

Severe Anti-epileptic Drug-induced Gingival Overgrowth in a Physically Disabled Patient

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ABSTRACT

Anti-epileptic drugs are considered to be the main drugs associated with gingival overgrowth. The co-administration of phenytoin and other anti-epileptic drugs, which increases the risk of phenytoin-induced gingival overgrowth, has been previously reported. However, no report has been done considering the new generation of anti-epileptic drug topiramate and its association with gingival overgrowth. High levels of dental plaque and calculus have also been reported as being a critical risk factor in the development and severity of drug-induced gingival overgrowth. Thus, this case report highlights the occurrence of severe gingival overgrowth and generalized periodontitis in a physically disabled patient with epilepsy who had been taking phenytoin and topiramate drugs for 10 years. It also emphasizes the importance for both medical and dental professionals to reduce the severity and impact of drug-induced gingival overgrowth.

Keywords: Anti-epileptic drugs, gingival overgrowth, periodontitis, physical disability

Agrandamiento Gingival Severo Inducido por Medicamentos Anti-epiléptico en un Paciente con Discapacidad Física

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RESUMEN

Los medicamentos anti-epilépticos son considerados los principales fármacos asociados con la hiperplasia gingival. La administración concomitante de la fenitoína y otros fármacos anti-epilépticos, que aumenta el riesgo de agrandamiento gingival inducido por la fenitoína, se ha reportado con anterioridad. Sin embargo, no se ha realizado ningún reporte teniendo en cuenta el topiramato – medicamento de la nueva generación de fármacos antiepilepticos – y su asociación con el agrandamiento gingival. Altos niveles de placa dental y cálculo han sido reportados también como factor de riesgo crítico en el desarrollo y severidad del agrandamiento gingival inducido por drogas. Así, este reporte de caso destaca la aparición de un agrandamiento gingival severo y periodontitis generalizada en un paciente con discapacidad física con epilepsia, que había estado tomando fenitoína y topiramato durante 10 años. También destaca la importancia que tiene para los profesionales médicos y dentales, el reducir la severidad y el impacto del agrandamiento gingival inducido por drogas.

Palabras claves: Antiepilepticos, agrandamiento gingival, periodontitis, discapacidad física

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INTRODUCTION

Anti-epileptic drugs are considered to be the main drugs associated with gingival overgrowth (1, 2). The incidence of adverse drug reactions can be as high as 65% in people with

epilepsy (2). Many studies have highlighted connections between anti-epileptic drugs, like phenytoin, phenobarbital, carbamazepine, valproic acid and vigabatrin and gingival overgrowth (3–5). Of the aforementioned drugs, phenytoin-induced gingival overgrowth was the most frequently reported. Clinically, gingival overgrowth begins in the dental papilla region, which increases and encroaches on the crowns of the teeth. The incidence and severity of gingival overgrowth is greatest on the labial surfaces of the anterior segment. Tissue appearance may range from normal to a hyperaemic state (6).

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The gingival overgrowth is normally confined to the attached gingiva but may extend coronally and interfere with aesthetics, mastication or speech (1). Various risk factors associated with drug-induced gingival overgrowth have been reported (7, 8). In addition, the role of dental plaque as a critical risk factor in the development and severity of drug-induced gingival overgrowth was recognized in the latest periodontal disease classification system (9).

Although the potential of phenytoin to induce gingival overgrowth has been established, with some reports suggesting that the co-administration of phenytoin and other anti-epileptic drugs – especially phenobarbitone and carbamazepine – increases the risk of phenytoin-induced gingival overgrowth (3), there is no evident report on the new generation of anti-epileptic drug topiramate and its relationship to gingival overgrowth. Therefore, the purpose of this report is to describe the clinical and histological features, aetiology, management and oral healthcare of severe anti-epileptic drug-induced gingival overgrowth, and generalized periodontitis in a physically disabled patient with epilepsy who had been receiving a combination therapy of phenytoin and topiramate drugs.

CASE REPORT

A 41-year old Thai male of very low socio-economic status and with a physical disability presented with severe gingival overgrowth, gingival bleeding, generalized periodontitis and tooth mobility over a period of two years. He had been suffering from epilepsy for 10 years and had been on a combination therapy of phenytoin (300 mg/day) and topiramate (100 mg/day) drugs for the same duration. The epileptic seizure attacks usually occurred at intervals of two months. The patient had many retained roots and large dental caries due to his inability to clean his teeth because of limb disability, as well as gingival overgrowth and bleeding. There was no history suggesting any haematological malignancy and he was not receiving any other drug treatment.

An oral examination of the patient revealed that both maxillary and mandibular arches were lobulated and inflamed, severe gingival overgrowth had extended along the labial, lingual and coronal aspects, the entire anatomical crowns of the teeth had been covered and poor oral hygiene status was visible. Throughout the overgrowth was generalized oedema with erythematous colour and easy bleeding (Fig. 1a–b).

A panoramic radiographic survey was then obtained and generalized severe periodontal involvement was seen around all of the teeth (Fig. 2). An incisional biopsy of the upper arch was performed. Histological sections showed parakeratinized stratified squamous epithelium with thin, elongated rete ridges. The underlying connective tissue demonstrated fibrocollagenous tissue infiltrated by numerous chronic inflammatory cells and small capillaries. However, as there was no sign of malignancy and the patient's haematological investigations were within the normal range, the histopathological diagnosis was reported as fibro-epithelial hyperplasia (Fig. 3).

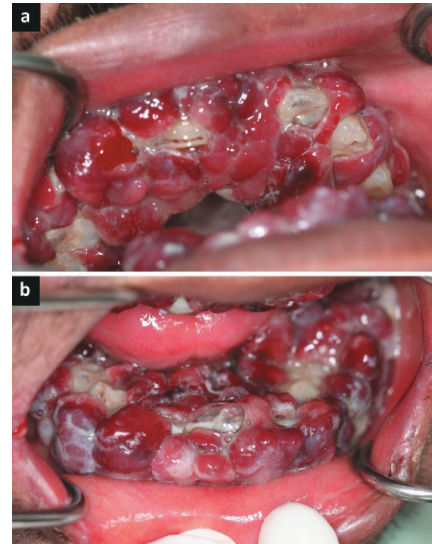


Fig. 1: Clinical appearances of gingival overgrowth in maxillary (a) and mandibular (b) arches.

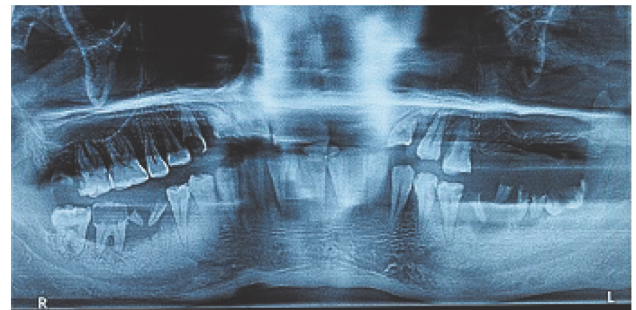


Fig. 2: Panoramic radiograph showing multiple retained roots, large dental caries and generalized periodontitis.

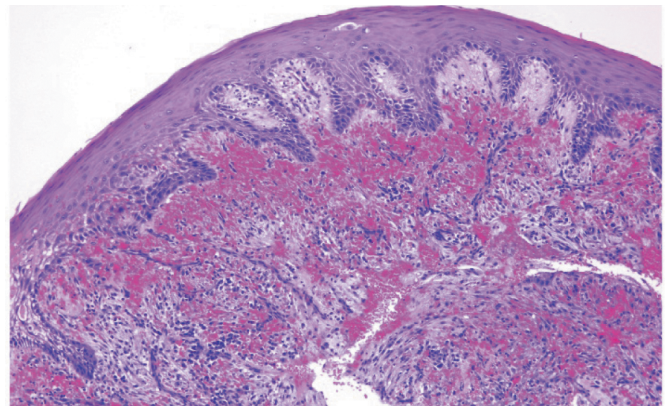


Fig. 3: Microscopic examination of gingival tissue (H&E, magnification 100×).

On the basis of the patient's history, clinical findings, radiographic examination, histological features and laboratory investigations, the final diagnosis of the gingival lesion was given as anti-epileptic drug-induced gingival overgrowth with generalized periodontitis. Because of very poor oral hygiene, poor prognosis of all remaining teeth, severe gingival over-

growth and an inability of the patient to control plaque due to limb disability, the treatment plan of this case was full dental clearance, mouth extraction, a gingivectomy, prosthodontics treatment and instructions for maintaining oral hygiene. In addition, the patient was advised by his physician to discontinue his previous therapy of anti-epileptic drugs and substitute with an alternative therapy.

After medical approval, full dental clearance extraction and a gingivectomy of gingival overgrowth were performed. Antibiotic and analgesic drugs and chlorhexidine mouthwash were prescribed. In addition, the patient's physician also prescribed sodium valproate (400 mg/day), carbamazepine (400 mg/day) and clonazepam (2 mg/day). The patient was then recalled after two weeks had elapsed for an intraoral examination, which showed a significant resolution of gingival overgrowth (Fig. 4a–b). On further examination six months later, the patient showed a complete resolution of gingival overgrowth (Fig. 4c–d). He was thereafter referred to the Department of Restorative Dentistry in the Faculty of Dentistry at Naresuan University, Thailand, for a complete denture fabrication for both maxillary and mandibular arches, and for aesthetics and masticatory functions. Unfortunately, the patient declined prosthodontics treatment because of an inconvenience with transportation when visiting the dentist; however, the patient's chief complaint was solved to his satisfaction.

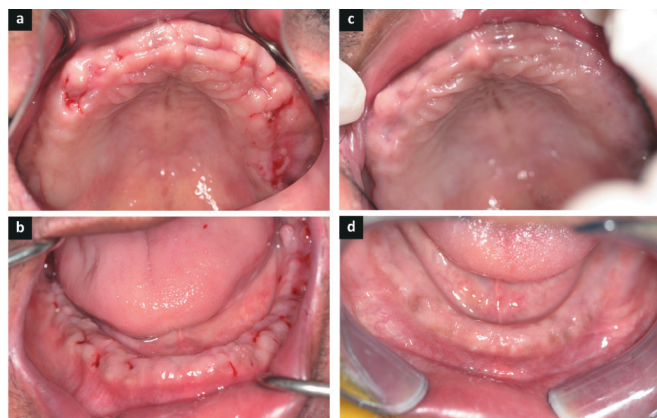


Fig. 4: Postoperative clinical appearances of gingiva at two weeks (a, b) and six months (c, d).

DISCUSSION

The main treatment options for patients suffering from epilepsy are anti-epileptic drugs. Phenytoin is generally prescribed in combination with other anti-epileptic drugs (4), and this is consistent with the patient in this case report who received a combination therapy of phenytoin and topiramate drugs. Gingival overgrowth is a common adverse side effect of phenytoin therapy and this phenomenon has several important medical and cosmetic implications, particularly in developing countries (1, 3). Some reports suggested that the co-administration of phenytoin and other anti-epileptic drugs, especially phenobarbitone and carbamazepine, increases the risk of phenytoin-induced gingival overgrowth, probably by

increasing the levels of certain phenytoin metabolites from hepatic enzyme induction (3, 7). In addition, receiving more than one anti-epileptic drug usually alters the pharmacodynamics of phenytoin, making the elucidation of dosage more complex (5). However, the synergistic action of combination anti-epileptic drug therapy remains obscure in the literature and needs to be further investigated in controlled trials (5, 6). Since there are no evident reports on topiramate and its relationship to gingival overgrowth, we therefore presented a case of severe gingival overgrowth in a physically disabled patient with epilepsy receiving a combined anti-epileptic drug therapy of phenytoin and topiramate drugs, possibly associated with the synergistic action of combination anti-epileptic drugs therapy.

Poor oral hygiene is a critical risk factor for the severity of drug-induced gingival overgrowth, which is a time-dependent process (3). However, overgrowth itself distorts the gingival contour, allowing plaques to accumulate easily and leading to exacerbation of local inflammation, gingival bleeding and complicated drug-induced gingival overgrowth, creating a vicious cycle (3). In this case report, anti-epileptic drug usage and poor oral hygiene over a long period of time are considered to be the significant risk factors of gingival overgrowth. The mechanisms of the development of anti-epileptic drug-induced gingival overgrowth are multiple and complex, including gingival fibroblasts, cytokines, growth factors, drug metabolism and genetic susceptibility at both cellular and molecular levels (1–3). Moreover, the degree of inflammation, fibrosis and cellularity depend on the duration of therapy, dose and identity of the drug, quality of oral hygiene and genetic factors (2). The most effective treatment of drug-induced gingival overgrowth is the withdrawal or substitution of medication (1, 5, 10) and the implementation of a plaque control programme (4).

In addition, surgery is the main option, and in most cases, gingivectomy is still the treatment of choice (10). If left untreated, gingival overgrowth can shift the patient's dentition or cover the entire crown of the affected teeth (4). Disfiguring of gingival overgrowth is not only aesthetically displeasing but also impairs nutrition and access for oral hygiene, resulting in an increased susceptibility to caries and periodontal diseases, as found in this case report. For the treatment of this case, full dental clearance extraction, surgical excision of gingival overgrowth, oral hygiene instruction and replacement of anti-epileptic drugs were accomplished. In conclusion, the effective management of patients with drug-induced gingival overgrowth requires the active involvement of both medical and dental professionals to reduce the severity and impact of the gingival overgrowth.

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