

Carbamazepine induced osteomalacia : Letter to the editor

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Case report

A 45 year-old woman with epilepsy who was treated with Carbamazepine (CBZ) 600 mg/daily for six years was seen at the neurology outpatient clinic with the complaints of back pain, weakness, fatigue, dizziness and recurrence of seizures during the last 2 months while she had been seizure free during the previous 4 years. She had been receiving no other medications. Detailed dietary and environmental (sun exposure) history did not suggest any risk factor for osteomalacia. Examinations of skin, eyes, respiratory, cardiovascular, gastrointestinal and neurological systems were all normal except for pain located bilaterally on the fifth and sixth thoracic rib areas by palpation. In laboratory examinations, thyroid hormones, complete blood cell count and erythrocyte sedimentation rate were normal. Her CBZ blood level was also in normal range : 29.75 mmol/L (N : 17-43 mmol/L). Biochemical analysis of the serum revealed. Alkaline phosphates (ALP) : 11.55 μ kat/L (N : 0-4.5 μ kat/L), calcium : 2 mmol/L (N : 2.20-2.55 mmol/L), phosphorus ; 0.61 mmol/L (N : 0.87-1.45 mmol/L), 25 (OH) D3 : 16.25 nmol/L (N : 25-110 nmol/L), Parathormone (PTH) : 395 ng/L (N : 10-65 ng/L). Serum calcitonin : 22 ng/L (N : 0-50 ng/L) and the urinary calcium excretion in 24-hours urine was 11.75 mmol/L (N : 12.5-75 mmol/L). ALP isoenzymes showed increased bone isoenzyme activity. 99m Tc-MDP bone scintigraphy of the patient showed focal regions of increased uptake at the ribs, bilateral humerus, proximal metaphysis and the left femur (Fig. 1).

The patient was diagnosed with anticonvulsant-induced osteomalacia. The Naranjo probability score (3) for the adverse drug reactions (+7) was suggestive for this diagnosis. Since, epileptic attacks of the patient were not under control, antiepileptic treatment was continued. Calcitriol (1,25-dihydroxyvitamin D3) : 0.5 mcg/daily and

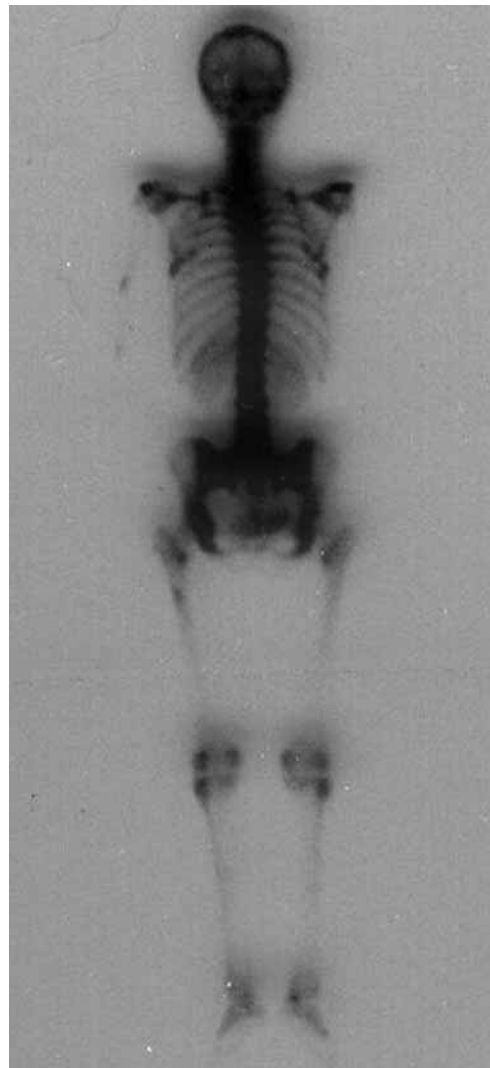


FIG. 1. — 99m Tc-MDP bone scintigraphy - high osteoblastic activity at the fifth ribs bilaterally, the sixth rib on the right, bilateral humerus shaft and the left femur.

calcium (elementary calcium) : 2 g/daily supplementations were initiated for the treatment of osteomalacia. Serum ALP and calcium concentration were monitored every each month during five months. At the end of this period, these critical bio-

chemical parameters were improved, together with the initial clinical symptoms.

Discussion

Antiepileptic drugs induced osteomalacia should be considered in epileptics receiving anticonvulsant drugs. Bone pains, fractures after minimal trauma, muscle weakness, or worsening of seizure control should be taken into consideration seriously for the diagnosis. The worsening of seizure control may be due to hypocalcaemia secondary to rickets or osteomalacia. Hypocalcaemia, increased serum ALP, and decrease in the 25-OH-vitamin D concentrations are hallmarks of this peculiar clinical entity (1, 2). However, the mechanism of CBZ for osteomalacia is controversial. Reduced 25-OH-vitamin D levels may result from the up regulation of the hepatic cytochrome P 450 enzymes by anticonvulsant inducers (2, 4) and this side effect can appear after a short period of therapy even normal plasma CBZ concentrations are found (6). Furthermore, a second hypothesis involves a form of high-turnover bone disease, with hypocalcaemia and secondary hyperparathyroidism that might occur despite normal serum levels of vitamin D metabolites (5-8).

The mechanism of osteomalacia in our patient may depend on CBZ induced reduction of 25-OH-vitamin D levels which may result from the up regulation of the hepatic cytochrome P 450 enzymes. Addition of adequate supplementation of calcium and vitamin D to the diet may be rational option and may reduce osteomalacia-developing risk.

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