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CASE REPORT

Thyrotoxic Neuropathy
A rare cause of acute flaccid paraplegia

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اعتلال عصبي متعلق بالتسمم الدرقي
حالة نادرة لشلل سفلي رخو

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ABSTRACT: Acute polyneuropathy is a rare manifestation of severe hyperthyroidism. We report a 22-year-old Omani male who presented to the Sohar Hospital, Sohar, Oman, in 2016 with acute-onset rapidly progressive flaccid areflexic paraplegia as the presenting manifestation of thyrotoxicosis. Nerve conduction studies revealed mixed axonal and demyelinating polyneuropathy in both the motor and sensory nerves. Treatment of the hyperthyroidism with β-blockers and carbimazole along with physiotherapy resulted in the patient's full recovery and the alleviation of his symptoms. Besides highlighting this rare association, this report underscores the importance of including thyroid function tests in the evaluation of patients with acute polyneuropathy.

Keywords: Thyrotoxicosis; Polyneuropathy; Hyperthyroidism; Flaccid Paraplegia; Case Report; Oman.

الملخص: يعد الاعتلال العصبي المتعدد الحاد عرضا نادرا لفرط الدرقية الوخيم. ونعرض هنا حالة مريض عماني عمره 22 عاما أحضر لمستشفى صحار، بمدينة صحار في عمان في عام 2016، وهو يشكو من شلل سفلي رخو ترقى وتضاعف بصورة حادة وسريعة. وقد كانت تلك الأعراض دالة على تسمم درقي. وأوضحت دراسات التوصيل العصبي عن حالة اعتلال عصبي متعدد محواري ومزيل للميالين في الأعصاب الحركية والحسية معا. وتم علاج فرط الدرقية باستخدام مضادات مستقبلات بيتا وكاربمازول، وبالعلاج الطبيعي. وأفضى العلاج لشفاء المريض شفاء تاما من الأعراض المذكورة. وتوضح هذه الحالة الارتباط النادر بين التسمم الدرقي والشلل السفلي الرخو، وتبين أيضا أهمية قياس مؤشرات وظائف الغدة الدرقية عند تقويم حالة المرضى المصابين باعتلال عصبي متعدد حاد.

الكلمات المفتاحية: التسمم الدرقي؛ الاعتلال العصبي المتعدد؛ فرط الدرقية؛ الشلل السفلي الرخو؛ تقرير حالة؛ عمان.

Thyrotoxicosis is associated with various neuromuscular illnesses like myopathy, periodic paralysis, ophthalmoplegia and *myasthaenia gravis*.[1,2] In contrast to muscles, the involvement of the peripheral nerves in hyperthyroidism has received little attention.[3,4] Even though the association between these two disorders has been questioned, electron microscopic studies of sural nerve biopsies have shown changes compatible with thyrotoxicosis.[5,6] This report describes a case of acute flaccid paraplegia which resolved upon treatment of the underlying hyperthyroidism.

Case Report

A 22-year-old Omani male presented to the Sohar Hospital, Sohar, Oman, in 2016 with a three-day history of progressive weakness in both lower limbs, resulting in him becoming bed-bound. There were no symptoms in the upper limbs or evidence of sphincter dysfunction. On examination, he was anxious, diaphoretic and had bilateral *exophthalmos* with lid lag. His pulse rate was 110 beats per minute and blood pressure was 130/82 mmHg. Motor weakness and reflex changes were confined to both of the lower extremities. The lower limbs were hypotonic and areflexic with a power grade of 2/5 both proximally and distally; there was no wasting or fasciculations. An examination of the feet revealed normal *flexor* plantar reflexes.

The results of routine blood tests were unremarkable, including serum electrolyte, creatine phosphokinase and antiganglioside antibody tests. A cerebrospinal fluid examination and electrocardiogram were normal. His serum thyroxine (T4) level was >100 pmol/L (normal range: 12–22 pmol/L), his triiodothyronine level was 11.77 pmol/L (normal range: 3.1–6.8 pmol/L) and his thyroid stimulating hormone (TSH) level was <0.005 IU/mL (normal range: 0.27–4.2 IU/mL). Levels of antithyroid peroxidase and TSH receptor antibodies were 16.2 IU/mL (normal range: <6 IU/mL) and 5.9 IU/L (normal range: ≥1.57 IU/L), respectively. Plain and contrast magnetic resonance imaging (MRI) of the brain and spine was essentially normal, although an MRI scan of the lumbosacral *plexus* was not performed. Tests

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Table 1: Sequential nerve conduction studies in a patient with acute-onset rapidly progressive flaccid areflexic paraplegia associated with hyperthyroidism

Nerve*		At baseline			After 12 weeks of antithyroid treatment		
		Distal latency in ms	Amplitude	Conduction velocity in m/s	Distal latency in ms	Amplitude	Conduction velocity in m/s
Motor nerves	**Peroneal**						
	Left	NR	0.0 mV	NR	6.0	3.5 mV	46.0
	Right	9.0	0.6 mV	39.3	4.0	4.1 mV	44.0
	Tibial						
	Left	-	-	-	3.7	2.1 mV	31.5
	Right	-	-	-	3.2	2.5 mV	36.0
Sensory nerves	**Sural**						
	Left	-	-	-	3.8	9.0 µV	36.8
	Right	-	-	-	3.9	9.7 µV	35.9
	Superficial peroneal						
	Left	4.8	0.6 µV	43.8	4.5	2.8 µV	45.6
	Right	6.0	0.0 µV	NA	NA	NA	NA

NR = not reproducible; NA = not assessed.

**Normal ranges for motor nerves are as follows: distal latency: 3.4–6.2 ms; amplitude: 6–15 mV; and conduction velocity: 42–55 m/s. Normal ranges for sensory nerves are as follows: distal latency: 2.5–3.6 ms; amplitude: >10 µV; and conduction velocity: 38–55 m/s.*[7]

for collagen vascular diseases (i.e. systemic *lupus erythematosus* or polyarteritis *nodosa*) were negative. Epstein-Barr virus, cytomegalovirus, hepatitis B and retroviral infections were also excluded by appropriate serology.

Two weeks after the onset of the patient's illness, nerve conduction studies revealed mixed axonal and demyelinating polyneuropathy in both the motor and sensory nerves. Concentric needle electromyography (EMG) showed moderate-to-severe active denervation in the bilateral *extensor digitorum brevis*, *tibialis anterior*, *gastrocnemius* and *vastus medialis* muscles. In contrast, nerve conduction was normal in the upper extremities. According to the EMG findings, there were no fasciculations in the lower extremities and the motor unit action potentials were of high amplitude with incomplete recruitment. The patient was prescribed a combination of a β-blocker (120 mg/day of propranolol) and 40 mg/day of carbimazole alongside intensive physiotherapy. After three weeks of treatment, thyroid function tests revealed T4 and TSH levels of 35.4 pmol/L and 0.01 IU/mL, respectively. After six weeks, the patient's tremors disappeared, the tachycardia stabilised and the motor power of the lower limbs improved to grade 4/5; moreover, reflexes were elicited as normal and the patient became ambulant. At this time, the T4 levels had decreased to 23.36 pmol/L and TSH levels remained at 0.01 IU/mL. Improvement in nerve conduction was noted after 12 weeks, coinciding with the patient's clinical and biochemical recovery [Table 1].[7]

Discussion

This case report describes a patient who presented with acute-onset rapidly progressive polyradiculoneuropathy involving only the lower limbs, without evidence of cranial nerve dysfunction or sphincter involvement. The absence of cranial nerve involvement, a normal cerebrospinal fluid examination and the presence of striking sensory involvement on electrophysiological studies made a diagnosis of Guillain-Barré syndrome unlikely.[8] Thyrotoxic periodic paralysis (TPP) was subsequently considered, since the patient's clinical signs correlated with hyperthyroidism. Patients with TPP usually present with muscle cramps with the lower extremities more often affected than the upper extremities in a proximal-to-distal pattern of involvement.[9] The attack can last for hours to days and improve with treatment of the thyrotoxicosis. However, the majority of patients with TPP have precipitating factors such as a carbohydrate-rich diet or muscle cooling immediately following exercise; moreover, hypokalaemia (serum potassium levels of <2.5 µmol/L) is also often detected, along with low TSH levels together with reduced-amplitude

Table 2: Other causes of acute polyneuropathy aside from hyperthyroidism[3,5,8]

Cause
Periodic paralysis (i.e. hypokalaemia)
Botulism
Collagen vascular diseases (i.e. SLE/PAN)
Lead poisoning
Poliomyelitis
Critical illness neuromyopathy
CMV, EBV and hepatitis B infections
Diphtheria
Retroviral infections (i.e. HIV)
Neurosarcoidosis
Tick paralysis
Spinal cord haemorrhage/epidural abscesses

SLE = systemic lupus erythematosus; PAN = polyarteritis nodosa; CMV = Cytomegalovirus; EBV = Epstein-Barr virus.

compound motor action potentials during clinical attacks.[9] Such features were not present in the current case; the patient's serum potassium levels were normal and his nerve conduction findings were not typical for TPP, although provocative tests were not carried out. Eventually, the patient's gradual clinical and electrophysiological response to antithyroid treatment confirmed the diagnosis of neuropathy.

Common causes of acute polyneuropathy aside from hyperthyroidism are presented in Table 2.[3,5,8] In the current case, these causes were considered but eventually excluded as a result of various investigations. Heavy metal poisoning was deemed unlikely from the patient's history, the electrophysiological findings and his rapid recovery. Spinal epidural abscesses, haemorrhage into the spinal cord and spinal cord injuries were also excluded by MRI. Acute porphyric neuropathy is rare in this geographical region of the world and neurosarcoidosis even more so.[5] Tick paralysis was also not considered in the present patient as, to the best of the authors' knowledge, this disease has never been reported in Oman. However, an acute polyneuropathy-like illness could also be a presenting feature of poliomyelitis, botulism, critical illness neuromyopathy and diphtheria.[5,8] Moreover, anterior horn cell syndrome secondary to hyperthyroidism (i.e. thyroid amyotrophy) may be possible.[3]

The association of thyrotoxicosis with acute peripheral neuropathy simulating Guillain-Barré syndrome has been reported in previous research; moreover, chronic subclinical peripheral neuropathy has been previously reported in hyperthyroidism, although less frequently than in hypothyroidism.[10,11] Paraplegia related to severe hyperthyroidism was first described by Charcot in 1889.[12] However, the association between hyperthyroidism and acute polyneuropathy has been questioned, with the muscle weakness believed to be secondary to a myopathic process rather than a polyneuropathy.[5] However, Pandit *et al*. reported a patient for whom electron microscopic studies on sural nerve biopsies revealed changes consistent with thyrotoxicosis, but different from Guillain-Barré syndrome.[6] Other researchers have also concluded that thyrotoxic myopathy is actually a neuropathic disorder in its early stage of denervation.[3] A prospective study of hyperthyroid patients found that 14% had numbness and paresthaesia and 19% had signs of distal sensory disturbances in the limbs with depressed ankle jerks.[13] Electrophysiological findings confirmed predominantly sensory axonal neuropathy among 24%; moreover, with treatment of the hyperthyroidism, the sensory symptoms resolved within seven months.[13] Surprisingly, acute thyrotoxic neuropathy has not been reported in children.[14]

The pathogenesis of neuropathy in hyperthyroidism is still obscure. It has been postulated to be either a direct effect of excessive thyroid hormones, immune-mediated or due to a hypermetabolic state depleting the nerves of essential nutrients.[3] A high index of suspicion of thyroid dysfunction is of paramount importance when evaluating a patient with acute polyneuropathy, even in the absence of overt thyromegaly or a history of thyroid disorders. Thyroid function tests should therefore be included in the routine work-up of acute polyneuropathy cases.

Conclusion

Acute polyneuropathy in hyperthyroidism is relatively rare. This report describes a patient who presented with acute polyradiculoneuropathy as the primary manifestation of thyrotoxicosis and for whom antithyroid treatment coincided with his clinical recovery.

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