

## PHENYTOIN-INDUCED RICKETS IN A TEN-YEAR-OLD GIRL WITH HYPOTHYROIDISM\*

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The rachitic effect of phenytoin and the sclerotic effect of hypothyroidism on bone are well known. We find this case interesting for the presence of both conditions in the same patient.

### Case Report

A 10-year-old girl was brought to the Karadeniz University Department of Pédiatrics for evaluation of the deformities of her legs, her difficulty in walking and in climbing stairs, her epileptic fits and goiter. The past history revealed that she had been receiving phenytoin treatment over the last six years for the epilepsy, that during the last five months the deformities in her legs had developed and that since then it had been increasingly difficult for her to walk and to climb stairs. On physical examination she was found to be 110 cm tall and weighed 20 kg. A stage III goiter was present with a nodule on the isthmus. Her gums were hypertrophic, she had knock-knees and enlarged wrists. Her skin was dry and she was mentally retarded (Figures 1, 2). Laboratory findings were as follows. Serum  $T_4$  was 1  $\mu$ g/dl,  $T_3$  was 1.2 ng/dl, TSH was 25  $\mu$ U/ml, Ca: 7.5 mg/dl, P: 2.7 mg/dl, alkaline phosphatase: 30 BU. The radiologic appearance of knees and wrists showed metaphyseal widening and irregularity, cupping and fraying (Figure 3). EEG findings were compatible with epilepsy. Vitamin D<sub>3</sub> 600,000 U was given in a single dose and repeated once a month later. L-Thyroxin 0.1 mg/day was prescribed. Three months later the symptoms and X-ray findings were improved.

### Discussion

During the past two decades it has become apparent that treatment with anti-convulsant drugs can produce a spectrum of disorders concerning Vitamin D and bone metabolism. The clinical abnormalities most commonly seen include hypocalcemia,

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Figure 1.  
**Knock-Knees.**



Figure 2.  
**Stage III goiter.**



Figure 3.  
**X-ray shows  
bone damage.**

elevated serum alkaline phosphatase, reduced serum 25-OH Vit D, mild elevation of serum PTH level, and radiological evidence of osteomalacia. In 1968 Kruse<sup>1</sup> reported the occurrence of hypocalcemia and radiological evidence of rickets in 15 percent of the German pediatric epileptic population. In subsequent years English investigators reported the presence of hypocalcemia in 23 to 30 percent of institutionalized adult and pediatric epileptic patients who were receiving long-term anticonvulsant drug therapy<sup>2</sup>. Most of the clinical manifestations of anticonvulsant induced osteomalacia appear to be the end result of two processes, a) drug mediated increase in the activity of hepatocyte endoplasmic reticulum resulting in increased vitamin D catabolism, and b) the direct inhibitory effects of drugs on intestinal and bone cell ion transport and metabolism<sup>3</sup>. The thyroid hormone affects bone by permitting its resorption<sup>4</sup>. In hypothyroidism there is a reduction in bone blood flow and a reduction in both bone formation and resorption. The disturbance of remodelling in children leads to a delay in skeletal maturation and to other disorders of growth. In addition there is an increase in intestinal calcium absorption. In hypothyroidic patients the radiological appearance of bones is of generalized osteosclerosis with unusually thick cortices<sup>5</sup>. In hypothyroidic patients PTH and 1,25 dihydroxy vitamin D levels were found to be elevated<sup>6</sup>. Decreased bone turnover and a tendency to hypocalcemia causing PTH hypersecretion and hypophosphatemia, raised the 1,25 dihydroxy vitamin D level<sup>6,9,10</sup>. Increased 1,25 dihydroxy vitamin D synthesis was shown as a cause of increased bone mass and increased intestinal calcium absorption<sup>7,8</sup>.

This case report is presented to show the effects of a coexisting deficiency of vitamin D and of thyroid hormone. It is seen that the rachitic effect of phenytoin is greater than the osteosclerotic effect of hypothyroidism.

This observation indicates that anticonvulsive drugs could produce rickets even in a child with hypothyroidism in whom growth is markedly restricted as a result of the basic disease.

## Summary

A 10-year-old epileptic and hypothyroidic girl who developed rickets while on phenytoin treatment is presented. Calcium and bone metabolism in the presence of both hypothyroidism and rickets is discussed.

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