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HYPOCALCEMIC MYOPATHY WITHOUT TETANY DUE TO IDIOPATHIC HYPOPARATHYROIDISM

Case report

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ABSTRACT - Myopathy due to idiopathic hypoparathyroidism is very unusual. We report on a 30 years-old man referred with complaints of sporadic muscle pain and mild global weakness for 10 years. His physical examination showed normal strength in distal muscle and slightly weakness in the pelvic and scapular girdles with no atrophy. Deep muscle reflexes were slightly hypoactive. Trousseau's and Chvostek's signs were absent. He had bilateral cataract and complex partial seizures. His laboratory tests showed decreased ionised and total calcium and parathyroid hormone and increased muscle enzymes. EMG and muscle biopsy was compatible with metabolic myopathy. After treatment with calcium and vitamin D supplementation he showed clinical, neurophisiological and laboratorial improvement. In conclusion: patients with muscle symptoms, even when non-specific and with normal neurological examination, should have serum calcium checked, as myopathy due to idiopathic hypoparathyroidism, even being rare, is treatable and easy to diagnose.

KEY WORDS: myopathy, hypocalcemia, hypoparathyroidism.

Miopatia hipocalcêmica secundária a hipoparatireiodismo idiopático sem tetamia: relato de caso

RESUMO - Miopatia secundária a hipoparatireidismo idiopático é enfermidade raramente descrita. Relatamos o caso de homem de 30 anos que procurou atendimento médico com queixas de dores musculares e discreta fraqueza há cerca de 10 anos. Ao exame físico apresentava leve diminuição de força na musculatura pélvica e escapular, sem atrofia, ou fraqueza distal. Os reflexos miotáticos fásicos eram hipoativos e não havia sinais de Trousseau ou Chevostek. Havia história de catarata bilateral e crises parciais complexas. Os exames laboratoriais demonstraram hipocalcemia, com diminuição do paratormônio, hiperfosfatemia e enzimas musculares elevadas. A EMG e a biópsia de músculo foram compatíveis com miopatia metabólica. Após reposição de cálcio e vitamina D houve melhora clínica e neurofisiológica. Em conclusão: em pacientes com sintomas musculares, mesmo não específicos para miopatia ou com exame neurológico normal, deve-se dosar cálcio sérico, já que miopatia associada a hipoparatireoidismo é uma doença facilmente diagnosticada e tratável.

PALAVRAS-CHAVE: miopatia, hipocalcemia, hipoparatireoidismo.

Myopathy due to idiopathic hypoparathyroidism (IHP) is an extremely rare condition, with little more than 10 cases described in the literature, and its pathophysiology is not well established[1-4]. IHP is an infrequent disease of unknown aetiology, caused by insufficient secretion of parathyroid hormone (PTH). Its estimated prevalence in Japan is 7.2 cases per million individuals[5]. The reduced secretion of this hormone leads to hypocalcemia and hyperphosphatemia, due to the inhibition in calcium reabsorption in distal tubules and bone matrix, and also to the deficiency in the synthesis of 1,25-dihydroxyvitamin D. The clinical manifestations of IHP are multiple and affect mainly tissues of ectodermic origin. Among the most common findings in these patients are cataracts, hair loss and dental abnormalities. Nervous system involvement can manifest as seizures, emotional lability, psychosis, cognitive slowing, mental retardation, dementia, symmetric basal ganglia calcifications and acroparesthesia. Cases of tetany and smooth muscle spasm in organs such as the larynx are also described, but muscular involvement is relatively rare[6]. Due to its varied and non-specific symptoms, IHP is usually diagnosed many years after its onset, and symptoms related to the involvement of muscular fibres

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can remain undetected even in diagnosed cases. These are usually discrete, with complaints of fadigue or slight proximal weakness, and in these cases there might be no abnormalities at routine neurological examination. Therefore, myopathy due to IHP is rarely diagnosed, both in patients with diagnosed IHP and in those with non-specific complaints suggesting muscle disease.

We describe the clinical and laboratory findings in a case of myopathy secondary to IHP, and discuss the pathophysiology and differential diagnosis of this little-known disease.

CASE

A 30 year-old man was referred to our service with a history of mild generalized weakness and sporadic muscle pain during the last 10 years. The patient complained of feeling fatigued with little variation throughout the day, but did not have difficulty in climbing stairs or carrying heavy objects. Because the symptoms were mild and did not have a major impact in his daily living, he did not seek medical help when they first appeared. At 25, he underwent surgery for correction of bilateral cataracts. Two years afters, he presented with a complex partial seizure and was started on carbamazepine. Shortly after, he underwent an EEG, which demonstrated epileptiform activity in the left temporal region, as well as a head CT that showed bilateral calcifications in the basal ganglia. When he was 30 years old, the patient was referred to our service due to slowness of thought, persistent fatigue and a feeling that his muscles were "hardened". He denied having a history of alcohol consumption, perinatal complications and developmental delays as a child, or a family history of neurologic or neuromuscular disease. He was alert and oriented, his speech was coherent and his general physical examination was positive only for a left corneal opacity. At neurologic examination, he had no alterations in cranial nerves, sensibility, coordination or balance. There was no evidence of involuntary movements, and Trousseau's and Chvostek's signs were negative. Strength was normal in distal muscle and slightly reduced in the pelvic and scapular girdles. Deep muscle reflexes were slightly hypoactive. Muscle tone was normal and there were no fasciculations or atrophy in any muscle group.

The patient underwent laboratory tests (Table 1), a new brain CT (Fig 1) and an ECG, which showed a prolonged QT interval. Electromyography (EMG) demonstrated normal insertional activity, a few fibrillation potentials of low amplitude, no fasciculation potentials, adequate muscle recruitment and the presence, in proximal muscle groups, of polyphasic, low-amplitude and short duration motor unit action potentials, in alternation with potentials of normal shape, amplitude and duration. Sensory and motor nerve conductions were normal, with no conduction blocks, and the latency of the F wave at the tibial nerve was normal. A biopsy of the left quadriceps showed discrete sarcolemmal alterations compatible with non-specific myopathy, without an associated inflammatory infiltrate.

Table 1. Laboratory tests.

Test	Result		
	Before treatment	After treatment	Reference values
Hemoglobin (g/dl)	12.45		
Leucocytes (/mm^3)	6580		
Urea nitrogen (mg/dl)	34	15-40	
Creatinine (mg/dl)	0.9	0.9	0.5-1.2
Glucose (mg/dl)	99		60-110
Sodium (mEq/L)	137	138	135-145
Potassium (mEq/L)	4.9	4,8	3.5-5.2
Calcium, total (mg/dl)	3.9	9.5	9-10.8
Calcium, ionised (mg/dl)	2	4.1	4-4.8
Magnesium (mg/dl)	1.9	2.0	1.9-2.5
Phosphorus (mg/dl)	6.9	5.1	3-5
AST (U/L)	31		9-43
ALT (U/L)	40		11-41
LDH (U/L)	756		<425
CK (U/L)	1361	166	0-190
Aldolase (U/L)	7	6	<7.6
ESR (mm/h)	37		0-15
PTH (pg/ml)	<1	1.1	12-72
Thyroxine (μg/dl)	8.97		4.5-12.5
TSH (μUI/ml)	2.25		0.4-4

According to the findings described above the diagnosis of hypocalcemic myopathy was established, and treatment with calcium and vitamin D was started. Few months after the patient begun his treatment he showed clinical, neurophisiological and laboratorial improvement.

DISCUSSION

The association of the patient's symptoms and physical findings with an EMG and a muscle biopsy that showed a non-specific, non-inflammatory muscle lesion and a significant hypocalcemia and hyperphosphatemia with a very low PTH, are consistent with the diagnosis of hypocalcemic myopathy secondary to idiopathic hypoparathyroidism. Myopathy associated with hypocalcemia is better described in the literature when associated with osteomalacia. In this cases, however, CK tends do be normal[7], whereas in our case it was strikingly elevated. Since the first description by Wolf et al.

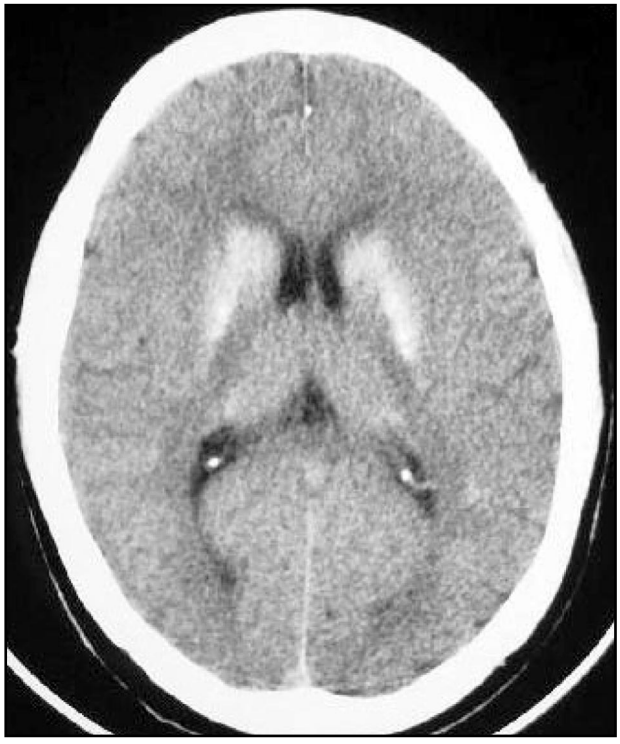

Fig 1. CT showing bilateral basal ganglia calcifications.

in 1972[3], there have been very few cases of hypocalcemic myopathy with an increased CK, and almost all of them were due to IHP[1,2,8-10], but this finding can also be observed in pseudohypoparathyroidism[11].

The reason for the increased CK levels found in these myopathies is not completely established. It has been proposed that it could be due to tetany, but there are reports of enzyme elevations unrelated to its occurrence[4,12]. Our patient, for example, had elevated CK levels with no evidence of tetany, and his Trousseau's and Chvostek's signs were negative. Another hypothesis is that hypocalcemia could induce functional alterations in the sarcolemma, leading to the release of CK and myoglobin[4,8]. Kruse[1] suggests that hypocalcemia can change the enzyme content of striated muscle with no significant morphologic or structural abnormalities. If this is the case, then the CK increase would not be secondary to tetany alone, and hypocalcemic myopathy would represent a distinct pathological entity[4]. The histological findings in our case are in agreement with the literature descriptions of mild alterations and no structural or inflammatory lesions at biopsy, indicating a mild, non-specific myopathy which supports the hypothesis of a functional change in striated muscle[4,11,13,14]. The very low serum levels of PTH, hypocalcemia and hyperphosphatemia seen in the patient are the characteristic findings of IHP. Mitochondrial myopathies, such as Kearn-Sayres syndrome (KSS) are also associated with endocrine and metabolic abnormalities such as hypoparathyroidism[15]. In KSS, however, the classic triad of pigmentary retinopathy, ophtalmoplegia and cardiac muscle conduction defects is almost always present before age 20, and frequently appears in the first decade of life[15,16]. None of these findings was seen in our case, and the onset of fatigue, weakness and bilateral cataracts at age 20 were the first symptoms of the patient's disease. Subsequently, there was the report of seizures and cognitive slowing. It is important to realise that, despite the patient's symptoms, a serum calcium measurement was not obtained until he was 30 years old. Barber et al.[13] have reported the importance of measuring serum calcium in patients with non-specific muscle symptoms, as this simple test can allow the diagnosis of hypocalcemic myopathy, an easily treatable condition. An early measurement of serum calcium is even more important when one consider that cases of proximal weakness with increased CK can be misdiagnosed as polymyositis and treated with corticosteroids. Besides being ineffective, steroids inhibit intestinal calcium absorption and increase renal calcium excretion, leading to a worsening of the hypocalcemia and, consequently, of the patient's symptoms.

The pathophysiology of the muscle lesion in IHP is not completely understood[14], although it probably relates to hypocalcemia. The decrease in calcium concentration causes an increase in excitability at the neuromuscular junction, with a smaller degree of depolarization being needed to generate an action potential[14], and these alterations can occasionally lead to tetany[4]. In addition, it is likely that there are ultrastructural modifications, which occur in response to the metabolic abnormalities and cause muscle function to be less effective. Therefore, we suppose that every patient with IHP or another disease causing chronic hypocalcemia probably suffers some degree of muscle damage[17].

We believe, therefore, that IHP-associated myopathy, although rare, can occur with a greater frequency than the one described in the literature. This is probably due to the fact that this myopathy is rarely diagnosed, even in patients with chronic hypocalcemia, as the clinical manifestations of these patients, except for those developing tetany, are subjective and non-specific. In some patients, for example, the only objective sign of disease

might be myoglobinuria[18]. Two recommendations should be made, therefore, to allow an early diagnosis of this disease and a better understanding of its pathophysiology. The first is to obtain CK measurements in every patient with a diagnosis of hypoparathyroidism or other conditions leading to chronic hypocalcemia. One should also keep in mind the possibility of performing EMG and muscle biopsy in these cases. The second recommendation is to perform serum calcium measurements in patients with myoglobinuria or nonspecific complaints suggesting muscle disease, such as fatigue, muscle aches and weakness, especially those with proximal weakness of unknown aetiology.

We emphasise that the diagnosis of hypocalcemic myopathy secondary to IHP is important not only for obtaining a better understanding the pathophysiology of this condition, but fundamentally because of the availability of unexpensive and effective treatment options for this disease, with a few simple measures leading to a great improvement in the patient's quality of life.

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