Diagnostic Challenge

A Diagnostic Challenge: Acute Flaccid Paralysis

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Keywords: paralysis, hypokalemia, hyperthyroid

THE CASE

A 37-year-old Filipino male presented to a community emergency department (ED) with acute bilateral flaccid leg paralysis. He had no known medical conditions, took no medications and denied any allergies or substance use. There had been no history of trauma.

On review of systems, he reported several weeks of intermittent leg weakness. He reported that this had mainly affected his proximal leg muscles, noting difficulty when attempting to rise out of a chair. He also described intermittent palpitations, tremor of his fingers, and a 10 pound weight loss over several months. He denied any paresthesia, headache, vision change, bowel change, or bladder change.

On examination he looked well and had stable vital signs with a heart rate of 90 bpm. Cardiac and respiratory examinations were unremarkable. Lower legs demonstrated markedly diminished strength and diminished deep tendon reflexes bilaterally. Sensation to fine touch was intact. He had symmetric and normal upper limb strength, reflexes and sensation to fine touch. A fine tremor was noted in the fingertips. Cranial nerve examination was unremarkable. Head and neck exam demonstrated eyelid retraction and lid lag, as well as a goiter. See Table 1.

Table 1. Laboratory Investigations

Results		Reference Range
WBC	6.1	4.5-11 x 10^9/L
HGB	133	140-180 g/L
PLT	189	140-440 x 10^9/L
INR	0.9	0.9-1.1
APTT	33.5	26-38 seconds
ESR	8	0-15 mm/h
Na	144	135-147 mmol/L
Cl	107	97-106 mmol/L
K	2.5	3.5-5.1 mmol/L
CO2 Total	24	22-30 mmol/L
Cr	48	44-106 umol/L
Ca	2.35	2.10-2.60 mmol/L
Mg	0.70	0.63-0.94 mmol/L
Phos	1.23	0.81-1.45 mmol/L
CK	84	52-175 U/L
Myoglobin	44	<50 ug/L
TSH	< 0.015	0.4-4.2 mU/L
Free T4	97.3	9.7-25.7 pmol/L
Free T3	32.9	3.7-6.9 pmol/L
Urinalysis	unremarkable	

Question 1 – What is the diagnosis?

He was diagnosed with thyrotoxic periodic paralysis

Question 2 – What is the appropriate management acutely?

Under the guidance of the endocrinology service, he was treated with IV potassium supplementation (10 mEq/hr x 8 hours) with complete and rapid resolution of his muscle weakness. He was observed in the ED for 15 hours and then discharged home after regaining normal extremity strength, with a serum potassium of 4.1 mmol/L.

Question 3 – What is the appropriate management on discharge?

Our patient was started on anti-thyroid treatment with methimazole 10 mg po TID, as well as propranolol 20 mg po TID. At his one week follow-up he had experienced no further episodes of weakness, and he had gained 3 pounds. His thyroid function tests had improved (TSH <0.015 mU/L, Free T3 11.1 pmol/L,

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 CJEM 2017;19(1):55-57 DOI 10.1017/cem.2016.355

Free T4 37.1 pmol/L), and his serum potassium was 4.4 mmol/L. No changes were made to his medical management.

Thyrotoxic periodic paralysis

Periodic paralysis is a muscle disease that presents with recurrent episodes of flaccid paralysis. Graves' disease is the most common underlying etiology, however, any cause of hyperthyroidism can be associated with TPP, including exogenous levothyroxine administration.[1,2] TPP most commonly effects Asian and Polynesian populations, with the majority of cases occurring in young males.[1-4]

Presentation

TPP presents with sudden attacks of painless generalized weakness. Attacks most commonly last several hours, but can persist for days. Patients may have multiple attacks per week, or alternatively be symptom-free for months.[4-7] The weakness preferentially affects the girdle muscles of the lower extremities; one typically finds decreased muscle tone, hyporeflexia. Tachycardia can be a sentinel finding.[4,5] Rarely, severe arrhythmias and respiratory muscle weakness necessitating mechanical ventilation have been documented.[5] Potassium levels are variable during these attacks, with reported values as low as 1.1 mmol/L (mean ~2.1 mmol/L). Lower potassium levels are associated with increased severity of clinical weakness.[5,8,9]

Attacks most commonly occur after large carbohydrate meals, strenuous physical activity, or stress, however, there may be no apparent precipitant. Though cold exposure is reported as a potential trigger, attacks occur more frequently in the summer.[1,4,10,11]

Pathophysiology

Increased Na-K-ATPase activity seen with hyperthyroidism can drive potassium intracellularly. This is thought to hyperpolarize the muscle membrane, leaving the fibers inexcitable. Indirect adrenergic stimulation also increases Na-K-ATPase activity, the probable explanation for the benefit seen with beta blockers. Insulin and testosterone can also stimulate the ATP activity.[12-14] Finally, a loss of function mutation in the potassium channel Kir2.6 is also thought to have a role.[2]

Table 2. Differential Diagnosis of Acute Weakness

Hypokalemia: due to intracellular shifts	Thyrotoxic periodic paralysis
	Familial periodic paralysis
	Drugs (beta-agonists, insulin, theophylline)
	Barium toxicity
Hypokalemia: due to potassium deficit	Gastrointestinal losses
	Renal losses
	Diuretic use
Other causes	Acute myelopathies
	Guillain-Barre syndrome
	Myasthenia gravis
	Myositis
	Tick paralysis
	Lyme disease
	Organophosphate poisoning
	Botulism

Management

A differential diagnosis is listed in Table 2.[1,2,5,15] Recommended acute medical treatment includes potassium supplementation.[1,2,5] This has been shown to result in more rapid improvement in muscle strength, particularly when given intravenously.[5,8,16] The minimal required dose of potassium replacement is unknown, but most sources report administering 10–20 mEq per hour, with total replacement in the acute phase ranging from 40–200 mEq. Cardiac monitoring is important during treatment, as rebound hyperkalemia occurs in over 40% of cases and can potentially be fatal.[2,5,17] A nonselective beta blocker like propranolol can reverse muscle weakness. Propranolol can be used in patients who are unresponsive to treatment with potassium, though rebound hyperkalemia can still occur with this treatment strategy. Propranolol 3 mg/kg orally or 1 mg IV repeated Q10 minutes (maximum 3 mg) has been reported to be effective.[15,18-20]

While potassium replacement is important in the acute phase, management of patients' hyperthyroidism is also necessary to prevent further attacks. Prior to achieving a euthyroid state, temporizing doses of propranolol ranging from 20–80 mg po Q6–8 h have been shown to reduce the frequency and severity of attacks.[2,5,15,21] Susceptible patients should avoid potential triggers as described earlier.[2]

Competing interests: None declared.

https://doi.org/10.1017/cem.2016.355 Published online by Cambridge University Press

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https://doi.org/10.1017/cem.2016.355 Published online by Cambridge University Press