Hypocalcemic Myopathy Secondary to Hypoparathyroidism

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ABSTRACT

Myopathy is a rare manifestation of idiopathic hypoparathyroidism. We report a 48-year-old man with a 6-year history of muscle pain and elevated creatine kinase levels. Laboratory analysis revealed low serum calcium, inappropriately low-normal parathyroid hormone, elevated phosphorus, and normal 25-hydroxy vitamin D levels. The patient was diagnosed with idiopathic hypoparathyroidism and treated with calcium and calcitriol. He demonstrated an excellent clinical response and creatine kinase values returned to normal. This case illustrates the subtle nature of hypoparathyroid myopathy and highlights the importance of measuring serum calcium in patients with unexplained myalgia and/or muscle weakness.

INTRODUCTION

Hypocalcemia may be associated with an array of seemingly unconnected symptoms and signs. Symptoms are often determined by the degree of hypocalcemia and how quickly the calcium level drops. Tetany, muscle cramps, carpopedal spasm, seizures, and laryngospasm are associated with acute hypocalcemia. Patients with chronic hypocalcemia frequently have nonspecific symptoms including fatigue, irritability, and anxiety. Other symptoms include dementia, papilledema, cataract formation, and ectopic calcification of the basal ganglia. Myopathy is a rare manifestation of hypoparathyroidism. The following case illustrates the uncommon nature of this diagnosis.

CASE REPORT

A 48-year-old man with muscle aches was seen in the internal medicine clinic. He denied severe muscle weakness but noted a slight loss of strength over the last few years that did not interfere with his job or activities of daily living. His past medical history was significant for hypertriglyceridemia and gout. He did not have any surgeries in the past. He drank between 6 and 12 beers per week. Family history was negative for hypocalcemia, hypoparathyroidism, connective tissue diseases, or myositis. His only medication was 300 mg of allopurinol daily for gout, which he was not taking regularly. Review of systems was negative for skin rash, photosensitivity, alopecia, mouth sores, sicca symptoms, Raynaud's phenomenon, pleurisy, prolonged morning stiffness, joint swelling, swallowing problems, or shortness of breath.

His physical exam was unremarkable and Chvostek's and Trousseau's signs were negative. Laboratory studies revealed a creatine kinase (CK) level of 461 IU/L (Normal value, 0-233 IU/L). The patient was referred to the rheumatology clinic for further evaluation.

Laboratory evaluation revealed a normal white blood cell count, hemoglobin, alanine transaminase, aspartate transaminase, Lyme titer, sedimentation rate, antinuclear antibody (ANA) screen, rheumatoid factor, C-reactive protein (CRP), serum protein electrophoresis (SPEP), aldolase and thyrotropin levels. His rheumatologist felt that the elevated CK level was related to physical exertion and perhaps alcohol use. He was recommended to have a repeat CK measurement after a week of abstinence from physical activity and alcohol. The patient, however, did not return for the study.

Four years later, the patient was referred again to the rheumatology clinic because of fatigue and elevated CK levels. He denied muscle pain but reported some morning stiffness that lasted for 5 to 10 minutes and resolved after a hot shower. Again, his blood tests were normal except for a CK level of 725 IU/L. Electromyography was recommended, but he did not follow through with this recommendation.

Two years later he was admitted to our hospital, with a subcapital femur fracture following a low impact injury sustained

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Table 1. Creatine Kinase and Calcium Levels Before and After Treatment of Hypoparathyroidism[a]

	Creatine Kinase	Calcium
	(0-233 IU/L)	(8.4-10.5 mg/dL)
August 29, 2002	365	
October 21, 2002	357	
November 21, 2002	461	
February 27, 2004	636	
April 3, 2006	635	
June 18, 2007	725	
September 4, 2007	415	
November 21, 2008	469	
March 5, 2009	734	
July 13, 2009	704	
September 10, 2009		6.1
October 5, 2009[b]	166	8.2
October 6, 2011[b]	139	8.6

[a]Normal values in parentheses.
[b]After treatment with calcium carbonate and calcitriol.

when he tipped over his motorcycle while stationary. His CK was noted to be high at 714 IU/L. A muscle biopsy done during the hip surgery was normal and did not display inflammatory infiltrates. He had undergone bilateral cataract extraction 2 months before this admission to the hospital.

At his follow-up appointment in the orthopedics clinic, a bone mineral density study showed lumbar spine density of 1.240 g/cm^2 at L1-L4, , consistent with a T-score of 0.2. The density of proximal left femur was 0.916 g/cm^2, consistent with a T-score of -1.3. The T-score of the left femoral neck was -1.9. He was diagnosed with osteopenia based on the World Health Organization classification.

The patient subsequently was referred to the endocrinology clinic, where serum calcium and parathyroid hormone measurements were obtained. They were inappropriately low at 6.1 mg/dL and 22 pg/ml respectively. His magnesium, albumin, TSH, and 25-hydroxy vitamin D levels were normal. Despite the absence of signs and symptoms of hypocalcemia, a diagnosis of hypoparathyroidism was made.

He was treated with 600 mg calcium carbonate twice daily and 0.75 mcg of calcitriol daily. He continued to complain of joint stiffness and occasional pain, but the muscle aching and pain improved and his CK levels returned to a normal level (Table 1). At a follow-up visit, his serum calcium level was 8.1 mg/dL and CK level was 166 IU/L.

DISCUSSION

Hypoparathyroidism is associated with a variety of symptoms that are due to hypocalcemia. Decreased parathyroid hormone secretion may be due to surgical destruction or removal of the parathyroid glands, autoimmune disease, irradiation of the neck, infiltrative diseases, or altered function of the parathyroid glands. Hypocalcemia is classically associated with hyperexcitability at the neuromuscular junction, which may result in tetany, muscle cramping, carpopedal spasm, laryngospasm, and seizures. Clinical problems seen with chronic hypocalcemia include cataract formation, papilledema, emotional instability, anxiety, depression, dry coarse skin, and brittle nails with transverse grooves, basal ganglia calcification, dementia, and extrapyramidal movement disorders. Myopathy with elevated CK enzyme levels is a rare manifestation of hypoparathyroidism.

Hypocalcemic myopathy due to hypoparathyroidism was first reported in 1972.[1] Since then, there have been only a small number of reports highlighting this association.[2-14] A summary of serum calcium levels, CK values, and presenting symptoms in published case reports can be found in Table 2.

Our patient did not experience or display symptoms or signs of acute hypocalcemia. He had bilateral cataract development and removal before the age of 55. It is well known that chronic hypocalcemia, especially associated with hypoparathyroidism, causes cataracts. The initial presentation of our patient's illness, elevated CK levels and myalgias, occurred 6 years prior to diagnosis. Some authors believe that the elevation in CK is the result of repetitive tetany or muscle spasm, resulting in leakage of CK from damaged muscle cells. Our patient denied muscle cramping, tetany, or carpopedal spasm. A muscle biopsy was not performed until the time of his hip surgery, and this showed no evidence of inflammation or structural alteration.

In a case describing the histological findings of a 65-year-old woman with hypocalcemic myopathy due to hypoparathyroidism, light microscopy and electron microscopy revealed type 2 fiber atrophy, perinuclear accumulation of mitochondria, and focal myofibrillar degeneration.[7] In addition, atrophic muscle fibers were negative for myoglobin staining, and normal fibers stained positive for myoglobin. The authors postulated that hypocalcemia resulted in the leakage of myoglobin from muscle cells, resulting in the elevated serum CK levels.

It has been postulated that patients with idiopathic hypoparathyroidism who develop myopathy with elevated CK probably remain minimally symptomatic due to the slow development of the hypocalcemia and the remarkable ability of the body to adapt to chronically low serum calcium levels.[2] A recent study retrospectively analyzed the clinical data of 9 patients with idiopathic hypoparathyroidism during the years 2006-2010 and found that there is an inverse relationship between serum calcium and CK.[15] Mild to moderate muscle cell degeneration was present in almost all patients. The degree of muscle change was related to the duration, but not the degree of hypocalcemia.

Table 2. Creatine Kinase, Calcium Values, and Presenting Symptoms from Case Reports

Authors	Year	Age	Sex	Duration of symptoms	Symptoms	Creatine Kinase[a]	Calcium[a]	Cataracts[b]
Wolf et al[1]	1972	53	M	5 years	Hand and feet cramps	1580 IU/L(5-50)	5.1mg% (9-11)	no
Barber et al[2]	2001	71	M	1 year	Anorexia, lethargy, stiffness	1600 U/L (<175)	1.13 mmol/L	no
Ishikawa et al[3]	1990	15	M	6 years	Seizures, mental retardation	315 IU/L (10-200)	6.2mg/dL (8.5-10.5)	no
Nora et al[4]	2004	30	M	10 years	Mild weakness, muscle pain	1361 U/L (0-190)	3.9mg/dL (9-10.8)	yes
Syriou et al[5]	2005	47	M	8 months	Myopathy, skin rash	3281 U/L (20-180)	1.1mmol/L (2.02-2.62)	no
Zambelis et al[6]	2009	62	M	1 year	Muscle weakness, paresthesias	1.29 U/L (26-174)	5.4mg/dL (8.1-10.4)	yes
Yamaguchi et al[7]	1987	65	F	20 years	Carpopedal spasm	756 IU/L (<110)	5.0mg/dL	yes
Roca et al[8]	1995	61	M	30 years, 2 years	Seizures, dementia	2220 U/L	5.5mg/dL	no
Kruse et al[9]	1982	13	F	2 years	Myopathy, waddling gait	268 U/L (<50)	0.98 mmol/L (2.2-2.6)	no
Van Offel et al[10]	2000	36	F	1 year	Fatigue, myalgia, muscle weakness	189 U/L(10-50)	5.1mmol/L (8.8-10.2)	no
Hower et al[11]	1974	8	F	7 years	Seizures	946 mU/mL (<50)	4.4 mg%	no
Walters[12]	1979	12	M	2 years	Muscle spasms, tingling	13.0 µmol/mL/hr (0.25 -3.6)	1.37 mmol/l	no
Wray et al[13]	1987	30	F	15 years	Muscle spasms ataxia	836 U/L	6.9 mg/dL	no
Akmal[14]	1993	45	F	5 days	Rhabdomyolysis	26080 U/L	4.1 mg/dL	no

[a]Normal values in parentheses.
[b]When cataracts were not mentioned in the published case report, it was assumed that there was no history of premature cataracts.

CONCLUSION

The association of hypoparathyroidism with myopathy and elevated CK levels is an important one to consider when evaluating patients with myalgias and muscle weakness. When this is recognized, treatment with calcium and calcitriol relieves symptoms and CK levels return to normal.

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REFERENCES

1. Wolf SM, Lusk W, Weisberg L. Hypocalcemic myopathy. *Bull Los Angeles Neurol Soc.* 1972;37(4):167-177.

2. Barber J, Butler RC, Davie MW, Sewry CA. Hypoparathyroidism presenting as myopathy with raised creatine kinase. *Rheumatology* (Oxford). 2001;40(12):1417-1418.

3. Ishikawa T, Inagaki H, Kanayama M, Manzai T. Hypocalcaemic hyper-CK-emia in hypoparathyroidism. *Brain Dev.* 1990;12(2):249-252.

4. Nora DB, Fricke D, Becker J, Gomes I. Hypocalcemic myopathy without tetany due to idiopathic hypoparathyroidism. *Arq Neuropsiquiatr.* 2004;62(1):154-157. Epub 2004 Apr 28.

5. Syriou V, Kolitsa A, Pantazi L, Pikazis D. Hypoparathyroidism in a patient presenting with severe myopathy and skin rash. Case report and review of the literature. *Hormones* (Athens). 2005;4(3):161-164.

6. Zambelis T, Licomanos D, Leonardos A, Potagas C. Neuromyotonia in idiopathic hypoparathyroidism. *Neurol Sci.* 2009;30(6):495-497.

7. Yamaguchi H, Okamoto K, Shooji M, Morimatsu S, Hirai S. Muscle histology of hypocalcemic myopathy in hypoparathyroidism. *J Neurol Neurosurg Psychiatry.* 1987;50(6):817–818.

8. Roca B, Mínguez C, Sáez-Royuela A, Simón E. Dementia, myopathy, and idiopathic hypoparathyroidism. *Postgrad Med J.* 1995;71(841):702.

9. Kruse K, Scheunemann W, Baier W, Schaub J. Hypocalcemic myopathy in idiopathic hypoparathyroidism. *Eur J Pediatr.* 1982;138(3):280-282.

10. Van Offel JF, De Gendt CM, De Clerck LS, Stevens WJ. High bone mass and hypocalcemic myopathy in a patient with idopathic hypoparathyroidism. *Clin Rheumatol.* 2000;19(1):64-66.

11. Hower J, Struck H, Tackmann W, Bohlmann HG. Myopathy and elevated serum enzymes in a case of hypoparathyroidism. *Z Kinderheilkd*. 1974;116(3):193-196.

12. Walters RO. Idiopathic hypoaparathyroidism with extrapyramidal and myopathic features *Arch Dis Child.* 1979;54(3):236-238.

13. Wray SH, Richardson EP Jr. Case records of the Massachussets General Hospital. Weekly clinicopathological exercises. Case 34-1987. A 30-year-old woman with an ocular motility disturbance, myopathy, and hypocalcemia. *N Engl J Med.* 1987;317(8):493-501.

14. Akmal M. Rhabdomyolysis in a patient with hypocalcemia due to hypoparathyroidism. *Am J Nephrol.* 1993;13(1):61-63.

15. Dai CL, Sun ZJ, Zhang X, Qiu MC. Elevated muscle enzymes and muscle biopsy in idiopathic hypoparathyroidism patients. *J Endocrinol Invest.* 2012;35(3):286-289.

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