

# Nerve, muscle or bone disease? Look before you leap

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## ABSTRACT

**Severe muscle weakness in osteomalacia may mimic a primary neuromuscular disorder like spinal muscular atrophy. A 32-year-old woman, initially diagnosed as a case of spinal muscular atrophy based on clinical presentation, electromyography and muscle biopsy, was later found to have osteomalacic myopathy due to primary hyperparathyroidism complicated by vitamin D deficiency. Before diagnosing a progressive, inevitably fatal degenerative condition like spinal muscular atrophy, one must rule out all possible treatable conditions with a similar presentation.**

**Keywords: primary hyperparathyroidism, myopathy, osteomalacic myopathy, spinal muscular atrophy**

*Singapore Med J 2009; 50(8): e293-e294*

## INTRODUCTION

Severe muscle weakness in primary hyperparathyroidism (PHPT) associated with vitamin D deficiency may mimic a primary neuromuscular disorder.<sup>(1,2)</sup> Before diagnosing a progressive, inevitably fatal degenerative condition like spinal muscular atrophy, one must rule out all possible treatable conditions with a similar presentation.

## CASE REPORT

A 32-year-old woman presented with progressive painful proximal muscle weakness of three years' duration. She initially noticed undue fatigue, and vague muscle and bone pains. Thereafter, she experienced difficulty rising from a squatting position and climbing stairs. Muscle weakness progressively involved upper limbs and trunk muscles, and she was bed-bound for six months prior to presentation. She had noted generalised thinning of her limbs with no twitching, stiffness or sensory loss. There was no cranial nerve deficit or sphincter disturbance. There was no fever, rash, arthritis, fracture or kidney stone. There were no symptoms suggestive of kidney or liver disease or malabsorption. She had been diagnosed to have primary hypothyroidism ten years ago for which she was on regular thyroxine supplementation with euthyroid

status. She had successfully delivered a healthy child four years prior, with no neonatal complications. She had poor milk intake, little sun exposure and had been irregular with calcium and vitamin D supplements during pregnancy, lactation and thereafter. There was no history of prolonged glucocorticoid or anticonvulsant drug intake or similar illness in the family.

She was initially evaluated by a neurologist who suspected a primary neuromuscular disorder. Serum potassium, muscle enzymes, creatinine phosphokinase, lactate dehydrogenase and renal and liver functions were normal. Serum vitamin B<sub>12</sub> level was normal. Magnetic resonance imaging of the cervical and dorsal spine showed no abnormality. Electromyography (EMG) showed variable amplitude of motor unit action potentials, and recruitment pattern with no spontaneous activity reported as neurogenic pattern. Nerve conduction studies showed normal amplitudes and velocities. Muscle biopsy showed Type II fibre atrophy with no inflammatory changes concluded as neurogenic atrophy. She was diagnosed to have anterior horn cell disease (spinal muscular atrophy) and prognosticated regarding its relentless downhill course and eventual fatal outcome.

She was reviewed on request for a second opinion. Detailed examination at this stage revealed a frail woman with generalised muscle thinning, diffuse muscle and bone tenderness. She was afebrile and normotensive with tachycardia, tachypnoea and shallow respiratory effort. A Grade II firm diffuse goitre was palpable with no other neck mass. Nervous system examination revealed diffuse muscle wasting, Grade II to III muscle power, sluggish deep tendon jerks and flexor plantar response. Respiratory muscle weakness was demonstrable by poor chest expansion and single breath count. Sensory examination was normal. There was no evidence of bulbar muscle weakness, cranial nerve deficit or autonomic dysfunction.

Laboratory evaluation was reviewed for reconsideration of the diagnosis and to rule out any treatable conditions. Serum chemistry for calcium, phosphorus, alkaline phosphatase (ALP), which was not done earlier, was ordered. A markedly elevated ALP 10,200 IU/L (normal range [NR] 60–120 IU/L) suggested the diagnosis of osteomalacic myopathy. An

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elevated calcium 11.2 mg/dL (NR 8.4–10.5 mg/dL) and simultaneous intact parathyroid hormone (PTH) 167 pg/ml (NR 10–65 pg/ml) was diagnostic of PHPT. Serum 25-hydroxy vitamin D was 2.1 ng/ml (NR > 30 ng/ml). A limited skeletal survey, including radiography of the hands, pelvis and skull, showed diffuse osteopenia, subperiosteal resorption, pseudofractures (Looser's zones), and a salt and pepper appearance of the skull bones. Ultrasonography of the neck showed a right inferior parathyroid gland adenoma, which was confirmed on computed tomography.

In view of the severe respiratory muscle weakness and poor respiratory reserve which precluded general anaesthesia for parathyroid surgery, initial stabilisation was planned. She was treated with a single dose of vitamin D<sub>3</sub> 600,000 IU intramuscular injection with daily oral calcium carbonate 1,000 mg. Oral calcitriol 0.25 mcg twice daily was administered for the first four weeks for rapid response. Her preoperative course was complicated by bilateral bronchopneumonia and Type I respiratory failure (hypoxaemia), which was managed with broad-spectrum antibiotics, oxygen by mask and chest physiotherapy. Over the next four weeks, as her general condition, including respiratory muscle strength, improved and chest infection resolved, she successfully underwent a parathyroid adenoma resection. Postoperatively, she had severe symptomatic hypocalcaemia due to hungry bone syndrome, which was managed with intravenous calcium gluconate infusion on a dose of 15 mg/kg body weight daily over the next two weeks. Oral calcium and vitamin D supplementation were continued thereafter. Serum calcium and phosphorus normalised in the postoperative week, and the ALP level gradually declined. Over the next 12 months, her bone and muscle pains subsided, and there was marked improvement in her muscle bulk and strength. She started walking with minimal support and resumed her activities of daily living.

## DISCUSSION

A young woman with severe progressive painful myopathy was diagnosed with anterior horn cell disease (spinal muscular atrophy) based on EMG and muscle histopathology. A review of the case, using a systematic algorithmic approach to rule out treatable causes of painful myopathy with simple biochemical evaluation, led to correct diagnosis, appropriate treatment and gratifying recovery. Clinical pointers to the possibility of PHPT complicated by osteomalacic myopathy were

a history of inadequate sun exposure, calcium and vitamin D intake, diffuse muscle and bone tenderness, and hypercalcaemia with elevated PTH and ALP levels. Neuromuscular involvement in hyperparathyroidism and vitamin D deficiency-related osteomalacia have been well documented.<sup>(3)</sup> With early diagnosis of asymptomatic PHPT by calcium screening and widespread vitamin D fortification, severe neuromuscular manifestation of PHPT and vitamin D deficiency are becoming a rarity in the developed world. However, such cases are still frequently encountered in the Indian subcontinent.<sup>(4)</sup>

Electromyographic changes in a case of osteomalacic myopathy may often mimic a primary neuromuscular disease.<sup>(1)</sup> Muscle fibre atrophy on muscle biopsy in cases with severe vitamin D deficiency and hyperparathyroidism may appear similar to the changes seen in anterior horn cell disease.<sup>(1,2)</sup> Hence these conditions may present as a diagnostic dilemma to the treating clinician. Serum ALP is a simple, widely-available and inexpensive screening tool in cases suspected to have osteomalacia. Dramatic response to vitamin D replacement with improved muscle strength and normalisation of ALP confirms the diagnosis of osteomalacic myopathy. Replacement of vitamin D in PHPT associated with vitamin D deficiency needs to be given without the fear of worsening hypercalcaemia, as has been shown in the literature.<sup>(5,6)</sup>

Treatable conditions like osteomalacic myopathy should be ruled out before establishing the diagnosis of a degenerative disorder like spinal muscular atrophy. A simple, algorithmic approach to a neuromuscular syndrome of this nature should include serum calcium, phosphorus and ALP estimation, to rule out osteomalacic myopathy.

## REFERENCES

1. Mallette LE, Patten BM, Engel WK. Neuromuscular disease in secondary hyperparathyroidism. *Ann Intern Med* 1975; 82:474-83.
2. Carvalho AA, Vieira A, Simplicio H, et al. Primary hyperparathyroidism simulating motor neuron disease. *Arq Neuropsiquiatr* 2005; 63:160-2.
3. Gilchrist JM. Osteomalacic myopathy. *Muscle Nerve* 1995; 18:360-1.
4. Harinarayan CV, Gupta N, Kochupillai N. Vitamin D status in primary hyperparathyroidism in India. *Clin Endocrinol (Oxf)* 1995; 43:351-8.
5. Grey A, Lucas J, Horne A, et al. Vitamin D repletion in patients with primary hyperparathyroidism and coexistent vitamin D insufficiency. *J Clin Endocrinol Meta* 2005; 90:2122-6.
6. Muthukrishnan J, Jagdish Kumar P, Ratan Jha, Modi KD. Vitamin D therapy in tertiary hyperparathyroidism: Is there a cause for being overcautious? *Ind J Nephrol* 2007; 17:187.