CASE REPORT

Phenytoin Induced Vitamin D Deficiency Presenting as Proximal Muscle Weakness

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A 6-year-old girl presented with proximal muscle weakness of lower limbs. She was receiving phenytoin for epilepsy for 2 years. Serum phenytoin level was within therapeutic range. Serum 25(OH) vitamin D was low (5ng/mL) and serum parathyroid hormone level was high. After administration of oral vitamin D, muscle weakness improved and vitamin D level increased to 39.11ng/mL. Proximal muscle weakness due to vitamin D deficiency following phenytoin intake is rare in children.

Key words: *Phenytoin, Proximal muscle weakness, Vitamin D deficiency*.

In children, muscle weakness due to vitamin D deficiency is rarely reported(1,2). We herein report one such case.

CASE REPORT

A 6-year-old female child presented with difficulty in walking and climbing stairs and a broad based gait for 10-15 days. She was being treated with phenytoin (5 mg/Kg/d) for generalized epilepsy, for last 2 years. The dietary intake was adequate, she was developmentally normal and anthropometry was appropriate for age. There was no sign of vitamin D deficiency on physical examination. Muscle bulk was equal on both sides, the muscle tone was normal; the muscle power was 3/5 in the flexors and extensors of the hip. Neurological examination revealed incomplete Gower's sign. There was no other neurological deficit. Serum phenytoin level was 2.7 µg/dL (normal 10-20 µg/dL), 25-OH vitamin D 5 ng/mL (normal 9-37.5 ng/mL), paratharmone 488 pg/mL (normal 10-69 pg/mL), total calcium 8.10 mg/dL (normal 8.8-10.8 mg/dL), inorganic phosphorus 4.0 mg/dL (normal 4.5-5.5 mg/dL), alkaline phosphatase 1622 U/L (normal 223-635 U/L) and CPK 171 U/L (normal <167 U/L). *X*-ray of both wrists and pelvis did not reveal any evidence of rickets or osteoporosis. Hemoglobin was 11 g/dL, and blood counts were normal. Electroencephalography (EEG) was also normal. Mother of the child did not give consent for electromyography.

Child was treated with oral vitamin D_3 (60,000 IU daily) for 10 days. Phenytoin was tapered and stopped. After one week, she was able to walk and go upstairs but waddling gait took almost 3 weeks to improve. After 4 weeks, the serum 25-OH vitamin D (39.11 ng/mL) and parathormone levels (25.50 pg/mL) normalized; serum alkaline phosphatase (809 IU/L) levels fell appreciably, serum calcium was 9 mg/dL and incorganic phosphorus 3mg/dL. A diagnosis of proximal muscle weakness due to vitamin D deficiency with secondary hyperparathyroidism was made. The child is well one year after stopping phenytoin.

DISCUSSION

The child had presented with proximal muscle weakness of lower limbs. Normal phenytoin levels eliminated phenytoin toxicity as a cause of waddling gait. Phenytoin therapy is known to affect bone

mineral density (BMD) but effect on BMD does not usually correlate with vitamin D levels, especially in ambulatory patients(3). There are numerous reports of elderly persons presenting with proximal muscle weakness, muscle pain, gait disturbances and frequent falls due to vitamin D deficiency(4,5), including a case report of muscular weakness with the concurrent use of phenytoin in an adult patient(6).

In children, muscle involvement due to vitamin D deficiency was reported in a 5-year-old child with cholestatic liver disease(1) and in another 11-year-old girl with celiac disease(2). In our case, vitamin D deficiency was associated with phenytoin therapy. All these children were successfully treated by vitamin D and calcium supplementation as in our case. Electromyography revealed a myopathic pattern in the affected muscles in one case(4). Muscle biopsy may reveal atrophy of type II fibers or may be normal. EMG would have confirmed myopathic involvement in our case but parents refused this invasive investigation.

In adults, the role of vitamin D in muscle function has been proved in the last decade(4,7). Skeletal muscles have a vitamin D receptor (VDR)(8). Vitamin D metabolites bind to VDR and mediate gene transcription leading to calcium uptake by the muscle cells, phosphate transport and maturation of muscle cells(7,8). Vitamin D also induces rapid changes in the calcium metabolism through direct action on calcium channels(4). Muscle strength also appears to be influenced by genotype of VDR on muscle cell(4,7, 8).

This case highlights vitamin D deficiency as rare cause of muscle pain and proximal muscle weakness in children. Children on phenytoin therapy should be carefully monitored and vitamin D rich diet and adequate sun exposure must be emphasized.

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