

Thyrotoxic Hypokalemic Periodic Paralysis as the Presenting Symptom in a Young Ashkenazi Jewish Man

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Thyrotoxic hypokalemic periodic paralysis is a rare manifestation of thyrotoxicosis characterized by recurrent episodes of muscle weakness and concurrent hypokalemia. THPP primarily affects people of Asian descent. The overall incidence of THPP among Chinese and Japanese thyrotoxic patients is 1.8% and 1.9%, respectively [1]. Only sporadic cases of THPP have been reported in non-Asian populations, namely Caucasian, Afro-American, American Indian and Hispanic [1–4]. However, due to immigration, THPP has become increasingly common in western countries.

Early assessment of thyroid function in patients with hypokalemic paralysis can distinguish THPP from other forms of hypokalemic periodic paralysis [1]. We present a case of thyrotoxic hypokalemic periodic paralysis in a young Jewish Ashkenazi man. We are aware of only one previous report of THPP in a man of Jewish Ashkenazi decent (East European origin), who immigrated to Israel from Romania [3].

PATIENT DESCRIPTION

A 21 year old healthy soldier was admitted to the department of emergency

medicine following recurrent attacks of muscle weakness. The symptom was first noticed one month earlier and there were several subsequent attacks. The attacks typically appeared a few hours after physical exertion. The proximal muscles of the legs were most severely affected. The attacks lasted for several hours and ended spontaneously. In the month preceding his hospitalization, the patient had lost 2 kg of his body weight. He was not taking any medication and there was no history of thyroid disorder in his family.

On physical examination the patient was calm. Body temperature was 36.6°C, heart rate 129/minute and blood pressure 133/89 mmHg. The skin was slightly warm. Very mild exophthalmus and a fine hand tremor were noticed. The thyroid gland was diffusely enlarged, and was twice the normal size. The rest of the examination, including neuromuscular, was unremarkable.

Laboratory findings on admission revealed hemoglobin 14.6 g/dl, white blood cells 5.760/ul, urea 25 mg/dl, creatinine 0.46 mg/dl, sodium 143 mEq/L, potassium 2.4 mEq/L, calcium 10.1 mg/dl, phosphorus 3.3 mg/dl, magnesium 1.43 mg/dl, creatine phosphokinase 147 U/L, myoglobin 216 ng/ml, blood pH 7.38 and bicarbonate 23.4 mmol/L. Repeated blood tests 2 hours later demonstrated spontaneous normalization of serum potassium concentration to 4.1 mEq/L, preceding any treatment, concomitant with disappearance of the muscle weakness. Further laboratory findings yielded thyroid-stimulating hormone < 0.05 IU/ml (normal 0.4–4), free triiodothyronine > 20 pg/ml (normal

2.5–4), free thyroxine 8.1 ng/dl (normal 0.8–2.4), anti-thyroglobulin antibody 98 IU/ml (normal < 100) and antithyroid peroxidase 335 IU/ml (normal < 50).

The patient was diagnosed with Graves' disease and thyrotoxic periodic hypokalemic paralysis. Treatment with potassium, propranolol and methimazole was initiated and he was discharged from the hospital in stable condition for ambulatory follow-up. Six months following his admission the patient was in complete clinical and biochemical remission and he reported no additional paralytic attacks following the initiation of antithyroid treatment

COMMENT

Our patient, a young Ashkenazi Jewish man, was diagnosed with thyrotoxic hypokalemic periodic paralysis, a rare condition among people of non-Asian decent that precedes other clinical manifestations of thyrotoxicosis and is associated with physical exertion. The muscle weakness disappeared concomitantly with spontaneous correction of serum potassium level following rest.

The first case of THPP was reported by Rossenfield in 1902 [2]. It is characterized by recurrent episodes of paralysis and hypokalemia during a thyrotoxic state. THPP usually manifests in young adults between the second and fourth decades. Physical exertion, warm temperature and carbohydrate-rich meals can precipitate an attack of muscle weakness. As in our patient, muscle weakness does not usually occur during exercise but rather during post-exertion rest. In Asians the symptoms of thyrotoxicosis

THPP = thyrotoxic hypokalemic periodic paralysis

are distinct and usually precede the first paralytic episode, whereas in non-Asian populations paralysis often precedes symptoms of thyrotoxicosis [5].

Paralytic attacks may last from a few hours up to 72 hours, with complete recovery between attacks. The intensity of the paralytic attack can range from mild weakness to complete flaccid paralysis. Muscle weakness may be asymmetric. Proximal muscle groups are more severely affected and respiratory muscles are seldom involved.

The hallmark of THPP is hypokalemia. The presenting serum potassium level is usually below 3.0 mEq/L and may be as low as 1.0 mEq/L. Fatal and life-threatening ventricular arrhythmia and respiratory failure can result from untreated THPP [1,2]. Concurrent hypomagnesemia and hypophosphatemia may occur, which were also noticed in a mild form in our patient. Hypokalemia results from a sudden intracellular shift of potassium and is not due to potassium deficiency caused by increased adrenergic activation of ATPase pump activity and enhanced insulin response. Thyroid hormones change the plasma membrane permeability to potassium by increasing beta-adrenergic receptors in skeletal muscles, and subsequently Na/K ATPase activity, resulting in a markedly increased intracellular shift of potassium [1,2].

Clinical features of hyperthyroidism in patients with THPP may be subtle. Non-selective beta-adrenergic blockers can ameliorate and prevent recurrence of the paralytic attacks, which finally disappear with control of the hyperthyroidism. Early recognition and immedi-

ate potassium supplementation can prevent life-threatening cardiopulmonary complications and hasten the recovery of muscle strength.

The genetic predisposition for THPP is not entirely clear. Various studies have suggested different candidate genes. Certain human leukocyte antigens have been reported to occur in higher prevalence (B46, DR9, and DQB1*0303 among Hong Kong Chinese, and HLA A2, Bw22, AW19, B17 and DRW8 among Singapore Chinese and Japanese, respectively, with THPP). However, it is uncertain whether these HLA genes are independently related to THPP, as they are also associated with Graves' disease [1]. None of the few mutation hot spots in the L-type calcium channel 1-subunit Cav1.1, which are associated with familial hypokalemic periodic paralysis (FHPP-1), were present in Asian or non-Asian patients with THPP. However, certain single-nucleotide polymorphisms of Cav1.1 were detected in THPP patients from southern China. The location of these single-nucleotide polymorphisms lies at, or close to, the thyroid hormone-responsive elements of the gene, suggesting that they may affect the binding affinity of the TRE and modulate stimulation of thyroid hormone on the Cav1.1 gene [1].

Because patients with THPP have increased Na/K-ATPase activity, the genes coding for the various subunits of Na/K-ATPase are examined, but no mutations have been identified in patients with THPP, nor has any asso-

ciation been found between the single-nucleotide polymorphisms of these five genes and THPP. No specific polymorphism in the β 2-adrenergic receptor gene has been associated with THPP. Thus, whether THPP is associated with a genetic predisposition to activation of the Na/K-ATPase genes remains to be determined [1].

The occurrence of THPP as a presenting symptom of Graves' thyrotoxicosis in our young Ashkenazi Jewish male patient posed a diagnostic challenge on two counts: the infrequent occurrence of Graves' disease in this particular gender and age group, and the almost unprecedented occurrence of THPP in this ethnic group. This case emphasizes the need for awareness regarding the possibility of THPP in patients of non-Asian origin as well.

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HLA = human leukocyte antigens
TRE = thyroid hormone-responsive elements

"Yes truly, there has been nothing but toil and care; and I may say that in all my 75 years, I have never had a month of genuine comfort. It has been the perpetual rolling of a stone, which I have always had to raise anew"

Johann von Goethe (1749-1832), German writer of poetry, drama, literature, theology, philosophy, humanism and science. Goethe's magnum opus, lauded as one of the peaks of world literature, is the two-part drama *Faust*

"You've got to do your own growing no matter how tall your father is"

Anonymous