SHORT REPORT

Secondary hyperkalaemic paralysis

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Abstract

Besides the hereditary hyperkalaemic paralysis, a secondary form exists which often mimicks Guillain-Barre syndrome. A 62 year old patient is reported on who developed severe hyperkalaemic paralysis on the basis of mild renal failure and additive spironolactone intake. Neurophysiological examinations disclosed normal muscle fibre activity but delayed nerve conduction velocities indicating that the mechanism underlying secondary hyperkalaemic paralysis is different from channelopathies. Haemodialysis led to complete recovery. Review of the medical literature showed that spironolactone intake is the most common cause of secondary hyperkalaemic paralysis. Typical symptoms are flaccid tetraplegia sparing the cranial nerves with only mild or lacking sensory impairment. Symptoms promptly resolve after haemodialysis or after glucose and insulin infusion. Only three out of 18 patients reviewed died, because of cardiopulmonary complications. Thus the prognosis of secondary hyperkalaemic paralysis is good.

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Hereditary episodic hyperkalaemic paralysis is a well known disease based on a dysfunction of sodium channels which has recently been attributed to a mutation on chromosome 17q23–25.[1] Besides the hereditary form, a secondary form of hyperkalaemic paralysis exists. Only few reports on secondary hyperkalaemic paralysis have been published so far,[2–16] most of them lacking neurophysiological findings. The basic mechanism underlying secondary hyperkalaemic paralysis is still unknown. Some authors discuss a direct influence of potassium on the muscle cell membrane or muscle fibre,[9 17] only one report suggests a functional disturbance of the peripheral nerves.[2]

Hyperkalaemia leading to paralysis can be induced by iatrogenic circumstances,[8 13] trauma[2 9], or misuse of diuretic drugs.[3 7 8 10] Therefore, secondary hyperkalaemic paralysis must often be considered in the differential diagnosis of flaccid palsies. In this paper, a systematic review of all reports on secondary hyperkalaemic paralysis published so far is provided in conjunction with a case report on secondary hyperkalaemic paralysis due to chronic renal failure and spironolactone intake.

Case report

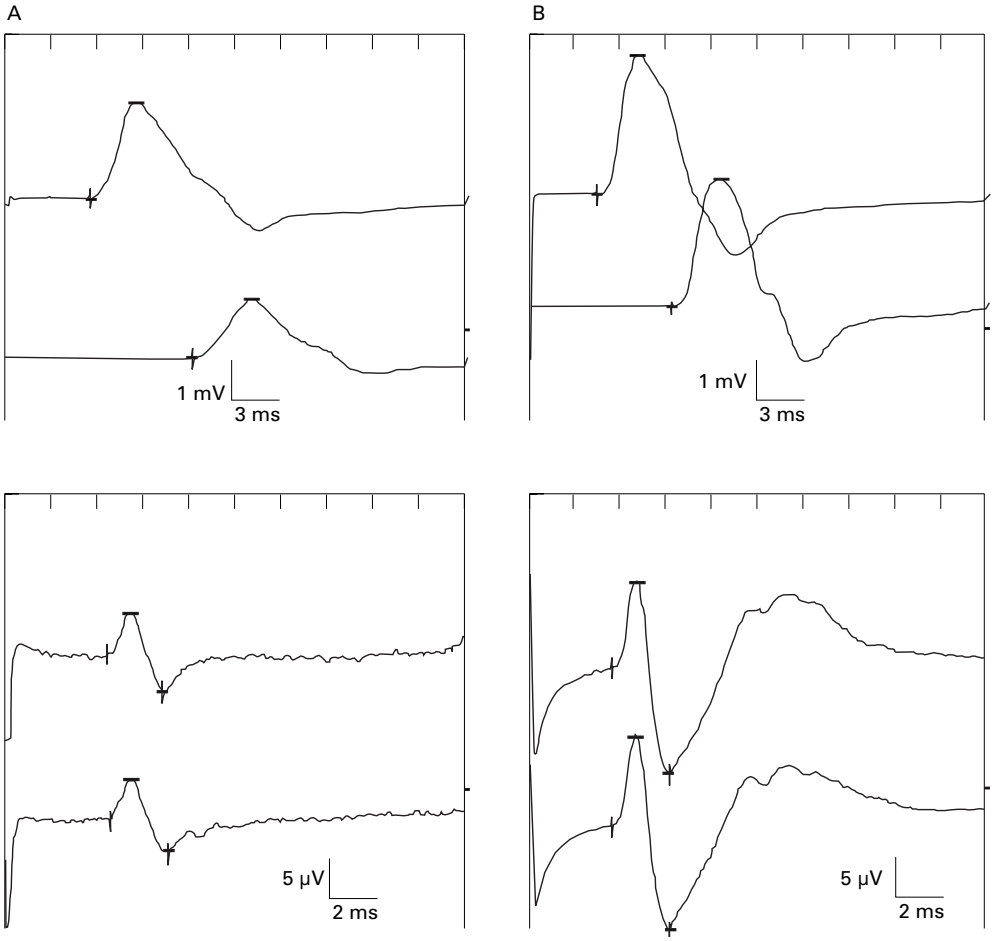
A 62 year old man was admitted to our hospital by his general practitioner because of progressive paralysis of all limbs over a period of one week. Magnetic resonance imaging of the spine and head performed two days before admission disclosed no abnormalities. As the patient had had a viral infection two weeks before, the initial diagnosis on admission was Guillain-Barré syndrome. The neurological examination showed typical symptoms of Guillain-Barré syndrome: areflexia of the Achilles tendon reflex, symmetric hyporeflexia of the other tendon reflexes, and distal dysaesthesia of all limbs. Motor paralysis was present in all limb muscles with a nearly complete symmetric paraplegia in the proximal muscles. Examination of the cranial nerves showed no abnormalities. No ventilatory problems occurred.

Neurophysiological examination showed prolonged sensory and motor nerve conduction velocities (NCVs), prolonged F wave latencies, and decreased amplitudes. Table 1 gives a synopsis of the values before and after haemodialysis. The figure summarises abnormal motor and sensory findings of the median nerve and in the M abductor pollicis brevis. The EMG of several distal and proximal muscles showed no pathological spontaneous activity and no myopathic or myotonic discharges. The mean duration of muscle potentials on voluntary activation was

Table 1 Neurophysiological examinations before and after haemodialysis and laboratory reference values

	Before haemodialysis (potassium 8.8 mmol/l)	*24 hours after haemodialysis (potassium 4.8 mmol/l)*	*Normal value*
Sural nerve:			
NCV (m/s)	Not done	53.8	>43.2
Amplitude(μV)	Not done	3.0	>2.4
Peroneal nerve (M extensor digitorum brevis):			
NCV(m/s)	22.9	43.2	>41.2
Distal latency (ms)	8.6	5.1	<4.9
Amplitude (mV)	2.0	3.2	>2.4
F wave latency (ms)	87.8	54.9	<56.1
Median nerve (M abductor pollicis brevis):			
NCV (sensory) (m/s)	33.3	43.2	>46.9
NCV (motor) (m/s)	28.3	43.7	>50.0
Distal latency (ms)	5.8	4.4	<4.5
Amplitude (sensory) (μV)	20.0	24.0	>6.9
Amplitude (motor) (mV)	2.4	6.9	>5.0
F wave latency (ms)	33.3	32.2	<31.2

NCV=nerve conduction velocity.



Motor potential of the M abductor policis brevis (upper panels) and sensory potentials (antidromic) of the median nerve (lower panels) (A) before and (B) after haemodialysis; motor stimulation of the median nerve at the wrist (first line) and at the elbow (second line); sensory stimulation of the median nerve at the wrist (second line: reproduction).

<10 ms, the amplitude ranged from 0.5 mV to 1.0 mV.

Analysis of CSF showed no typical results for Guillain-Barré syndrome: 426 mg/l protein; 1/μl leucocytes; normal IgG, IgM, and glucose ratios; absence of oligoclonal antibodies; and lack of intrathecal IgG production. The ECG showed sinus rhythm, a mild intermittent increase in T wave amplitude, and a prolonged QRS complex. Laboratory analysis on admission showed a severe hyperkalaemia of 8.8 mmol/l (control after 30 minutes 8.6 mmol/l), and a mildly increased creatinine concentration (0.17 mmol/l). Other routine laboratory tests, including urea and uric acid, were normal.

Because of the severe life threatening hyperkalaemia, the patient was immediately given haemodialysis. Recovery from motor paresis started already during this procedure, within one hour. After three hours of haemodialysis, the potassium serum concentration was decreased to 5.1 mmol/l and remained constant during the following weeks with concentrations ranging between 4.7 and 5.6 mmol/l. Neurological examination five hours after haemodialysis showed no abnormalities except hyporeflexia of the Achilles tendon reflex. Examination one day after haemodialysis showed almost normal values in all nerve conduction studies (table 1, figure).

The patient had a one year history of mild chronic renal failure with mild arterial hypertension, treated with 10 mg enalapril/day since diagnosis. Serum concentrations of uric acid were normal, concentrations of creatinine were mildly increased (about 0.15 mmol/l). The definite aetiology of the renal failure could not be evaluated despite extensive investigations including renal biopsy. Before admission, however, the patient had been taking a daily dose of 200 mg spironolactone for two months.

Review of the medical literature

Based on all available medical reference systems, we reviewed the reports published on secondary hyperkalaemic paralysis without any relevant family history of paralysis. Only 17 patients could be identified. Table 2 shows a synopsis of all important data and features of these patients including our patient.

The age of all 18 patients analysed (12 men, six women) ranged between 21 and 76 years. Fifteen patients presented with tetraparesis or tetraplegia. In three patients, there was paraparesis of the legs. The paralysis usually started distally with an ascending course. Sensory symptoms were reported in five patients. The serum potassium concentration leading to hyperkalaemic paralysis ranged from 7.0 to

Table 2 Patients with secondary hyperkalaemic paralysis (synopsis of the literature)

Report	*Age/ sex*	*Clinical symtoms*	*Potassium (mmol/l)*	*Creatinine (mmol/l)*	*CSF*	*Possible reason for hyperkalaemia*	*ECG findings*	*Neurographic and EMG findings*	*Treatment*	*Outcome*
This case	62/M	Tetraplegia and distal areflexia within one week; distal dysaesthesia; cranial nerves normal	8.2	0.17	Normal	Mild renal failure; spironolactone intake	QRS prolonged T raised	Decreased NCV and amplitudes; F waves increased; EMG normal	Haemodialysis; Ca infusion	Completely resolved
Naumann et al[4]	36/F	Symmetric tetraparesis, dysaesthesia and areflexia; cranial nerves normal	8.4	1.47	Normal	Nephrosclerosis; chronic renal failure	QRS prolonged; T sharp	Decreased NCV; EMG normal	Haemodialysis	Completely resolved
Khullar et al[6]	50/M	Ascending tetraparesis; anaesthesia in feet	7.0	1.01	Nd	Diabetes; anuria	Nd	Nd	Haemodialysis	Completely resolved
Freeman and Fale[5]	75/M	Distal tetraplegia, no areflexia; cranial nerves normal	10.2	0.21	Normal	Diabetes; amiloride intake	QRS prolonged	Nd	Insulin and glucose infusion	Completely resolved
Tamm[3]	a: 66/M	Tetraparesis, tremor	11.2	2.06	Nd	Renal failure; spironolactone intake	QRS prolonged; P absent	Nd	Haemodialysis; Ca infusion	Completely resolved
	b: 65/M	Ascending paraparesis	9.3	1.20	Nd	Chronic renal failure; excessive cherry intake	QRS prolonged; P absent	Nd	Haemodialysis; Ca infusion	Completely resolved
	c: 73/F	Tetraplegia	8.6	Nd	Nd	Spironolactone intake; no renal failure	Normal	Nd	Insulin and glucose infusion; diuresis	Completely resolved
Rado[10]	76/F	Pure motor tetraplegia within one month; cranial nerves normal	8.8	Nd	Nd	Spironolactone intake; chronic renal failure	QRS prolonged; P absent; T raised	Nd	Ca and insulin infusion; resonium	Completely resolved
Shinotoh et al[2]	38/M	Tetraplegia and areflexia within one week; distal paraesthesia; cranial nerves normal	8.7	1.26	Nd	Traumatic rupture of urinary bladder	QRS prolonged	Decreased motor CNV; increased distal latency	Haemodialysis; insulin infusion	Completely resolved
Palmer and Wikström[7]	68/M	Pure motor tetraparesis	7.9	0.10	Nd	Spironolactone intake; normal renal function	T raised	Nd	Insulin and glucose infusion	Completely resolved
Jaffey and Martin[11]	69/F	Tetraparesis with hyporeflexia and paraesthesia	9.3	Nd	Nd	Spironolactone intake; mild renal failure	"Bizarre" QRS; P absent	Nd	Ca and insulin infusion	Completely resolved
Udezue and Harrold[8]	69/M	Progressive ascending pure motor paralysis and areflexia	9.3	Nd	Nd	Spironolactone (100 mg/day)	QRS prolonged; P absent	Nd	Insulin and glucose infusion; peritoneal dialysis	Died of pulmonary embolism; paralysis resolved
Livingstone and Cumming[9]	38/M	Ascending paraparesis and areflexia of the lower limbs; no sensory symptoms; cranial nerves normal	9.3	1.25	Nd	Traumatic urine excretion failure	"Typical signs of hyperkaliaemia"	Nd	Peritoneal dialysis	Completely resolved
Gelfand et al[14]	44/F	Tetraplegia; mental disorientation	9.8	Nd	Nd	Geophagia (clay); chronic renal failure	Arrhythmia	Nd	Nd	Completely resolved
Kalbian[13]	46/M	Paraparesis of the lower limbs	8.0	Nd	Nd	Spironolactone intake; potassium supplement	T raised	Nd	Insulin and glucose infusion	Completely resolved
Herman and Rado[12]	43/M	Tetraplegia and areflexia; pain in all limbs	9.5	0.40	Nd	Spironolactone intake; diabetic nephropathy	T raised	Nd	Insulin and glucose infusion	Died because of cardic arrest
Richardson and Sibley[16]	21/M	Tetraplegia and areflexia	9.9	Nd	Normal	Glomerulonephritis	T raised	Nd	Insulin and glucose infusion	Died because of "convulsions"
McNaughty and Burchell[15]	49/F	Tetraplegia	8.6	11.2	Nd	Renal failure; pyelonephritis	P absent; T raised	Nd	Glucose and Ca infusion	Completely resolved

m=Male, f=female, nd=no data available, NCV=nerve conduction velocity, EMG=electromyogram, Ca=Calcium.

11.2 mmol/l with a mean of 9.0 mmol/l. In one patient the serum creatinine concentration was normal; in the others it ranged from 0.17 to 11.2 mmol/l.

The most probable causes of the sudden hyperkalaemia were spironolactone or amiloride intake (10), trauma of the bladder (two), excessive cherry intake (one), and geophagia of clay (one). Chronic renal failure was the underlying mechanism of hyperkalaemia in 12 patients. In the three patients in whom neurophysiological examinations were performed, decreased NCVs and increased F wave latencies but normal EMG findings were found. Normal cell count and protein was obtained in all patients with CSF analysis (four).

The treatment concepts of acute hyperkalaemia included intravenous infusion of insulin and glucose (10), infusion of calcium (seven), haemodialysis (six), or peritoneal dialysis (two). All patients had complete resolution of symptoms within hours or days with the exception of three who died within three days, either of cardiac arrest or convulsions due to hyperkalaemia (two) or of pulmonary embolism (one).

Discussion

We describe a patient with secondary hyperkalaemic paralysis who promptly recovered after haemodialysis. The hyperkalaemia in this patient was most probably due to an additive effect of his mild chronic renal failure in conjunction with spironolactone medication. Spironolactone is known to induce hyperkalaemia[18] and has previously been reported as the cause of hyperkalaemic paralysis.[7 8 10]

Our patient was first misdiagnosed as having Guillain-Barré syndrome, a phenomenon already described previously.[3–5 8 9] The reason is that the clinical features of hyperkalaemic paralysis are very similar to those of Guillain-Barré syndrome in most patients. In our patient, even the neurophysiological findings (reduced NCVs, increased F wave latencies) would have confirmed Guillain-Barré syndrome. In four of the patients presented, CSF was analysed and was normal. As normal CSF does not exclude Guillain-Barré syndrome in the early stages, measurement of potassium concentrations can be the key to the diagnosis of progressive distal paralysis.

The neurophysiological examinations performed in our patient suggest a totally or mainly neurogenic mechanism in the aetiology of secondary hyperkalaemic paralysis. We found extremely decreased motor and sensory NCVs and very low amplitudes fulfilling demyelinating criteria. However, the reduced compound muscle potential amplitudes can also be explained by a concomittant loss of muscle fibre membrane activity. In episodic familial hyperkalaemic paralysis, abnormal depolarisation of the muscle membrane due to channelopathy is the cause underlying muscle weakness.[1] We could not confirm this finding in the secondary form. On the basis of our NCV studies, we assume that secondary hyperkalaemic paralysis is probably caused by an abnormal depolarisation of the nerve membrane occurring with excessive increase of serum potassium concentrations.

In most patients, chronic renal failure or diuretic intake, especially spironolactone, is the cause of secondary hyperkalaemic paralysis. The prognosis of secondary hyperkalaemic paralysis is usually good. Haemodialysis, peritoneal dialysis, or infusion therapy with insulin and glucose led to complete recovery in nearly all of the patients reported. Only two patients died, the cause malign arrhythmia due to untreatable hyperkalaemia. In patients with chronic renal failure and muscle weakness, serum potassium concentrations should be monitored carefully to identify threatening hyperkalaemia and to initiate early therapy.

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