Case report

Complications of long-term phenytoin use

An 18-year-old man with a background of mental retardation and epilepsy presented with a history of poor seizure control complicated by repeated head trauma and aspiration pneumonia. Notably, he had been on phenytoin since the age of 3.

Clinically, the patient was febrile and tachycardic but haemodynamically stable. He had severe gingival hypertrophy, with markedly poor dentition and gingival abscesses secondary to long-term phenytoin use. He was tachypnoeic, with asymmetric chest expansion and evidence of lung consolidation in the right lower zone. He had poor secondary sexual characteristic development with no pubic or axillary hair, mild gynaecomastia and a single small left testis.

Chest radiography confirmed the pneumonia but interestingly a radiographic skeletal survey revealed severe generalised osteopenia, multiple rib fractures and delayed bone age. Consequently, low serum testosterone and vitamin D levels were noted. In addition, his serum alkaline phosphatase levels were elevated but his serum calcium, phosphate and parathyroid hormone levels were normal. In the absence of a tetracycline-labelled bone biopsy, a diagnosis of osteomalacia was suggested.

Discussion

Phenytoin is inexpensive and a commonly used first-line anti-epileptic drug (AED). Gingival hypertrophy, hirsutism and coarsening of facial features are well-recognised adverse effects; however, side-effects such as osteomalacia are often forgotten.

Interestingly, the incidence of osteomalacia in long-term users of phenytoin has been estimated in the literature to be about 50%. However, these data are challenged by limitations such as small sample sizes, lack of suitable control groups and confounding variables such as smoking and polypharmacy. Despite this, treating physicians generally tend not to consider this side-effect, which may lead to patients presenting with severe, debilitating osteomalacia. The mechanism by which phenytoin and other AEDs cause bone loss is not entirely clear, but relates to hepatic microsomal induction of enzymes that enhance the metabolism of 25-hydroxyvitamin D to inactive metabolites.

One must remember that the bone effects are often multifactorial with lack of sunlight exposure, immobility and poor nutrition together with phenytoin use all contributing. In our patient, his hypogonadotrophic hypogonadism was an additional aggravating factor. Anticonvulsant choice in all patients, especially those at risk of bone adverse effects, should be carefully considered. Furthermore the significant cosmetic effects of phenytoin warrant an alternative choice, particularly in younger patients. It is suggested that patients on long-term phenytoin therapy should be monitored with serum calcium and DEXA scans at baseline and during follow-up. Unfortunately this practice is not widespread and does offset the cost-effectiveness of phenytoin. Vitamin D and $Ca2^{+}$ supplementation is recommended in patients on AEDs, although there is no controlled trial evidence.

Summary

We report a young man who presented with several adverse effects related to long-term phenytoin use. Gingival hypertrophy, for example, is a well-known adverse effect of phenytoin use; however, the metabolic bone effects are less well known. We therefore suggest the prudent use of phenytoin in those at risk. Alternatively, one must use less toxic anti-epileptic drugs and if phenytoin is to be used, screening for bone side-effects is advised.

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Single suture

An unwanted side-effect of weight loss

Weight loss has a serious problem – it leads to the release of persistent organic pollutants (POPS), which may be detrimental to health. POPS enter the food chain from sources such as pesticides and have been linked to an increased risk of diabetes, cancer and dementia.

Once they are eaten, POPS collect in fatty tissue, where they are not thought to be harmful. However, Duk-Hee Lee of Kyungpook National University in Daegu, South Korea, has shown that weight loss releases POPS, leading to their build-up in the blood.

Lee compared weight changes in 1 100 adults over 10 years, with blood levels of seven POPS. People who had lost 10 kg or more during the decade had the highest levels of blood-borne POPS, while those who had gained 10 kg or more had the lowest.

However, the level of POPS needed to have adverse effects on health is not known, so this should not be used as an excuse not to lose weight.

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