INTRODUCTION

Antiphospholipid syndrome (APS) is also known as antiphospholipid antibody (APLA) syndrome, Hughes Syndrome (Graham Hughes),[1] or “Sticky Blood.” APS is an acquired autoimmune condition, defined by the occurrence of venous and arterial thrombosis, often multiple, and recurrent fetal losses, frequently accompanied by a moderate thrombocytopenia, in which the body recognizes the normal components of blood and/or cell membrane (phospholipids, fatty molecules) as foreign substances and produces APLA’s namely lupus anticoagulant, anticardiolipin antibodies, or anti-b2 glycoprotein-I antibodies.[2] Single vessel involvement or multiple vascular occlusions may give rise to a wide variety of presentations which included thrombocytopenia (3.7%), livedo reticularis (2.6%), stroke (2.4%), transient ischemic attacks (2.3%), deep vein thrombosis (2.1%), pulmonary embolism (2.1%), epilepsy (1.7%), valve vegetations (1.4%), and myocardial infarction (1%) among others.[3]

Pathogenic mechanism common to autoimmune[4] and periodontal diseases[5] is the increased production of the cytokines tumor necrosis factor and interleukin 1 beta. Susceptible patients exhibit an abnormal immune-mediated inflammatory response.[4] The APS can be found in patients having neither clinical nor laboratory evidence of another definable condition (primary APS) or it may be associated with other diseases (secondary APS), mainly systemic lupus erythematosus, but occasionally with other autoimmune conditions,[6] infections,[7] drugs,[2] and malignancies[8] or in a small subset of patients, as a life-threatening form characterized by a rapid development of microthrombosis that led to rapid multiorgan failure, which is termed catastrophic APS.[9] Venous thrombosis in APS most commonly affects deep vein of the lower limb and/or pulmonary embolism, but any part of the venous system may be involved. The most frequent site of arterial thrombosis in APS in the cerebral vasculature results in transient cerebral ischemia/stroke.[10] These antibodies themselves may be directly implicated in causing epilepsy[11] such as decreasing the

Abstract:
Antiphospholipid antibody (APLA) syndrome is a noninflammatory autoimmune disease, with innumerable clinical manifestations ranging from recurrent thrombosis and pregnancy morbidity to valvular lesions, transverse myelitis, thrombocytopenia, and hemolytic anemia. APLAs in antiphospholipid syndrome (APS) are well-known risk factors for cerebrovascular accidents. Stroke is the most common manifestation of APS in the central nervous system. Gingival enlargement is a known side effect of phenytoin which is an antiepileptic drug. This can have a significant effect on the quality of life as well as increasing the oral bacterial load by generating plaque retention sites. The management of gingival overgrowth seems to be directed at controlling gingival inflammation through a good oral hygiene regimen. Thus, this case report aims to describe the conservative management of phenytoin-induced gingival enlargement combined with inflammatory enlargement in a patient with APLA syndrome.

Key words:
Antiphospholipid syndrome, gingival hyperplasia, periodontal therapy

Case Report

Management of phenytoin-induced gingival enlargement in a patient with antiphospholipid antibody syndrome: A rare case report

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activity of the neurotransmitter gamma-aminobutyric acid. Considering this autoimmunity mechanism, autoimmune components (antiphospholipid) might be important in the pathogenesis that can recognize various brain endothelial cells.

Phenytoin is an antiepileptic drug commonly used as drug of choice for epileptic patients. Gingival enlargement is a well-recognized adverse effect and occurs in about 50% of patients receiving phenytoin. As per evidence, drug-induced gingival enlargement may improve by substitution with other anticonvulsant drugs, along with reinforcement of good oral hygiene regimen. Surgical excision of hyperplastic gingival is often necessary to correct the esthetic and functional impairment associated with this condition to successfully manage it. Thus, this case report emphasizes the challenges that oral and medical health practitioners face when developing appropriate treatment modalities for epileptic patients associated with APLA syndrome, particularly those with periodontal disease which often could be missed by general practitioners. Here, we present a rare case of management of phenytoin-induced gingival enlargement in a patient with APLA syndrome.

CASE REPORT

A 38-year-old male patient reported to the department of periodontics with chief complaint of bleeding gums and also with the history of seizures for 3 years and on medication for the same. He first noticed that his gums had become thick and swollen before 1½ years which gradually started to bleed while brushing for 6–8 months. Medical history revealed that the patient was a known case of APLA syndrome and had a history of cerebrovascular thrombosis before 3 years and had undergone a burr hole craniotomy for the same to relieve the decompression. The patient also gave history of generalized tonic–clonic seizures since then and was on medication, i.e., phenytoin sodium for the same. The patient was on oral anticoagulants (warfarin sodium 5 mg 1-0-0, i.e. sofarin tablet and anticonvulsants tablet eptoin 100® 1-0-2).

On intraoral examination, there was presence of moderate amount of local factors, generalized bleeding on probing (Muhlemann and Son bleeding index score was 4), and suppuration was present. The gingiva revealed generalized puffy and erythematous enlargement [Figure 1]. Generalized pockets were present with Grade I mobility (tooth #11–18, 24, 35, 37, and 38), Grade II mobility (tooth #28, 31, 32, 41, and 42), and Grade II furcation involvement (tooth #27). Routine blood examination revealed that there was slight increase in total white blood cell count of 11,300 cells/mcL and a slight raise in the international normalized ratio values of 2.03. Full-mouth radiographs revealed generalized bone loss whereas panoramic X-ray revealed vertical bone loss in relation to 13–21, 26, and 32–42 [Figure 2]. Many teeth had a questionable prognosis because of the simultaneous occurrence of gingival enlargement and chronic periodontitis. Clinically, inflammatory gingival enlargement, drug-induced enlargement, conditioned gingival enlargement, and gingival enlargement associated with systemic diseases were considered in the differential diagnosis. Based on the clinical findings and medical history, it was diagnosed as phenytoin-induced gingival enlargement combined with inflammatory enlargement. The patient’s neurologist was consulted, and medication could not be deferred or changed.

Treatment

Considering compromised medical condition, conventional flap therapy was avoided because of the risk of hemorrhagic episodes. Hence, a conservative treatment (scaling and root planing with maintenance and regular follow-up) under antibiotic coverage was planned for this patient after taking opinion from neurologist and consent from patient’s caretaker. The periodontal treatment included several scaling sessions...
and gingival debridement, accompanied by ample washings with oxygenated water and 3% chloramine solution. Systemic antibiotic therapy included administration of amoxicillin 500 mg and metronidazole 400 mg three times a day, for 7 days. Antiseptic mouthwash 0.2% chlorhexidine mouthrinse was prescribed twice daily for 3 weeks. As a result of the antibiotics and periodontal therapy, satisfactory results were seen at the follow-up visit, with the presence of pockets and gingival enlargement in some areas [Figure 3]. Oral hygiene practice was stressed to the patient during regular follow-up visit with the continuation of the drugs for the main disease.

**DISCUSSION**

Immune mechanism shares a common pathway both for systemic autoimmune diseases and periodontal diseases. Increased production of cytokines and abnormal immune-mediated inflammatory response[46] are the pathogenic mechanisms in both the conditions.[35] Studies have been conducted to find the association between periodontal diseases and various systemic autoimmune diseases independently. One such study done by Ramesh Kumar et al.[16] showed that the presence of systemic autoimmune diseases may pose a risk for the development of periodontal diseases. He also showed that all patients with APS had periodontal disease. Epilepsy is the utmost common chronic neurological disorder in human, and phenytoin remains the drug of choice for control of seizures in cerebral palsy.[14] Clinically, gingival enlargement frequently appears within 1 year of the initiation of treatment with the phenytoin drug.[17]

The precise mechanism by which phenytoin-induced enlargement occurs is still not completely understood although a number of hypotheses have been suggested.[18] Expression of these gingival changes can be related to numerous variables such as type of drug, dosage levels, interactions with other drugs, preexisting periodontal disease, presence of dental plaque, current oral hygiene care, and individual variations of response, i.e., genetic factors the latter determining the heterogeneity of the gingival fibroblasts.[19] Patients who are on anticoagulant therapy with coexisting autoimmune disease undergoing elective invasive procedures are at high risk. Hence, patients in primary care setting have to be managed with utmost care after outweighing the benefits and risks involved in the treatment plan. Similar to our case report, Giurgiu and Dumitriu[20] reported one such case report where the patient was managed by a complex treatment especially, when the general condition of the patient was not favorable.

Based on this, a multidisciplinary approach including medication adjustments followed by periodontal therapy with supportive care is recommended for this patient. Unfortunately, in the present case, the patient’s neurologist did not give an opinion for change of drug because of severe compromised medical condition. The risks involved in undertaking a surgical approach were more as compared to the benefits and also there were many teeth with a questionable prognosis. Considering all the above factors and the clinicopathological and radiographic findings, conservative treatment with scaling, root planing, and curettage under antibiotic coverage was planned. Regular follow-up was done with maintenance, and the results of this treatment approach were quite satisfactory.

**CONCLUSION**

The present case emphasizes on wide diversity in clinical presentation of phenytoin-induced gingival enlargement in epileptic patients associated with APLA as well as significant diagnostic challenges and relevant management by the clinicians. In numerous situations, a complex treatment is necessary; however, it may not be always possible to go for the surgical correction because of medically compromised condition and hemorrhagic episodes. Therefore, early identification of susceptible patient, maintaining them under constant supervision, and a multidisciplinary approach are critical steps in the successful management of drug-induced enlargement in APLA patients.

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**Conflicts of interest**
There are no conflicts of interest.

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