three days later, nerve conductions were normal when he had completely recovered. Azotemia and hyperkalemia were considered to arise from "*autodialysis feedback*" due to reabsorption of urinary constituents and excreted potassium from large quantity of beer that had leaked into the peritoneal cavity.[3]

A young lady with chronic renal failure admitted with SHP had reduced amplitudes of compound muscle action potential (CMAP) and conduction velocity with absent sural potential, which recovered after hyperkalemia correction. In addition, partial conduction block was demonstrated in the median nerve. Needle EMG did not reveal abnormal spontaneous activity or smaller MUPs.[5] A 62-year-old man with SHP was initially considered to have GBS when he developed acute quadriparesis preceded by viral infection. Nerve conductions revealed features consistent with GBS and the EMG did not reveal abnormality. Hemodialysis initiated for hyperkalemia (8.8 mEq/L) corrected the quadriparesis and nerve conduction abnormalities.[6] Similar reversible motor nerve conduction abnormalities with slow conduction velocities and conduction blocks were reported in a young woman who developed SHP while taking NSAIDs.[8]

Our patient had marked prolongation of DML with slowed conduction velocities in the upper limb, which recovered significantly following hemodialysis. Lower limb motor nerve conduction abnormalities reversed partially. Clinically, he had subacute-onset neuropathy, which could be from diabetes and chronic renal disease. Nutritional deficiency could have contributed as he had dimorphic anemia with early megaloblastic changes in bone marrow. EMG findings of neurogenic pattern with denervation and partial reinnervation along with residual nerve conduction abnormalities favor additional longstanding neuropathy. As the nerve conductions revealed "demyelinating neuropathy" features at admission, electromyography had not been performed and could have added additional information.

The pathogenic process causing neuromuscular paralysis in SHP has been variably localised to muscle, neuromuscular junction and nerve. If the pathogenic process were to be primarily in the muscle, it can explain the reduced amplitudes of the CMAP but not the reduced velocities and impairment of sensory conductions that have been documented in SHP. Primary neuromuscular junction abnormality would be negated on the same grounds. Impairment of neural excitability produced by hyperkalemia can explain slowed conductions and amplitude changes.

Hyperkalemia reduces the transmembrane gradient between the intracellular and the extracellular compartments producing partial neuronal depolarization proportional to degree of hyperkalemia. Potassium equilibration potential is shifted by about 12 mV when the serum potassium increases to 7 mM, making the nerve and muscle depolarized.[11] This inactivates the voltage-gated sodium channels and makes the axons refractory to excitation, which explains the amplitude reductions in motor and sensory NCS.[8,9] This could impair the propagation of action potential, reducing the conduction velocities with prolongation of distal motor and F-wave latencies. Conduction failure across a segment can result in partial conduction block as well. However, exact pathogenesis of the slowed conduction velocities and conduction blocks needs further investigations in basic electrophysiology.

Potassium has been implicated in contributing to the pathogenesis of neuropathy of chronic renal disease.[11,12,15] Presence of sustained hyperkalemia is considered to exert its effect on the nerves by impairing the generation of action potentials and the impulse conduction. NCS studies before, during and after dialysis in patients with chronic renal disease revealed increased refractoriness and reduced nerve excitability correlating with degree of hyperkalemia and not with other markers of renal dysfunction, including elevated urea and creatinine. Interference with functioning of Na/K pump by hyperkalemia was considered to contribute to these changes in addition to its effects on voltage-gated sodium channel.[12,15]

The rapid improvement of the neuromuscular paralysis in patients with SHP and resolution of the nerve conduction abnormalities with correction of hyperkalemia augurs the hypothesis of hyperkalemia-induced conduction failure causing reversible weakness and electrophysiological abnormalities.

Conclusion

Hyperkalemic paralysis is an important and rapidly reversible cause of acute flaccid paralysis. It is characterized by slowing of nerve conduction velocities, reduction in amplitudes and conduction blocks, which can easily be confused with GBS.

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