2 **Krahn LE**, Maraganore DM, Michels VV. Childhood-onset schizophrenia associated with parkinsonism in a patient with a microdeletion of chromosome 22. *Mayo Clin Proc* 1998;**73**:956–9.
3 **Zimprich A**, Grabowski M, Asmus F, *et al*. Mutations in the gene encoding ε-sarcoglycan cause myoclonus-dystonia syndrome. *Nat Genet* 2001;**29**:66–9.

Phenobarbitone induced gingival hyperplasia

Among the long term adverse effects of anticonvulsants, gum hyperplasia is cosmetically disturbing and can give rise to complications such as bleeding and gingivitis.[1 2] Long term use and high doses of phenytoin sodium (diphenylhydantoin) have been implicated in the occurrence of gingival hyperplasia.[3] Serum phenytoin level in these patients are high.[3] Rarely other drugs such as primidone, sodium valproate, nifedipine, and cyclosporin have also been implicated.[1 2] Treatment consists of stopping the offending agent and providing corrective surgery.[4] Phenobarbitone (phenobarbital) has not yet been reported to cause gum hyperplasia. We describe a patient who developed this complication in association with the long term use of phenobarbitone.

Case report

A 26 year old man had been suffering from hot water reflex epilepsy and primary generalised tonic-clonic seizures since he was 12 years of age. The seizures were poorly controlled because of his inability to avoid taking hot baths, inadequate dosage of anticonvulsants, and poor compliance. Since 1987, he had been taking phenobarbitone, 60 to 90 mg/day. In 1988, phenytoin (100 mg twice daily) was added for six months but was stopped because there was no benefit. In 1989, carbamazepine (200 mg twice daily) was added but was discontinued by the patient in 1996 for unspecified reasons. From 1996 onwards he had been receiving only phenobarbitone 120 mg/day. He was referred to us for progressive gum hyperplasia with bleeding from the gums, both spontaneously and with tooth brushing, since 1996. There was no history suggesting any haematological malignancy, and he was not on any other drug treatment.

On examination, he had gingival hyperplasia involving both the upper and the lower jaws (fig 1). There was occasional bleeding from the hyperplastic gum tissue. General physical examination did not reveal any pallor, hepatosplenomegaly, or lymphadenopathy and neurological evaluation was unremarkable.

Haematological investigations, including haemoglobin, white blood count, erythrocyte sedimentation rate, and peripheral smear, were all normal. Blood glucose, renal and liver function tests, serum electrolytes, and urine analysis were normal. Scalp electroencephalography and cranial computed tomography were normal. Serum concentrations of phenobarbitone, phenytoin, and carbamazepine were measured. Phenobarbitone was within the therapeutic range (11.2 μg/ml) while the other two drugs were not detectable.

Discussion

This patient with longstanding epilepsy probably had phenobarbitone induced gingival hyperplasia. He had used phenytoin in 1988 for only six months without developing this symptom, and it only appeared later in 1996 when he was on phenobarbitone alone. After that time it ran a progressive course. Primidone, the metabolites of which contain phenylethylmalonamide and phenobarbitone, has also been reported to be a rare cause of gingival hyperplasia.[1 2] However, it is difficult to state which of the two components contributes to the hyperplasia.

Figure 1 Gum hyperplasia caused by phenobarbitone.

Phenytoin sodium is known to be the most common cause of gingival hyperplasia.[1 4] A minor degree of hyperplasia occurs quite commonly and this generally causes only cosmetic problems, especially for women. However, when phenytoin is used for prolonged periods in high dosage a severe degree of gingival overgrowth occurs. In such cases the hyperplastic gingiva bleed with minimal trauma or spontaneously, and may sometimes become secondarily infected.[3]

The mechanism of anticonvulsant induced gingival hyperplasia is not known. It is believed that these drugs cause tissue collagen proliferation but the reason for this is unknown. It has been speculated that a high phenytoin concentration in the pituitary and adrenal glands may be related to hirsutism and gingival hyperplasia. However, there is at present no evidence that high concentrations of phenytoin in these tissues produce changes in their secretion rate, or indeed that these alterations cause hirsutism and gingival hyperplasia.[5]

Antiepileptic drug levels are generally high in cases of gingival hyperplasia. However, in our case the phenobarbitone level was within normal therapeutic limits, while phenytoin and carbamazepine were undetectable. Buchnann *et al* reported nine cases of phenytoin induced moderate to severe gingival hyperplasia who underwent corrective gingivectomy. It was found that in eight of these cases the tissue diphenylhydantoin levels were higher than the plasma levels.[5]

Treatment consists of stopping the offending drug and providing supplements of folic acid and ascorbic acid. If regression does not occur, reconstructive surgery of the hyperplasic gingival tissue is advised. Our patient has been switched to sodium valproate, and reconstructive cosmetic surgery is planned.

In conclusion, we report a case of phenobarbitone induced gingival hyperplasia because of its rarity. The mechanism of this side effect remains unclear. Accurate drug history, thorough investigations, and punctilious reporting of such cases may help us gain a better understanding of the condition.

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References

1 **Meinardi H**, Stoel LMK. Side effects of antiepileptic drugs. In: Magnus O, Lorentz de Haas AM, eds. *Handbook of neurology – the epilepsies*. Amsterdam: North Holland, 1974:705–38.
2 **Scheuer ML**, Van Cott AC. Antiepileptic drugs. In: Rowland LP, ed. *Current neurologic drugs*, 2nd ed. Philadelphia: Williams and Wilkins, 1998:127–66.
3 **Perli F**, Kolinova J, van Patzelo U. Phenytoin as a risk factor in gingival hyperplasia. *Ther Drug Monitor* 1995;**17**:445–8.
4 **Darbari UR**, Hopper C, Speight PM, *et al*. Treatment approach to gingival hyperplasia due to drug therapy. *J Clin Periodontol* 1996;**23**:941–4.
5 **Buchnann RA**, Kinkel AW, Goulet JR, *et al*. The metabolism of DPH following once daily administration. *Neurology* 1972;**22**:126–30.

Hashimoto's encephalopathy mimicking Creutzfeldt-Jakob disease: brain biopsy findings

A previous report in this journal described seven cases of Hashimoto's encephalopathy (HE) clinically resembling Creutzfeldt-Jakob disease (CJD).[1] Brain biopsies in such cases are rare and have suggested "vasculitis".[2] We contribute a report of rapidly progressive dementia in a patient undergoing brain biopsy before the diagnosis of HE was established, showing features suggesting early spongiform change but with inflammation.

A 57 year old woman was taken to a local hospital following a generalised seizure. She was discharged that night after negative cranial computed tomography and cerebrospinal fluid (CSF) analysis. Within a few days she was noted by family members to be acting strangely and hallucinating. Her doctor found her to be somnolent and rigid without focal neurological findings. Magnetic resonance imaging of the brain showed a questionable increase in gadolinium contrast uptake in a 7 mm area of the left medial frontal cortex. An electroencephalogram (EEG) showed bihemispheric slowing without epileptiform activity. Despite an extensive inpatient evaluation (including biochemical, haematological, endocrine, infectious, autoimmune, and toxic analyses), no cause for the encephalopathy could be found. The patient was then referred to our institution for brain biopsy and further care.

Samples of left frontal cortex showed light microscopic evidence of rare vacuoles abutting neurones, suggesting early spongiform