

Osteomalacia in adolescents presenting as proximal myopathy

Hessah M. AL-Otaibi, Nasir A.M AL-Jurayyan, Sarar Mohamed, Mustafa A. M. Salih

Department of Pediatrics, College of Medicine and King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia.

Abstract

We report three adolescent patients with osteomalacia who presented initially with clinical features consistent with proximal myopathy. All patients had low serum level of 25 hydroxy vitamin D. Furthermore, radiological investigations confirmed osteomalacia. Myopathy responded well to appropriate treatment of osteomalacia. Possible pathophysiologic explanation of myopathy in patients with osteomalacia is discussed, and this report highlights that osteomalacia is an important treatable cause of proximal myopathy in adolescents.

Key words: Osteomalacia, Myopathy, Vitamin D deficiency.

Accepted September 06 2011

Introduction

Rickets and osteomalacia are two distinct conditions arising from the common event of mineral insufficiency. Rickets is often referred to as failure of mineralization of a growing bone, whereas osteomalacia indicates failure of a mature bone to mineralize [1]. In developing countries, vitamin D deficiency rickets is still considered as a major community health problem in infants and children. Likewise, Osteomalacia is reported with increasing frequency among adolescents [2-6]. Despite having economic affluence and adequate sunlight all over the year, rickets and osteomalacia emerged as a significant risk for Saudi children and adolescents [7-11]

Proximal myopathy may occur in association with several muscle diseases. However, myopathy associated with endocrinopathies is rare. Vitamin D deficiency is an unusual cause of myopathy [12-17]. This causative association can easily be overlooked although the condition is readily treatable.

In this article, we present our experience with three adolescent patients with osteomalacia who presented with proximal myopathy. Our patients responded to vitamin D therapy. This report elucidates the importance of considering rickets and osteomalacia in the assessment of patients presenting with myopathy.

Case 1

A 15-year-old female presented to our endocrinology clinic with history of progressive weakness, fatigability and lethargy. Her condition worsened in the last two years

prior to presentation to our clinic. She complained of difficulty in climbing stairs and standing up from sitting position. She had been on regular family diet with low milk intake. She reported minimal sun exposure in her daily life. She had no symptoms to suggest malabsorption, liver and renal diseases. She has no history of fracture. Examination revealed a fully conscious, alert girl with stable vital signs. Growth assessment indicated that her weight was 48 kg at 50th centile, and her height was 152cm at 25th centile. She had no dysmorphic features. Cardiovascular, chest and abdomen examination was normal. Examination of the central nervous system revealed normal higher centers and cranial nerves. Patient had waddling gait, was unable to rise from squatting position with proximal muscle weakness which was easily demonstrated by failure to overcome mild resistance at lower limbs and by moderate resistance at upper limbs. There was no evidence of muscular atrophy or tenderness either in the upper or lower limbs. Deep tendon reflexes and sensation were intact.

Laboratory investigations showed normal complete blood count (CBC), ESR, renal function, blood gas, liver function, CPK, celiac screening and thyroid function. Serum corrected calcium was 1.68 mmol/l (N= 2.1-2.55), phosphorus 1.06 mmol/l (N= 0.87-1.45) and ALP, 1325 U/L (N= 50-136). PTH was normal while 25 hydroxy vitamin D was very low as shown in Table 1. X-ray of skeleton showed severe generalized osteopenia with no fractures. DEXA scan of the spine and long bones confirmed osteopenia with T score < -2.5 SD below expected mean for sex and age. EMG was normal. In view of confirmed osteomalacia biochemically and radiologically, our pa-

tient was commenced on alphacalcidol one microgram twice daily for two months. After which the patient improved dramatically in terms of mobility, muscle power and feeling of well-being.

Case 2

A 13-year-old girl presented to our pediatric neurology clinic with leg pain and progressive difficulty in walking for two years. She had difficulty in standing up from a sitting position as well as in climbing stairs. Later, she developed leg deformity of both lower limbs. She had no history of renal, gastrointestinal or liver disease. Examination showed a well nourished girl with no dysmorphic features. Her weight was 50 kg at 50th centile and her height was within the predicted genetic height 140 cm at 10th centile. All systems were normal apart from a waddling gait, knock knees and reduced muscle power to grade four in both upper and lower limbs with proximal muscles more affected than distal muscles. Routine investigations including CBC, CPK, renal, liver and thyroid functions were within the normal limits. Bone profile showed hypocalcaemia, hypophosphatemia together with high ALP. 25-hydroxyvitamin D was low and PTH was

elevated as shown on Table 1. X-ray showed generalized osteopenia. EMG showed non-specific changes. Based on these abnormal biochemical and radiological findings our patient was diagnosed as osteomalacia secondary to vitamin D deficiency. She was treated with vitamin D, calcium, and phosphate supplements. She responded well to treatment. Muscle power and gait returned to normal within two months of therapy.

Case 3

A 13-year-old girl presented to the Neurology Clinic with severe proximal muscle weakness for three years. She could not climb stairs, stand from sitting position and was bound to wheel chair most of the time. Clinical examination confirmed presence of proximal myopathy affecting both the upper and lower limbs. Routine laboratory workup for proximal myopathy was normal including CPK. Bone profile revealed low calcium, low phosphorus, high ALP together with low 25 hydroxy vitamin D as shown in Table. X ray showed severe osteopenia with no fractures. Few months following treatment with vitamin D and calcium, our patient improved and was able to walk and perform her daily activities unassisted.

Table 1. Biochemical profile of patients with Osteomalacia

Parameters	Normal range	Patient 1	Patient 2	Patient 3
Total protein	60-80 g/L	76	78	75
Albumin	30-50 g/L	40	36	45
Total calcium	2.1-2.55 mmol/L	1.68	1.96	2.05
Corrected calcium		1.7	2.04	1.95
Phosphorus	0.87-1.45 mmol/L	1.06	0.85	0.8
ALP	50-136 U/L	1325	1052	774
25 hydroxy vitamin D	23-113 nmol /L	1	11	13
PTH	1.65-6.9 pmol /L	7.26	272	15.24
CPK	30-200 mmol/L	71	46	94

Discussion

Vitamin D deficiency is the commonest cause of osteomalacia in adolescents. It is usually caused by low intake of vitamin D and calcium or resulting from limited sun exposure [18,19]. In Saudi Arabia, the exposure of people, especially females, to the sun is limited, despite of abundant sun light for different reasons including sociocultural factors and lack of awareness of the importance of sun exposure for bone health(9). Several studies from Saudi Arabia showed that vitamin D level tend to be low among the general population especially children and females [11,2].

In this report we describe three females with clinical and radiological evidence of osteomalacia who presented with symptoms and signs suggestive of proximal myopathy.

The association of vitamin D deficiency and myopathy can easily be overlooked in young adults as the signs of osteomalacia are not readily recognized compared to the clinical features of rickets in young children. CPK level was normal in our three patients whereas it is usually elevated in primary muscle diseases and is remarkably raised in muscular dystrophies. Normal CPK in the context of clinical evidence of myopathy may alert physicians to think of vitamin D deficiency as being the underlying cause. Few previous studies reported the association of myopathy with vitamin D deficiency [14-17]; and the response to treatment in our patients was remarkable in agreement with these reports [14-17]. This may be explained by the severe and long standing deficiency of vitamin D.

This present report provides further clinical evidence that vitamin D deficiency is implicated in the pathogenesis of

myopathy. However, the exact mechanism of muscle weakness in vitamin D deficient individuals is poorly understood [14,20]. It has been well established that vitamin D plays an essential role in the regulation of calcium and phosphate homeostasis and in bone development. Clinically vitamin D is known to exert its function on target organs, such as intestine, kidneys, parathyroid glands, and bones. Over the last two decades, however, there has been increasing evidence that vitamin D plays an important role in many other tissues including skeletal muscle [14, 15,17,20]. Early clinical descriptions of a reversible myopathy associated with vitamin D deficiency and or chronic renal failure recognised a potential association between vitamin D and muscle [14,15,17,20]. The identification of the vitamin D receptors (VDR) in muscle cells provided further support for a direct effect of vitamin D on muscle. Recent studies on animal cell culture have advanced our understanding of some of molecular mechanisms through which vitamin D targets skeletal muscle, however, much remains to be characterised [20].

Clinically, patients with parathyroid excess (such as hyperparathyroidism) share similar symptoms of muscle weakness and fatigue as in vitamin D deficiency. Furthermore, muscle biopsies demonstrate atrophy of type II muscle fibre in patients with PTH excess [20]. The question of whether vitamin D deficiency itself or secondary hyperparathyroidism is the primary cause of muscle abnormalities is still not fully answered [21]. Low vitamin D levels stimulate PTH production and PTH may have direct effect on skeletal muscle. Studies in animals have demonstrated that PTH induces muscle catabolism, reduces calcium transport and impair mitochondrial fatty acid oxidation in skeletal muscle [14,15,17,20]. All these may contribute to the development of myopathy associated with excess parathyroid hormone.

In conclusion, proximal myopathy is an uncommon but important feature of osteomalacia or rickets. In this article we highlight the importance of considering rickets or osteomalacia as one of the differential diagnosis of any patient who presents with muscle weakness.

Abbreviations

PTH Parathyroid Hormone
CPK Creatinine Phosphokinase
ALP Alkaline Phosphatase
EMG Electromyogram
DEXA Dual Energy X-ray Absorbtiometry

References

1. Harrison HE, Harrison HC. Rickets and osteomalacia. In: Scnafeer AJ, Markovitz M editors. Disorders of calcium and phosphate metabolism in children and ado-

1. lescence.Phildelphia (PA) W.B.Saunders 1979 p 141-256.
2. Lubani MM, ALSahb TS, Al Saleh QA, Sherda DC,Quattawi SA, Ahmed S.A , vitamin D deficiency in Kuwait, the prevalence of a preventable disease. *Ann Trop Paediatrics* 1989; 3: 134-139
3. Majid- Molla A, Badawi MH, AL-yashi S , Sharma P, EL Salaam RS, Molla A.M risk factors for nutritional rickets among children in Kuwait, *paediatric international* 2000; 42: 280-284
4. Ahmed I, Atiq M, Iqbal J, Khurshid M, Whittaker P, vitamin D deficiency rickets in breast fed infants presenting with hypocalcemic seizures. *Acta Pediatr* 1995; 84: 941-942.
5. Al-Atawi MS, Al-Alwan IA, AlMutair AN, Tamim HM, Al Jurayyan NA. Epidemiology of nutritional rickets in children. *Saudi Journal of Kidney Disease and Transplantation* 2009; 20: 260-265.
6. Erfan AA, Nafie OA, Neyaz AH, Hassanein MA. Vitamin D deficiency rickets in Maternity and Children Hospital, Makah, Saudi Arabia. *Ann Saudi Med* 1997; 17: 371-373.
7. Al Jurayyan NA, El Desouki ME, Al Herbish AS, Al Mazyad AS, Al Qhani MM, Nutritional rickets and osteomalacia in school children and adolescents. *Saudi Med J* 2002; 23: 182-185.
8. Abdullah MA, Salhi HS, Bakry LA et al .adolescent rickets in Saudi Arabia: a rich and sunny country. *J Pediatr Endocrinol Metab* 2002; 15: 1017-1025.
9. Siddiqui AM, Kamfar HZ, Prevalence of vitamin D deficiency rickets in adolescence school girls in western region, Saudi Arabia. *Saudi med J* 2007; 28: 441-444
10. Sedrani SH. Are Saudi at risk of developing vitamin D deficiency? *Saudi med J* 1986; 7: 427-433.
11. Sedrani SH, Abanamy A, Salman H, Al-Arabi K, EL Idrissi ATH , vitamin D status of Saudi children. Are Saudi children at risk of developing vitamin D deficiency rickets? *Saudi Med J* 1992; 13: 430-433
12. Dent, CE and Stamp, TCB hypophosphatemic osteomalacia presenting in adults. *Quarterly Journal of Medicine* 1971; 40: 303-329.
13. Pfeifer M, Begerow B, Minne HW. Vitamin D and muscle function. *Osteoporosis Int* 2002; 13: 187-94
14. Glerup H, Mikkelsen K, Poulsen L, et al. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. *Calcif Tissue Int* 2000; 66: 419-424.
15. Russell JA, Ostemalacic Myopathy. *Muscle Nerve* 1994; 17: 578-580
16. Swash M, Schwartz MS, Sergeant MK. Osteomalacic myopathy: an experimental approach. *Neuropathol Appl Neurobiol* 1975; 5:295-302
17. Skaria J, Katiyar BC, Srivastava TP, Dube B. Myopathy and neuropathy associated with osteomalacia, *Acta Neurol Scand* 1975; 51: 37-58
18. Bhan A., Rao AD, Rao AS. Osteomalacia as a result of vitamin D deficiency. *Endocrinology and Metabolism clinic* 2010; 39 (2): 321-331.

19. Rico H, Gomez F et al. Adult hypophosphatemic osteomalacia: report two cases. *Clinical Rheumatology* 1985; 4: 325-334.
20. Ceglia L. Vitamin D and skeletal muscle tissue and function, *Molecular Aspects of medicine* 2008; 29: 407-414.
21. Zanello SB, Collins ED, Marinissen MJ, Norman AW, Boland RL, Vitamin D receptor expression in chicken muscle tissue and cultured myoblasts. *Horm Metab Res* 1997, 29: 231-236.

Correspondence:

Hessah M AL-Otaibi
Department of Pediatrics
King Khalid University Hospital
King Saud University, Riyadh
Saudi Arabia