Difficulty in Walking: An Ancient Presentation of an Old Endocrine Disease: Case Report

Yürümekte Zorlanma: Eski Bir Endokrinolojik Hastalık İçin Tarihi Bir Yakınma

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ABSTRACT A fourty-years-old female presented with gait disturbance. Physical examination revealed a proximal muscle weakness in the lower limb. Electromyographic evaluation was normal and magnetic resonance imaging (MRI) of the lumbar region revealed serious osteoporosis. On biochemical analysis calcium was 10.7 g/dL, phosphorus 1.7 mg/dL, alkaline phosphatase (ALP) 559 U/L, with normal levels of albumin. On hormonal analysis, intact parathormone (i-PTH) was elevated, and 25-OH colecalciferol was remarkably low. Ultrasonography of the parathyroids revealed a suspicious, right-sided parathyroid adenoma and dual energy X-ray absorptiometry (DEXA) suggested the osteoporosis. A right-sided parathyroidectomy was performed and decrease in serum calcium levels necessitated parenteral calcium infusion on postoperative period. She used oral calcium and vitamin D, and her osteoporosis improved spontaneously on her first year follow up visit. This patient's gait disturbance seems to be related to primary hyperparathyroidism which clinicians did not recognize the high-normal calcium levels because of an associated vitamin D deficiency, severe vitamin D deficiency and hypophosphatemia. Recognition of a parathyroid adenoma with gait disturbance is a rare occurrence in the 21st century.

Key Words: Muscle weakness; primary hyperparathyroidism; parathyroid neoplasms; hypophosphatemia; vitamin D deficiency

ÖZET Kırk yaşında kadın hasta yürüme bozukluğu ile kliniğimize başvurdu. Fizik muayenede alt ekstremite proksimal kaslarında güçsüzlük saptandı. Elektromiyografik incelemesi normal bulunan hastanın lomber manyetik rezonans görüntülemesinde (MRG) ağır osteoporoz izlendi. Biyokimyasal testlerde albumin düzeyi normal, kalsiyumu 10.7 g/dl, fosfor 1.7 mg/dl, alkalen fosfataz (ALP) 559 U/l olarak tespit edildi. Hormonal incelemede intakt parathormon (i-PTH) yüksek ve 25-OH kolekalsiferol düzeyi belirgin düşük bulundu. Paratiroid ultrasonografisinde sağ tarafta şüpheli bir paratiroid adenom görüntüsü ve DEXA'da osteoporoz izlendi. Hastaya sağ paratiroidektomi uygulandı ve operasyon sonrasında kalsiyum düzeyindeki düşüş parenteral kalsiyum infüzyonu gerektirdi. Hastaya daha sonra oral kalsiyum ve D vitamini başlandı ve bir yıl sonraki takibinde osteoporozun düzeldiği görüldü. Bu hastadaki yürüme bozukluğunun sebebi olarak, eşlik eden ciddi D vitamin eksikliği nedeni ile klinisyenlerin yüksek-normal kalsiyum düzeylerini fark etmediği primer hiperparatiroidizm, ciddi D vitamin eksikliği ve hipofosfatemi birlikteliği gibi görünmektedir. Bir paratiroid adenomunun yürüme bozukluğu nedeni ile fark edilmiş olması XXI. yüzyılda nadir bir durumdur.

Anahtar Kelimeler: Kaslarda güçsüzlük; primer hiperparatiroidizm; paratiroid adenomu; hipofosfatemi; D vitamin eksikliği

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Primary hyperparathyroidism is an old disease, first described in 1925 by Mandl.[1] Because of the availability of routine biochemical screening, the term classical hyperparathyroidism was replaced by modern

hyperparathyroidism, referring to an early diagnosis of the patients without any symptom related to hyperparathyroidism.[1] Classical hyperparathyroidism is a more severe disease when compared with modern hyperparathyroidism, with its bone and renal involvement, and neuropsychiatric and neuromuscular signs and symptoms.[1] In 1949, a special form of hyperparathyroidism-related neuromuscular syndrome was described with proximal muscle weakness and atrophy, gait disturbance, abnormal electromyography and hyperreflexia.[2]

We described a patient with primary hyperparathyroidism who presented with gait disturbance, which is an extremely rare presentation for primary hyperparathyroidism for the modern world in the 21st century.

CASE REPORT

A fourty-year-old female presented with a history of difficulty in walking for one year. Her previous and family history was unremarkable. On physical examination, she had gait disturbance and was unable to stand up from a chair. On neurological examination, proximal muscle strength of both lower limbs were 3/5, muscle weak examination other than lower limbs and deep tendon reflexes were normal. On electromyography, sensory and motor nerve conductions were normal without a decrease in amplitude of action potentials and conduction slowing. Lumbar magnetic resonance imaging (MRI) showed osteoporosis. On biochemical analysis, calcium was 10.7 g/dL (8.5-10.5 g/dL), phosphorus 1.7 mg/dL (2.5-4.5 mg/dL), albumin 4.6 mg/dL (3.5-5.5 mg/dL) and ALP 559 U/L (15-250 U/L). On hormonal evaluation, intact-PTH (i-PTH) was 1314 pg/mL (12-72 pg/mL) and 25-OH-cholecalciferol was 14.1 ng/mL. She had 288 mg/day urinary calcium excretion with a normal creatinine clearance rate. Urinary ultrasonography which was performed for possible renal involvement was normal. On DEXA, femoral neck T score was –5.4 and lumbar total T score was -5.2. On parathyroid ultrasonography a suspicious parathyroid adenoma was observed in the inferior pole of the right thyroidal lobe. Because of a current technical problem we could not perform a parathyroid scintigraphy. After a successful parathyroidectomy, hungry bone syndrome occurred necessitating intravenous calcium infusion. She was discharged following the restoration of calcium levels and prescribed an oral calcium and vitamin D. On the third month follow up visit she was able to stand up from chair, and proximal muscle weak strength of the lower limbs were improved to 5/5. On her first year follow-up visit, femoral neck T score was -1.2 and lumbar total T score was -1.3, suggesting a spontaneous improvement.

DISCUSSION

Although primary hyperparathyroidism is an old endocrine disease, the presentation spectrum of the disease has changed during the time course.[1] Wide availibility of routine biochemical studies increased the proportion of asymptomatic hyperparathyroid patients when compared with the classical hyperparathyroid ones and led to identification of a new terminology named as modern hyperparathyroidism.[1] Classical hyperparathyroidism is a severe disease with its bone and renal involvement, and neuropsychiatric and neuromuscular signs and symptoms. In 1949, a special form of hyperparathyroidism-related neuromuscular syndrome was described with proximal muscle weakness and atrophy, gait disturbance, abnormal electromyography and hyperreflexia.[1,2] Our patient presented with neuromuscular symptoms, which is actually a rare presentation for primary hyperparathyroidism in the 21st century. Routine biochemical analysis is also available in our country, but our patient had high-normal calcium levels with high ALP levels on repeated examinations, which clinicians did not recognize. High-normal serum calcium and normal urinary calcium levels which may be explained by an associated severe vitamin D deficiency, might protected the patient from renal involvement of a severe hyperparathyroid diseases reported before.[3] In severe primary hyperparathyroidism, neuromuscular signs including the muscle weakness are thought to be due to hypercalcemia.[4,5] Our patient did not show a remarkably high serum calcium and we did not find hyperreflexia, so her neuromuscular findings can not be explained with

high-normal hypercalcemia alone.[6] Although neuromuscular complaints in the hyperparathyroid disease are referred to hypercalcemia, the impact of mild hyperparathyroidism on neuromuscular function in asymptomatic hyperparathyroid disease remains controversial.[5-7] Vitamin D deficiency and hypophosphatemia have shown to be cause proximal muscle weakness.[8-10] Spontaneous improvement of the symptoms with parathyroidectomy, calcium and vitamin D supplementation make it difficult to predict the actual cause of the gait disturbance, but it seems to be related with combination of three diseases affecting the neuromuscular system; primary hyperparathyroidism, vitamin D deficiency and hypophosphatemia.

Two sources of Vitamin D in human are diet and cutaneous synthesis after sun exposure. Because of the geographical settling, sunlight exposure is not a problem in our country, but traditional clothing style in women wearing concealing clothes like our patient may be a cause of vitamin D deficiency, which was reported before.[1] In low sun exposure states, standard diets can not provide the daily need of vitamin D and it is well known that vitamin D intake should be increased by fortified foods in such states.[11] These fortified foods are not available in our country, so clothing style seems to be the main etiology of vitamin D deficiency in our patient who has standard dietary habits. Absence of a disease leading to malabsorption in this patient is a suggestion of our theory.

In conclusion, primary hyperparathyroidism presenting like a neuromuscular disease is a rare occurrence in the modern world. But association with vitamin D deficiency may aggravate the neuromuscular symptoms related to hyperparathyroidism and cause a presentation like classical hyperparathyroidism.

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