Young man with acute flaccid tetraparesis

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CASE PRESENTATION

A 26-year-old Brazilian man, previously well, developed acute-onset flaccid tetraparesis. He had retired to bed at 11 p.m. without neurological symptoms and had awoken at midnight with weakness in all four limbs and unable to walk. He took no medications, drugs (including nitrous oxide) or alcohol and had no history of intense physical exertion, fever, recent vaccination, recent trauma and loss of sphincter control. The previous night, he had eaten a meal with a higher carbohydrate content than usual. Four months before, he had experienced one episode of sudden lower limb weakness lasting for minutes. He reported persistent tremors in both his hands and feet, along with unintentional weight loss of 45 kg over 6 months. There was no relevant family history.

On examination, he was alert and orientated. Pupils were equal, rounded and reactive to light. Extraocular movements were normal, with no ptosis or fatiguability. Visual fields were intact, and his face was symmetrical. There was weakness in both upper (proximal Medical Research Council grade 2/5 and distal 4/5) and lower limbs (proximal 3/5 and distal 4/5). All four limbs were hypotonic. Deep tendon reflexes were normal and symmetrical. Coordination and sensory systems were normal. He had a tachycardia with a regular rhythm and normal blood pressure.

Question: what are the differential diagnoses for this patient's flaccid paralysis?

This patient presented an acute-onset symmetrical tetraparesis with hypotonia and normal deep tendon reflexes: an acute flaccid paralysis. Differential diagnoses include myopathies, neuromuscular transmission disorders, neuropathies and acute myelopathies.[1]

The most common global cause of acquired flaccid paralysis is Guillain-Barré syndrome, a polyradiculoneuropathy. Patients present acute, symmetrical paralysis, usually ascending and progressive. Frequently beginning in the lower limbs, symptoms progress over days to weeks, with decreased or absent deep tendon reflexes and cranial nerve involvement. A history of recent vaccination or infection is common. The diagnosis is typically clinical, supported by altered cerebrospinal fluid findings and electromyography.[2] However, it does not typically recur.

Other causes of weakness include inflammatory myopathies that present progressive muscle weakness, mainly in proximal limbs, often with elevated muscle enzymes. Metabolic myopathies, rare genetic diseases, usually manifest with exercise intolerance or previous rhabdomyolysis episodes. Neuromuscular junction disorders, such as myasthenia gravis, are characterised by muscle fatiguability, typically involving the eye muscles. Acute myelopathies, such as transverse myelitis, can present with acute flaccid tetraparesis but this is usually associated with dysautonomia, pyramidal or sensory signs, particularly a sensory level. Again these conditions are not recurrent.

This patient's recurrent weakness episodes raise the possibility of periodic paralysis. Periodic paralysis encompasses a rare group of skeletal muscle channelopathies, marked by recurrent muscle weakness. These episodes may correlate with varying serum potassium concentrations, presenting with hypokalaemia or hyperkalaemia.[3,4] Two notable examples include familial periodic paralysis, an autosomal dominant disorder, and thyrotoxic periodic paralysis.

Question: what investigations would you perform?

The initial evaluation should include basic serum chemistries for metabolic abnormalities, such as electrolytes—especially serum potassium—blood glucose, arterial blood gases, lactate, muscle injury markers, liver enzymes, thyroid function and thyroid antibodies, depending on initial results. An electrocardiogram should aid in establishing the diagnosis.

The most relevant finding was a serum potassium of 2.89 mEq/L (normal 3.5–5.5). Transaminases, lactate and creatine kinase were normal. Arterial blood gas showed no acidosis, and neuroimaging was normal. He received intravenous potassium replacement, and 4 hours later his muscle strength had completely recovered.

Blood test results also showed low TSH (<0.01 mU/L; normal 0.4–4.3) and high free T4 (6.11 ng/dL; normal 0.78–2.9) and thyrotropin receptor antibody (TRAb) (4.7 UI/L; normal <1.75). Thyroid ultrasound scan showed heterogeneous echogenicity of the gland, with increased dimensions and hypervascular flow (thyroid imaging reporting and data system (TI-RADS)) 1. He was then treated with thiamazole for hyperthyroidism and a beta-blocker for control of adrenergic symptoms.

Question: what is the likely diagnosis and prognosis?

The resolution of acute-onset tetraparesis after potassium supplementation and hyperthyroidism treatment supports the diagnosis of thyrotoxic hypokalaemic periodic paralysis with Graves' disease as the underlying disorder; familial periodic paralysis is not associated with altered thyroid function.[4 5] When identified and treated, thyrotoxic hypokalaemic periodic paralysis has an excellent prognosis and may be completely reversible in euthyroid status.

At outpatient follow-up 5 months later, his thyroid function was normal and there had been no new episodes of acute tetraparesis. His neurological examination was normal, with normal strength in all limbs.

DISCUSSION

Thyrotoxic hypokalaemic periodic paralysis is a rare condition manifesting as episodes of flaccid muscle paralysis, low serum potassium and hyperthyroidism. While more common in Asians, this Brazilian patient reinforces that thyrotoxic hypokalaemic periodic paralysis is not limited to specific populations and is becoming more frequent in Western countries. Although hyperthyroidism is more common in women, thyrotoxic periodic paralysis occurs more frequently in men.[5 6]

The patient's Graves' disease, the underlying disorder in most cases, points to the role of thyroid overactivity in causing flaccid paralysis, possibly related to increased sodium–potassium-adenosine triphosphatase (Na/K-ATPase) pump activity. Excessive thyroid hormones, β-adrenergic catecholamine and insulin can increase Na/K--ATPase activity in skeletal muscle, liver and kidney; thus, resulting in an influx of potassium into the intracellular space, leading to low plasma potassium concentrations with no change to the total body potassium. It may be more common in men because testosterone increases Na/K-ATPase activity.[6 7]

Restoration of euthyroidism prevents new attacks of thyrotoxic hypokalaemic periodic paralysis. Beta-blockers decrease attack incidence and should be administered to relieve adrenergic symptoms. Avoiding triggering events such as strenuous activity, stress, high-carbohydrate intake, cold exposure and alcohol is recommended.[6 7]

Key points

- It is essential to check thyroid function in patients with acute flaccid tetraparesis.
- Timely recognition and treatment of thyrotoxic hypokalaemic periodic paralysis can reduce the risk of severe complications.

Suggested reading

- Falhammar H, Thorén M, Calissendorff J. "Thyrotoxic periodic paralysis: clinical and molecular aspects." *Endocrine*. 2012.
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Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and was approved by the Institutional Review Board of Secretaria Municipal da Saúde de São Paulo—SMS/SP, under reference number CAAE 59842722.0.0000.0086. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study complied with all relevant local, national and international regulations governing research involving human participants. Participants gave informed consent to participate in the study before taking part.

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