CASE REPORT

Diphenylhydantoin Induced Severe Gingival Hyperplasia

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ABSTRACT

Gingival overgrowth (GO) is a side effect, associated with some distinct classes of drugs, such as anticonvulsants, immunosuppressant, and calcium channel blockers. One of the main drugs associated with GO is the antiepileptic, diphenylhydantoin (DPH)/ phenytoin¹, which affects gingival tissues by altering extracellular matrix metabolism. Phenytoin (DPH)-induced gingival overgrowth (PIGO) due to chronic administration remains an unsolved problem especially in cases where this drug is taken without any supervision due usually to poor follow-up. Younger age groups experience more lesions than adults and in the mentally handicapped the prevalence appears to be highest. The most satisfactory treatment is the replacement of the drug by a safer antiepileptic. Patients who are to be maintained on DPH respond well to a program of meticulous oral hygiene at home along with frequent professional prophylaxes. We present a case of seizure disorder with mental retardation who developed severe gingival overgrowth wherein teeth are almost buried, caused by unsupervised intake of phenytoin. JMS 2017; 20(1):44-46

INTRODUCTION

Gingival overgrowth (GO) comprises of any clinical condition in which an increase in the size of the gingiva is observed. Several causes of gingival hyperplasia are known, and the most recognized is drug-induced. Gingival overgrowth, also known as gingival hyperplasia secondary to drugs, was first reported in the dental literature in institutionalized epileptic children who were receiving therapy with phenytoin (DPH) for the treatment of seizures.

Other drugs like Cyclosporine, a potent immunosuppressant widely used since the early 1980s, and numerous calcium channel blocker agents, including nifedipine and amlodipine, have also been associated with gingival overgrowth.

Because not all patients on phenytoin, cyclosporine, and/or calcium antagonists develop gingival overgrowth, identifying patients at risk is important in order to take all the necessary measures to minimize the onset and severity of this condition.

CASE REPORT

A 25 year old mentally retarded male had generalized tonic-clonic seizures for 12 years. Previous records revealed a normal computed tomographic scan of brain and an abnormal electroencephalogram showing generalized epileptiform discharges in the form of bilaterally symmetrical spike wave discharges lasting for 1-4 seconds. Treatment with 200 mg of phenytoin along with 60 mg of phenobarbitone per day was started. However patient continued these drugs without any supervision and was taking double the prescribed dose of these anti-epileptics for last many years. Examination revealed coarse facial features and severe gingival hyperplasia to an extent that his teeth were almost buried in the gums (Fig. No.1). There was generalized fibrotic gingival enlargement in upper as well as lower jaw (Fig. No.2). Gingiva were inflamed, bright red with irregular margins. There was bleeding on probing with scalloping of the interdental gingiva and presence of stippling (Fig. No.3). Due to these side effects phenytoin was replaced by sodium valproate. Presently patient is on regular follow-up of Neurology Department as well as a dentist.

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Figure.1: Severe Gingival Hyperplasia With Coarse Thick Lips.

Figure. 2: Generalized Fibrotic Gingival Enlargement In Upper As Well As Lower Jaw With Buried Teeth.

Figure 3: Showing Bleeding Of Enlarged Gums On Probing.

DISCUSSION

Epilepsy is the most common chronic neurological disorder in humans². The prevalence of epilepsy in developed countries reaches approximately 1%, rising to 2% in developing nations³. Epilepsy treatment is based on drug-therapies which aim to help patients to achieve seizure

freedom without adverse effects. However, in several cases the first-choice drug fails in the treatment due to a lack of efficacy or to the patient failure to tolerate the medication due to side effects^{4,5}. Among the drugs that induce GO, the antiepileptic agent phenytoin has been widely related to this condition¹.

The first report of GO associated with the chronic use of phenytoin was made in 1939⁶. This agent remains as one of the most commonly prescribed medications to treat epilepsy and it may also be used in cases of neuralgias, myotonia and cardiac arrhythmias⁷. It is estimated that about 30 to 50% of patients taking phenytoin develop significant gingival alterations⁸. Till date several studies have tried to determine the pathogenesis of drug-induced GO but the mechanisms that trigger such condition are not fully elucidated. Several studies have shown that the interaction of phenytoin, cyclosporine, and nifedipine with epithelial keratinocytes, fibroblasts, and collagen can lead to an overgrowth of gingival tissue in susceptible individuals.

Phenytoin has been shown to induce gingival overgrowth by its interaction with a subpopulation of sensitive fibroblasts. Gingival overgrowth is more pronounced on the labial aspect of the maxillary gingiva and in the interdental papillae.

It is customary in medical practice to treat untoward drug reactions by eliminating the drug causing the problem. This is probably the most satisfactory treatment of PIGO. In patients where the gingival overgrowth is severe and difficult to control, the patient's physician should be warned of the situation and consulted about the feasibility of changing the anticonvulsant drug. In many cases PHT proves to be the drug of choice for seizure control and this usually takes precedence over the gingival overgrowth. Withdrawal of the drug will usually result in a spontaneous disappearance of the gingival overgrowth within three to six months, if the lesions are moderate in size and upto a year or longer if the lesions are large. Surgical removal is indicated when the severity of the gingival overgrowth is such that an esthetic problem exists, speech or mastication is impeded, severe secondary inflammation is occurring, and when oral hygiene procedures have not succeeded in controlling the overgrowth. Surgery is not a permanent solution. If DPH therapy continues, the gingival overgrowth will invariably recur. Repeated gingivectomies may be necessary in these

patients and recurrence of the lesion has been observed as early as three weeks after surgery. Meticulous oral care will, however, markedly delay the recurrence.

REFERENCES

1. McLeod DE, Stoeckel D, Contreras J, Reyes E. Severe postpartum gingival enlargement. *Journal of Periodontology*. 2009;80(8):1365-1369.
2. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy. *Epilepsia*. 1993;34:592-596.]
3. Sander JW, Shorvon SD. Epidemiology of the epilepsies. *Journal of Neurology Neurosurgery and Psychiatry*. 1996; 61(5):433-443.
4. Garnett WR, St Louis EK, Henry TR, Bramley T. Transitional polytherapy: tricks of the trade for monotherapy to monotherapy AED conversions. *Current Neuropharmacology*. 2009;7(2):83-95.
5. Maschio M, Dinapoli L, Vidiri A, et al. The role side effects play in the choice of antiepileptic therapy in brain tumor-related epilepsy: a comparative study on traditional antiepileptic drugs versus oxcarbazepine. *Journal of Experimental and Clinical Cancer Research*. 2009;28(1, article 60)
6. Kimball OP. The treatment of epilepsy with sodium diphenyl hydantoinate. *The Journal of the American Medical Association*. 1939;112:1244-1245.
7. Guncu GN, Cxaglayan F, Dincel A, Bozkurt A, Sayg S, Karabulut E. Plasma and gingival crevicular fluid phenytoin concentrations as risk factors for gingival overgrowth. *Journal of Periodontology*. 2006;77:2005-2010.
8. Modr T, Domeij H, Andurn I, Mustafa M, Brunius G. Effect of phenytoin on the production of interleukin-6 and interleukin-8 in human gingival fibroblasts. *Journal of Oral Pathology and Medicine*. 2000; 29(10):491-499.