

THYROTOXIC PERIODIC PARALYSIS AS A FIRST SIGN OF GRAVE'S DISEASE

Case Report

GRAVES HASTALIĞININ İLK BULGUSU OLARAK TİROTOKSİK PERİYODİK PARALİZİ

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ABSTRACT

Thyrotoxic periodic paralysis; is a rare sign of thyrotoxicosis and characterised by attacks of muscle weakness. Hypokalemia is usually present during attacks. A 33-year-old male patient admitted to emergency service of our hospital with complaints of generalised muscle weakness which was more prominent in his lower extremities. Thyrotoxicosis and hypokalemia were detected in his examination. Hypokalemia signs were present in electrocardiography; intravenous potassium replacement had been started immediately. After potassium replacement; his complaints rapidly recovered. Thyrotoxic signs in Thyrotoxic periodic paralysis can be overlooked because neurological signs are more prominent during attacks. Early diagnosis in these patients prevents severe cardiopulmonary complications.

Key words: hypokalemic periodic paralysis, thyrotoxicosis, Graves Disease

ÖZET

Tirotoksik periyodik paralizi tirotoksikozun nadir bir bulgusudur ve ataklar şeklinde jeneralize güçsüzlük ile karakterizedir. Ataklar sırasında hipokalemi genellikle saptanır. 33 yaşında erkek hasta acil servise alt ekstremitede daha belirgin olan jeneralize kas güçsüzlüğü yakınmasıyla başvurdu. Yapılan tetkiklerinde hipokalemi ve tirotoksikozis saptandı. EKG sinde hipokalemi bulguları saptanan hastaya, acil olarak intravenöz potasyum verildi ve hastanın bulguları hızla iyileşti. Tirotoksik PP hastalarının tirotoksik bulguları nörolojik semptomların daha ön planda olması nedeniyle gözden kaçabilmektedir. Bu hastalarda erken tanı ciddi kardiyopulmoner komplikasyonları önlemektedir.

Anahtar kelimeler: hipokalemik periyodik paralizi, tirotoksikozis, Graves Hastalığı

INTRODUCTION

Thyrotoxic periodic paralysis (Thyrotoxic PP) is a sporadic form of hypokalemic periodic paralysis and related with hyperthyroidism. Thyrotoxic PP can be seen in all conditions that cause hyperthyroidism. Grave's disease is the most common cause in etiology of thyrotoxic PP (1,2). Thyrotoxic PP cases are more oftenly seen in Asian populations. Incidence of Thyrotoxic PP in Asian hyperthyroid patients is about %2 (3,4). Relation between hyperthyroidism and hypokalemic periodic paralysis is well known but diagnosis of these patients usually delays because neurological signs are more prominent in first admission.

CASE REPORT

33 year old male patient admitted to emergency service with complaint of muscle weakness. His complaints were more prominent in his lower extremities and accrued gradually. In his first evaluation; we detected his blood pressure 120/70 mmhg, heart rate 72/min, body temperature 36.3 °C. He had no hyperthyroidism symptoms as; weight loss, heat intolerance, diarrhea. He had no history of chronic disease or drug usage. Also he had no family history of familial hypokalemic periodic paralysis. Our patient stated that he had admitted to hospital with similar complaints at about one month ago.

In his neurological examination; tetraparesis was present, he had no sensory deficit. In biochemical tests we detected; potassium 2 mmol/l, sodium 137 mmol/l, chlorine 105 mmol/l, creatinine 0.80 mg/dl, magnesium 2.4 mg/dl, phosphate 3.5 mg/dl, creatine kinase 435 u/l, PH 7.44, HCO₃ 26 mmol/l, PO₂ 92 mm hg, PCO₂ 37 mm hg. In his 24 hours urine analysis; there was no potassium loss. In electrocardiography; we observed decrease in T wave amplitude and U wave formation in v4-v6 derivations. In thyroid function tests; we detected free T4 3.8 µg/dl (0,61-1,12) , free T3 16.30

pg/dl(2.5-3.9), TSH 0.06 µIU/ML (0.34-5.86), anti-tpo 260 iu/ml, antithyroglobulin 98 u/ml.

Thyroid gland ultrasonography revealed that size of thyroid gland was increased, thyroid gland parenchyma was heterogeneous and milimetric multiple hypoechoic nodules were present in heterogeneous background. Also we performed thyroid gland scintigraphy; technetium uptake of thyroid gland was diffusely increased in a non-homogeneous pattern.

40 meq/l potassium replacement was made in emergency service and control potassium level of patient was 3.5 mmol/l after 6 hours. Complaints of our patient recovered rapidly, in 24 hours he was able to walk alone. After his first treatment in emergency service; propranolol and methimazole treatment was started. During 2 months he had no recurrent attacks.

DISCUSSION

Hyperthyroidism incidence is higher in females than males; but %95 of reported thyrotoxic PP cases is male (5,6). Symptoms begins between ages of 20-39 (3,6). In differential diagnosis; familial periodic paralysis should be considered. But familial periodic paralysis is seen in younger ages. Clinical features are similar with thyrotoxic PP. Mechanism of thyrotoxic PP in hyperthyroidism is not well known. Thyroid hormone increases sensitivity of tissues to beta adrenergic stimulus. In skeletal muscles; Na/K/ATPase activity increases also (7). Hypokalemia occurs as a result of massive shift of potassium into the cells. Urinary potassium excretion is usually normal or decreased (8,9). In our case urinary potassium excretion was normal. Level of hypokalemia is related with severity of paralysis but not with thyroid hormone levels.

Fatal and life threatening ventricular arrhythmias were reported in literature (10,11). In our patient's electrocardiography; hypokalemia signs were present, but recovered after

immediate potassium replacement. Besides hypokalemia; in these patients hypophosphatemia and hypomagnesemia can be seen; these effects occur with intracellular shift of phosphorus and magnesium like potassium. In our patient, magnesium and phosphate levels were normal.

Attacks of muscle weakness may occur suddenly; severity of attacks varies in a range of mild weakness to complete flaccid paralysis. Proximal muscles are more affected than distal muscles. Attacks begin with weakness in lower extremities, afterwards upper extremities are affected. Sensorial functions are not affected (2,6,12,13). Respiratory muscles are rarely affected, but cases with total paralysis of respiratory and ocular muscles had been reported (14,15). In our case, muscle weakness had started in lower extremities afterwards tetraparesis occurred.

If a patient admits with acute attack, differential diagnosis must be made from causes of tetraparesis such as myasthenia crisis, Guillain Barre syndrome, transverse myelitis and botulism. Presence of hypokalemia usually alerts the physician, if there was not any family history of periodic paralysis, TPP must come to the mind. In thyrotoxic PP patients; frequency and duration of attacks are various. Cases having more than one attack in a week had been reported in literature (6,16). Physical activity, stress and high carbohydrate diets may precipitate attacks. Increase in epinephrine and insulin secretion cause intracellular shift of potassium and hypokalemia occurs (3,17). In many instances, no obvious precipitant is identified, in our patient there was not any precipitant factor. Genetic predisposition is included in thyrotoxic PP pathogenesis. Polimorphism in calcium channel alpha 1 subunit gene and SCN4A, CACNA 15 mutations had been shown (18,19). In %33 of Thyrotoxic periodic paralysis patients, mutation of Kir 2.6 gene had been determined (20).

Emergency treatments of familial hypokalemic periodic paralysis and thyrotoxic PP are similar. Firstly, potassium replacement must be made. Aggressive potassium replacement must be avoided because total body potassium is not deficient and rebound hyperkalemia may occur (21).

In a retrospective case serial, it was shown that intravenous potassium replacement provides recovery rapidly than oral potassium treatment does (22). During potassium replacement; cardiac monitoring and frequent potassium measurement are suggested. If there is no obvious improvement of symptoms with potassium replacement; it is considered that intravenous propranolol can provide recovery in muscle weakness and hypokalemia (23,24). In a study, it is stated that oral propranolol without potassium replacement may improve muscle weakness and hypokalemia (25). Propranolol is a non selective beta blocker and decreases increased activity of NaKATPase in these patients. Second stage of Thyrotoxic PP treatment includes prevention of attacks by providing euthyroidism with antithyroid drugs. Potassium replacement is not suggested in prevention of attacks in Thyrotoxic PP. But severe exercises, high carbohydrate diets and alcohol should be avoided in these patients. In our case after potassium replacement we started methimazole and propranolol treatment with diagnosis of Grave's disease. During 2 months our patient was in euthyroid state and he had no recurrent attacks.

When 20-40 year old patients admit to hospital with acute paralysis; Thyrotoxic periodic paralysis should be evaluated in differential diagnosis if hypokalemia is present. Family history and age are important in differential diagnosis from familial hypokalemic periodic paralysis. Hyperthyroidism symptoms can be mild like our patient but thyroid functions must be evaluated in hypokalemic patients with muscle paralysis.

REFERENCES

- 1) Chen YC, Fang JT, Chang CT, Chou HH. Thyrotoxic periodic paralysis in a patient abusing thyroxine for weight reduction. *Ren Fail* 2001; 23:139.
- 2) Pompeo A, Nepa A, Maddestra M, et al. Thyrotoxic hypokalemic periodic paralysis: An overlooked pathology in western countries. *Eur J Intern Med* 2007; 18:380.
- 3) Ober KP. Thyrotoxic periodic paralysis in the United States. Report of 7 cases and review of the literature. *Medicine (Baltimore)* 1992; 71:109.
- 4) Kelley DE, Gharib H, Kennedy FP, et al. Thyrotoxic periodic paralysis. Report of 10 cases and review of electromyographic findings. *Arch Intern Med* 1989; 149:2597.
- 5) Hsieh MJ, Lyu RK, Chang WN, et al. Hypokalemic thyrotoxic periodic paralysis: clinical characteristics and predictors of recurrent paralytic attacks. *Eur J Neurol* 2008; 15:559.
- 6) Okinaka S, Shisume K, IINO S, et al. The association of periodic paralysis and hyperthyroidism in Japan. *J Clin Endocrinol Metab* 1957; 17:1454.
- 7) Rhee S. *N Engl J Med* 2012; 366:553.
- 8) Nora NA, Berns AS 1989 Hypokalemic, hypophosphatemic thyrotoxic periodic paralysis. *AM J Kidney Dis* 13:247-249
- 9) Lin SH 2005 Thyrotoxic periodic paralysis. *Mayo Clin Proc* 80:99-105
- 10) Fisher J 1982 Thyrotoxic periodic paralysis with ventricular fibrillation. *Arch Intern Med* 142:1362-1364
- 11) Loh KC, Pinheiro L, Ng KS 2005 Thyrotoxic period paralysis complicated by near-fatal ventricular arrhythmias. *Singapore Med J* 46:88-89
- 12) Shiang JC, Cheng CJ, Tsai MK, et al. Therapeutic analysis in Chinese patients with thyrotoxic periodic paralysis over 6 years. *Eur J Endocrinol* 2009; 161:911.
- 13) Li J, Yang XB, Zhao Y. Thyrotoxic periodic paralysis in the Chinese population: clinical features in 45 cases. *Exp Clin Endocrinol Diabetes* 2010; 118:22.
- 14) Liu YC, Tsai WS, Chau T, Lin SH 2004 Acute hypercapnic respiratory failure due to thyrotoxic periodic paralysis. *Am J Med Sci* 327:264-267
- 15) Crane MG 1960 Periodic paralysis associated with hyperthyroidism. *Calif Med* 92:285-288
- 16) Venance SL, Cannon SC, Fialho D, et al. The primary periodic paralyses: diagnosis, pathogenesis and treatment. *Brain* 2006; 129:8.
- 17) Wong P. Hypokalemic thyrotoxic periodic paralysis: a case series. *CJEM* 2003; 5:353.
- 18) Kung AW, Lau KS. Association of novel single nucleotide polymorphisms in the calcium channel alpha 1 subunit gene (Ca(v)1.1) and thyrotoxic periodic paralysis. *J Clin Endocrinol Metab.* 2004;89:1340-1345.
- 19) Raja Rayan DL, Hanna MG. Skeletal muscle channelopathies: nondystrophic myotonias and periodic paralysis. *Curr Opin Neurol.* 2010;23:466-476.
- 20) Ryan DP, da Silva MR. Mutations in potassium channel Kir 2,6 cause susceptibility to thyrotoxic hypokalemic periodic paralysis. *Cell.*2010;140:88-98.
- 21) Chou HK, Tsao YT, Lin SH. An unusual cause of thyrotoxic periodic paralysis: triiodothyronin-containing weight reducing agents. *Am J M Sci.*2009;337:71-73.
- 22) Cesur M, Bayram F, Temel MA, et al. Thyrotoxic hypokalaemic periodic paralysis in a Turkish population: three new case reports and analysis of the case series. *Clin Endocrinol (Oxf)*2008;68:143.
- 23) Tassone H, Moulin A, Henderson SO. The pitfalls of potassium replacement in thyrotoxic periodic paralysis: a case report and review of the literature. *J Emerg Med* 2004; 26:157.
- 24) Yu TS, Tseng CF, Chuang YY, et al. Potassium chloride supplementation alone may not improve hypokalemia in thyrotoxic hypokalemic periodic paralysis. *J Emerg Med* 2007; 32:263.
- 25) Lin SH, Lin YF. Propranolol rapidly reverses paralysis, hypokalemia, and hypophosphatemia in thyrotoxic periodic paralysis. *Am J Kidney Dis* 2001; 37:620.