Case Report

Rare Treatable Limb Girdle Muscle Disease

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Abstract

We report two cases of Limb Girdle pattern of muscle weakness caused by hyperparathyroidism due to parathyroid adenoma. It can be easily missed as early symptoms are non specific but once diagnosed it is easily treatable and complete recovery occurs over a period of time.

Introduction

Proximal muscle weakness of upper limbs and lower limbs are commonly seen in patient with degenerative diseases like spinal muscular atrophy, dystrophic muscle disease and also endocrine, metabolic inflammatory and myoneural junction disease. Always an attempt should be made to look for treatable cause. Other evidences of endocrine dysfunction, joints, skin and other system involvement, rapid progression, significant pain, constitutional symptoms and well elicited reflexes point to possible secondary cause. It is always important to look for such clues clinically as even laboratory data can be misleading unless they are directed specifically at suspected diagnosis. Here we report two cases of muscle weakness associated with hyper parathyroidism.

Case 1

Thirty two year old female presented with the following history, during July 2005 at Medical College Thiruvanathanpuram. Her illness started nine years ago as recurrent dislocation of the patella. This was followed by fatigue, difficulty in climbing up, getting up from sitting posture and frequent buckling. She experienced disabling pain in the infrascapular, sub costal region and low back. This was followed by difficulty in lifting objects and drooping of shoulders (Figure 1).

She was evaluated at several places with MRI spine, electrophysiological studies and muscle biopsy. Electrophysiology showed mixed picture in the form of positive sharp waves in the resting muscle and motor unit action potentials were showing myopathic picture. Muscle biopsy showed group atrophy (Figure 2). There were no inflammatory cells. Hence, she was diagnosed as suffering from degenerative muscle disease. However as her symptom was progressive she was brought to Medical College Hospital, Thiruvananthapuram. Examination showed pallor, hyper extensible joints and mild hypertension 150/100mm Hg.

Neurological evaluation showed normal cranial nerves. Her power was grade four proximally and normal distally in the upper limbs and grade three proximally and grade four distally in the lower limbs. There was no wasting, hypertrophy, pseudo hypertrophy or fasciculation. Deep tendon reflexes were grade three in all groups. Superficial reflexes, organic reflexes, primitive reflexes and sensations were normal. This finding of exaggerated reflexes in the setting of a muscle disease prompted us to examine her thyroid gland. There was a palpable circumscribed swelling about one cm in size seen at the right inferior pole of thyroid gland. She had no goitre.

Her investigations showed normal urine examination, Hb: 9.1gm%, TC: 5600 cells/ cu.mm, Neutrophil 49%, Lymphocyte: 50%, Eosinophil :1%, ESR 40mm/hr. Platelet count 3.2lac/cu mm.

Peripheral smear showed normocytic normochromic anemia, random blood sugar 95mg/dl, urea 30mg, creatinine 1mg, CPK 35 u/l(25 to 1950),LDH 657 u/l (163-518),alkaline phosphatase 1038 u/l (15- 1450), serum calcium1mg/dl on admission and when repeated six days later showed 12mg/dl, phosphorus 2mg/dl (2.5 to 4.5). Magnesium levels were not done. Parathormone level was 100 pg/ml (10 to 60). Anti nuclear antibody, Rheumatoid factor, LE cell, Anti double stranded DNA antibody and thyroid functions were normal. ECG and echocardiogram were normal. EMG repeated in our institution showed myopathic pattern in the following sampled muscles, right quadriceps femoris, right biceps, right adductor pollicis brevis and deltoid.Muscle biopsy was not repeated in our department. Muscle biopsy is a invasive procedure and it was not considered necessary in this case, for the following reason. Denervation changes are common in chronically disused muscles. The fast twitch fibres when not put in use undergo atrophy irrespective of the cause of the patients problem, especially type 2 fibres become angular and appear to group themselves. This picture should not be interpreted as anterior horn cell disease without correlating with other phenotypic characters.

Ultrasound scan of thyroid showed 22 x18 mm hypo echoic lesion in relation to posterior and inferior part of right lobe of thyroid gland and 8 x 6.7 mm lesion with tiny calcification in the left inferior lobe. Ultrasound scan of abdomen showed tiny calcifications involving medullary region and calyces of both kidneys. Parathyroid scintigraphy using 99 MTC- methoxy isobutyl isonitride showed bilateral inferior parathyroid adenoma; right larger than the left. (Figure 3). X-ray skull lateral view showed classical pepper salt skull (Figure 4). X-ray pelvis and chest showed diffuse osteopenia involving all bones. There was narrowing of pubic symphysis (Figures 5 and 6). X ray of both hands showed sub-periosteal bone resorption. (Figure 7)

Patient underwent para-thyroidectomy of both inferior and left superior gland and subtotal thyroidectomy. (Figure 8) Post operatively patient’s serum calcium rose to 13.6 mg/dl and remained at 11mg /dl until the fourth post operative day. This was treated with 0.9 % Sodium chloride intravenously at 20 ml/kg in the first one hour followed by slow continuous infusion along with 20 mg of Frusemide fourth hourly to facilitate renal excretion of calcium. Reassessment of calcium on the sixth day showed 8.5mg/dl and patient clinically developed features of hypocalcaemia in the form of muscle cramps. This was treated

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with 1.5gms of oral calcium /day. By the end of six months her phenotypic characters including myopathy completely reverted to normal. (Figure 9) Her hypertension was treated with beta blockers which could be withdrawn after few months completely.

**Case 2**

Twenty year old female was treated with plaster of paris cast for a fracture which she sustained in the lower end of right femur following a fall in the year 1999. Two months later when she started bearing weight it was found that she could not get up from sitting posture and was buckling while standing. She had a collapsing chest cage with limb girdle pattern of weakness. Her deep tendon jerks were exaggerated and superficial reflexes were normal. She had no cranial nerve palsy or sensory symptoms. She had normal thyroid gland with palpable nodule about one centimeter in size in the left inferior pole. Ultra sound scan abdomen showed bilateral stag horn calculi. Skeletal survey showed diffused osteopenia. Her serum calcium was 11.6 mg per and phosphorus 2.1 mg/dl, parathormone level 110 pg/dl. She opted to undergo surgery at her native state. However it was reported that in the postoperative period she went in stupor and could not be saved. No pictures with reference to this patient is available. In view of the unfortunate eventuality which happened to this patient.

**Discussion**

The most common manifestation of primary hyperparathyroidism is asymptomatic hypercalcemia accidentally detected. Severe bone and stone disease is seen in places where hypovitaminosis D exists. The symptoms and signs are due to the combined effect of increased parathormone secretion and hypercalcemia. Non specific symptoms like fatigue, anorexia, depression are common. Five percent of patients present with bone disease and 15 to 20% with nephrolithiasis.

The neuro muscular syndrome associated with hyperparathyroidism is extremely rare. Clinically exaggerated reflexes and histopathologically type II fibre atrophy can be seen.

Neuropsychiatric manifestations in the form of lethargy, depressed mood, and cognitive decline can occur. However improvement after surgery is variable. Fractures are common at distal forearm, pelvic and vertebra. Bone thinning due to endosteal bone resorption appears to be the cause.

Hypertension is a common association with hyperparathyroidism. Left ventricular hypertrophy and diastolic dysfunction are also known. However, evidence for improvement of these features after surgery is lacking. Rheumatological complications in the form of pseudo gout with pyrophosphate crystals in the joints hyper uricaemia, gout and calcifications of articular cartilage are common.

Severe classical hyperparathyroidism is associated with increased mortality due to cardiovascular disease. There is a small increase in the risk of death from cancer. Parathyroid crisis is severe hypercalcemia with serum calcium more than 15 mg/dl and central nervous system dysfunction in the form of coma and confusion. This can be precipitated by associated inter current infection and dehydration.

The pathogenesis of neuro-muscular complications have been described. Serum phosphate concentration decreases because parathormone inhibits proximal tubular reabsorption of phosphate leading to increased phosphate excretion. This is due to decreased activity of sodium phosphate co-transporter in the luminal membrane. So entry of filtered phosphate into tubular cells and its return to systemic circulation is reduced. Hypophosphatemia limits the phosphorylation reaction and synthesis of ATP in muscles and this leads to weakness. Hypocalcaemia is expected due to reuptake of calcium in to the hungry bones once parathormone level comes down.
Limb girdle pattern of muscle weakness occurs in a vast majority of conditions. Painless non selective wasting, weakness, areflexia, fasciculations and tremors with normal muscle enzymes, denervation pattern in EMG and biopsy suggest spinal muscular atrophy. Painless muscle weakness with selectivity pseudo hypertrophy, retained ankle jerk, abnormal muscle enzymes, myopathic pattern in EMG and biopsy suggest dystrophic muscle disease. Painful muscle weakness with brisk reflexes, mild to moderate enzyme changes, inconclusive electrophysiology and histology with evidence for other system involvement should alert the physician regarding treatable
Lessons learnt

Primary hyperparathyroidism is a condition to be remembered in patients with muscle weakness and exaggerated reflexes. As the symptoms and signs can be evasive, diagnosis can be easily missed. If not treated on time multisystem involvement occurs and can result in mortality. Denervation pattern in EMG can be seen in less used muscle and does not always indicate anterior horn cell disease. Immediate post operative hypercalcemia and later hypocalcemia are expected complications and should be managed adequately.

Conclusion

Whatever may be the duration of the illness when unusual features complicate common illnesses, it’s always worthwhile to look for less common and treatable factors. Primary Hyper parathyroid myopathy is a relatively less common limb girdle muscle disease which presents with exaggerated tendon reflexes and is completely reversible with surgery of parathyroid adenoma.

References