

# Phenytoin-Induced Gingival Overgrowth in Un-Cooperated Epilepsy Patients

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Phenytoin-induced gingival overgrowth is a well-known and frequently reported gingival lesion, which was first detected in 1939. However, there are conflicts in the literature about the agents which affect the severity of the lesion. Un-cooperative dental patients are one of the most unsuccessfully treated periodontal patient groups because of the difficulty in maintaining their oral hygiene. This case report consists of two cases with the same characteristics: phenytoin usage, comprehension and speech defects and poor oral hygiene, but each case differs in the duration of the phenytoin therapy. Both of the cases received scaling, root planning and a gingivectomy.

**Key Words:** Phenytoin, gingival overgrowth, co-operation defects

## INTRODUCTION

Epilepsy is a disease where a person has recurrent seizures due to a chronic underlying process. The currently available anti-epileptic drugs act either by depressing the neuronal activity at the focus of origin, or by blocking the spreading mechanisms.<sup>1,2</sup>

Phenytoin (PHT, 5,5-diphenylhydantoin) was first introduced as an anti-epileptic drug in 1938.<sup>3</sup> It is slowly absorbed from the gastrointestinal track, and shows marked inter individual variation.<sup>4</sup> PHT is known to concentrate in the brain, at levels 5 to 10 times that found free in the serum.<sup>5</sup> The drug is extensively metabolized in the liver by microsomal enzymes, with the major me-

tabolite (50-5% of the PHT dose) being 5-(p-hydroxyphenyl)-5-phenylhydantoin (p-HPPH).<sup>6</sup> The drug has been proposed to act via stabilization of the neuronal cell membranes and through suppression of synaptic transmissions. Depending on the membrane conditions, the drug concentration and the timing, it appears that PHT acts by affecting the (Na<sup>+</sup>K) pump, Ca<sup>++</sup> transport or the sodium influx at a cellular level.<sup>7-9</sup>

Gingival overgrowth is one of the most common side effects associated with the administration of phenytoin, the most frequently used anti-epileptic drug. Gingival overgrowth, in relation to phenytoin, was first described in 1939, with several other subsequent authors reporting the overgrowth associated with phenobarbital, valproic acid and vigabatrin.<sup>10-13</sup>

The prevalence of Phenytoin-induced gingival overgrowth has been shown to vary, from 13 to 50%, in community based studies on institutionalized patients.<sup>14-16</sup> Some authors have observed a lower prevalence of gingival overgrowth, and explained this situation in relation to the interaction of phenytoin with phenobarbital and/or carbamazepine. However, this relationship is controversial.<sup>12,14</sup>

Our study outlines two cases with common findings: epilepsy, phenytoin usage, and speech and comprehension retardation.

## CASE REPORT

### Case 1

A 33-year-old male, who had moderate gingival

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swelling, was referred to the Department of Periodontology, Faculty of Dentistry at the University of Cumhuriyet. The patient had not received any prior dental therapy. He began to use Carbamazepine and Phenytoin at the age of 8, and for the last 5 years had also used Phenobarbital. His medical doctor prescribed all the drugs. He had no medical history of serious illness. A radiographic examination revealed no bone loss; however in all quadrants, the first, second and third molars had been extracted due to serious caries. (Fig. 1)

Comprehension and speech retardation were evident, however communication was achieved with the help of his parents. (Fig. 2)

One week after scaling and root planning, a full-mouth gingivectomy was performed. His response to scaling and root planning were mode-

rate; however as a result of patients co-operation retardation, meticulous oral hygiene applications could never been achieved. Also, the 2 week post-operative results were unsatisfactory due to the lack of adequate plaque control.

## Case 2

A 32-year-old male, who complained of gingival overgrowth, was referred to the Department of Periodontology, Faculty of Dentistry at the University of Cumhuriyet. In his medical history, it was determined that he had suffered severe epilepsy attacks, with variable intervals, since the age of 5 years. He had been administered Phenytoin (100 mg 3 × 1 daily) as the frequency of the attacks increased over the years, however the dosage had been increased to 200 mg every 12



Fig. 1. Clinical appearance of the first case from the initial visit.



Fig. 3. Clinical appearance of the second case from the initial visit.



Fig. 2. Panoramic appearance of the first case from the initial visit.



Fig. 4. Panoramic appearance of the second case from the initial visit.

hours, on a daily basis, as the seizure frequencies had not reduced. He had difficulty with speech, and consumed half a pack of cigarettes per day.

The patient noticed a gingival overgrowth after taking the medication. Clinically, there was a fibrotic gingival overgrowth, with a lobular appearance, found in most of the affected areas on labial surfaces. (Fig. 3 and 4)

It was thought the gingival overgrowth was due to Phenytoin usage. However, it was not possible to stop, or decrease, the drug dosage for our patient, therefore oral hygiene instruction, scaling and root planning, and gingivectomy operations were performed as treatments. With similar results to the case 1, inadequate plaque control, due to co-operation defects, made the results of the periodontal therapy insufficient.

## DISCUSSION

A gingival overgrowth is a common feature of a gingival disease. There are many types of gingival overgrowth, with the types varying according to the etiological factors and pathological processes producing them.

The term 'hyperplasia' refers to an increase in the size of a tissue, or an organ, produced by an increase in the number of component cells. Non-inflammatory gingival hyperplasia is produced by factors other than local dental plaque or dental calculus irritation. It is very common, with most cases occurring after therapy with drugs, such as phenytoin, cyclosporine and nifedipine.

Overgrowth of the gingiva, caused by Phenytoin, usually begins as a painless, bead-like, and diffuse swelling of the interdental papillae, which enlarge and coalesce, leaving a nodular appearance. As the condition progresses, the marginal and papillary overgrowths unite; they may develop into a massive tissue fold covering a considerable portion of the crowns. The overgrowth is chronic, and slowly increases in size, recurs when surgically removed, and has been reported to spontaneously disappear, soon after the discontinuation of the drug.<sup>17</sup>

A phenytoin-induced gingival overgrowth begins as hyperplasia of the connective tissue core of the marginal gingiva, followed by proliferation

of the epithelium. The overgrowth increases by proliferation and expansion of the central core beyond the crest of the gingival margin.

There are various risk factors that have been elucidated for a drug-induced gingival overgrowth. The identifiable factors can be considered under the following headings; age, oral hygiene, daily dose and duration of drug therapy.<sup>18</sup>

Despite the studies confirming a relationship between the age of the patient and a gingival overgrowth, uncertainty about the issue still remains.<sup>9</sup> Both of the subjects of our case study were in the same age, and therefore, it is not possible to discuss the effect of age on gingival overgrowth for this case report. The duration of the drug therapy has also been associated with a higher frequency and severity of overgrowth.<sup>18</sup> However, both our cases showed similar severities of overgrowth, and the results do not confirm this idea. However, we also accept that the study of only two cases does not allow for adequate interpretation in this particular situation.

The role of oral hygiene in the pathogenesis of a gingival overgrowth is also complex. The presence of the overgrowth makes plaque control difficult, resulting in a secondary inflammatory process, complicating the gingival hyperplasia caused by the drug. Both subject in this case report had comprehension retardation, which also made the appreciation of the professional oral hygiene instructions by the patients difficult. However, it is not easy to explain whether the plaque induces the overgrowth, or if the overgrowth helps the retention of the plaque. Both cases showed marked improvement in their oral hygiene habits, and a post-operative follow-up will help to explain the relationship.

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