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Ligneous Periodontitis with Type-I Plasminogen Deficiency in Two Siblings: Thirty-six Months of Follow-up

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ABSTRACT

Hypoplasminogenemia is a rare condition associated with ligneous conjunctivitis, pseudomembranous lesions on the tarsal conjunctiva, and oral lesions. Lignous periodontitis is a periodontal disease characterized by nodular gingival enlargements and progressive tissue destruction, which is part of a systemic disease due to fibrin deposition and causes rapid bone loss despite treatment attempts. It usually ends with the early loss of teeth. Defective fibrinolysis and abnormal wound healing are the primary pathogenetic factors and differ from other mucosal systemic disorders. In this case report, we describe the treatment of ligneous periodontitis secondary to plasminogen deficiency in two siblings aged 12 and 14 years, respectively. In the treatment of lignous periodontitis, a 12-year-old male patient underwent calculus removal, root correction and gingivectomy under local anesthesia and improved oral hygiene. The gingival enlargement of the patient recurred in a short time. A 14-year-old female patient underwent tartar cleaning and root correction. Improvement was observed in oral hygiene, gingival bleeding and patient complaints decreased. According to the results of this case report, we concluded that maintaining oral hygiene is very important to reduce the clinical symptoms of ligneous periodontitis and we can say that ligneous periodontitis is a genetic disease.

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INTRODUCTION

Hemostasis depends on vasoconstriction, the formation of blood coagulation factors, and fibrinolysis, especially plasmin. Plasmin is derived from plasminogen (plg), which is present in plasma and synthesized in the liver. When bound to fibrin, plg converts into plasmin, the active fibrinolysin. The protease plasmin plays a vital role in hemostasis through a controlled dissolution of the fibrin blood clot (1).Plasminogen and plasmin are very important for the destruction of fibrin. They are also important in epithelial regeneration and wound healing.

Hypoplasminogenemia or Type-I plg deficiency is a rare disease associated with total deficiency and functional activity of immunoreactive plg. Impaired fibrinolysis results in nodular subepithelial accumulations consisting mainly of fibrin (2-5).

The term "ligneous periodontitis" was first used to describe a destructive membranous periodontal disease characterized by gingival enlargement and periodontal tissue destruction due to the accumulation of amyloid-like material (3-6). Ligneous mucosal pathologies related to hypoplasminogenemia are rare inherited chronic disorders, causing the typical clinical appearance of rigid, stalkless, fibrin-rich, woody-like pseudomembranous mucosal masses, mainly on the tarsal conjunctiva. Ligneous conjunctivitis is a rare form of chronic conjunctivitis that affects girls more often than boys (gender ratio of 3:1) (4).

The conjunctiva and gingival mucosa are frequently involved, and the lesions usually begin in childhood (2-4,7,8). Simultaneous involvement of other regions such as the tracheobronchial tree, kidneys, female genital tract, and skin may be observed (4). Less common manifestations include ligneous vaginitis (8%) and involvement of the respiratory tract (ligneous laryngitis) (16%), the ears (14%), the gastrointestinal tract (2%) and the central nervous system (occlusive hydrocephalus) (5-9).

A large-scale epidemiological study in the United Kingdom reported the prevalence of (heterozygous) Type-I plg deficiency as 0.26% (25 of 9.611 subjects) (4). The predicted prevalence of homozygotes/compound heterozygotes was estimated to be within the range of 1.6 per 1 million people in Europe (1,4,10).

The conjunctival mucosa and gingiva are easily exposed to external injury, which can lead to sustained low-level inflammation and regeneration. These tissues being amenable to injury is probably the reason why most patients initially present with conjunctival or gingival symptoms. Local injuries, infections, irritations and surgical interventions can trigger new mucosal lesions (11).

This case report describes a case of ligneous periodontitis in two siblings (a boy and girl) who were referred to the Department of Periodontology by their medical doctors with complaints of gingival enlargement and bleeding. A written patient consent statement form had been read by patients and their parents. Also, oral explanation was made. Thereafter the form including name and signature of the parents was received before treatments. Since the patients had symptoms of ligneous conjunctivitis and intraoral lesions, the authors decided to perform a biopsy. Histopathological examinations of the gingival samples obtained from the patients were made, and the two siblings were diagnosed with ligneous periodontitis.

CASE DESCRIPTION

Case Report 1

After clinical and radiographic examination of a 12-year-old male patient, endodontic treatment was performed in the right first mandibular molar tooth. Difficulty in closing the eyelids, increased tear secretion, extreme sensitivity to light, and 80% vision loss were identified. Severe gingival enlargement, spontaneously gingival bleeding, conjunctivitis was detected, and ligneous periodontitis was diagnosed. The 12-year-old male patient had more severe gingival enlargement on his oral examination when compared to his 14-year-old elder sister.

Gingival enlargements were nodular, and no pseudomembrane formation was observed. The molar teeth had Miller class-1 mobility (Figure 1).

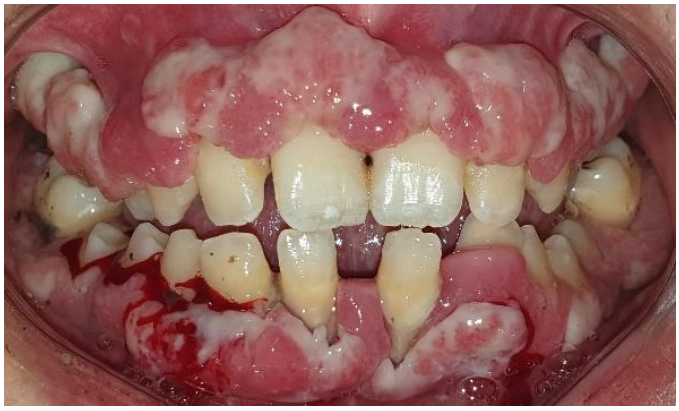

Figure 1. Before initial therapy in case 1. Gingival enlargements were nodular and revealed pseudomembrane formation. Miller class-1 mobility was observed in the molar teeth.

Radiographic examination revealed that all first molar teeth had caliceal bone loss and mild bone loss around the anterior mandibular teeth (Figure 2).

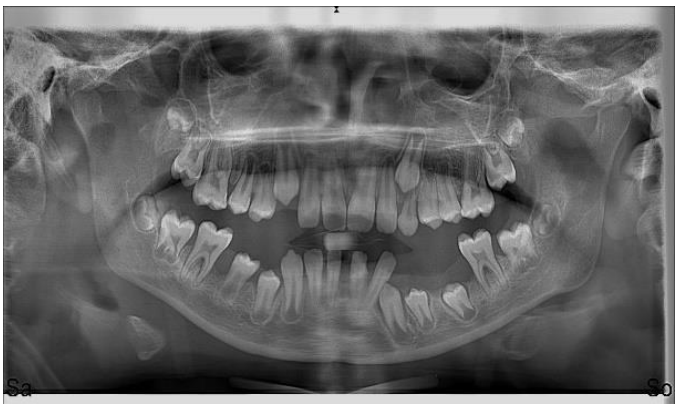

Figure 2. Before treatment, in case 1, severe alveolar bone loss in the molar teeth and mild bone loss in the mandibular anterior teeth was observed.

Case 1 Management

Scaling and root planning were performed on all patient teeth under local anesthesia. Following surgical treatment, nonsteroidal anti-inflammatory drugs and chlorhexidine gluconate were administered. Following these processes, chlorhexidine gluconate was administered. One month later, at the follow-up, it was observed that bleeding and complaints of the patient reduced, and oral hygiene improved.

Histological examination was performed for this case due to his severe gingival enlargements. Histological samples were derived from gingiva in the gingivectomy operation session (Figure 3, 4). Then, a gingivectomy was performed to provide better oral hygiene for the patient. The gingivectomy operations of the patient's entire mouth were completed within four weeks (Figure 5, 6).

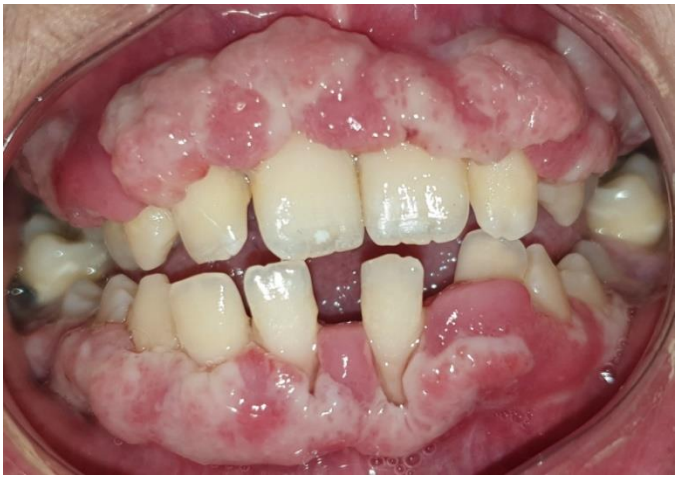

Figure 3. Follow-up at one month after scaling and root planing in case 1. Oral hygiene improved and gingival bleeding significantly reduced.

In case 1, after surgical procedures were accomplished, gingival enlargements were observed to recur in a short time all over the mouth. The patient was followed-up with periodic examinations to reassess her periodontal condition (Figure 3, 5, 6, 7, 8). The patient has visited for control after three years (Figure 7, 8, 9).

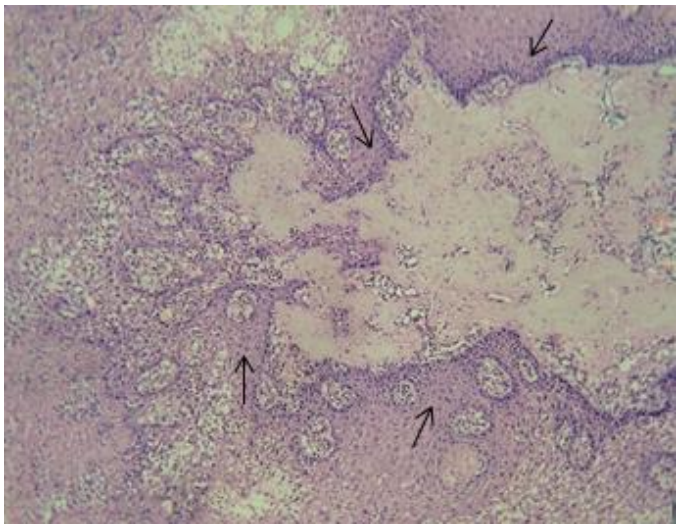

Figure 4. Histological section of tissue sample derived from gingiva of the upper jaw at the time of gingivectomy operation. Chronic phase of ligneous periodontitis. Black arrows show fibrin accumulation beneath the epithelium.

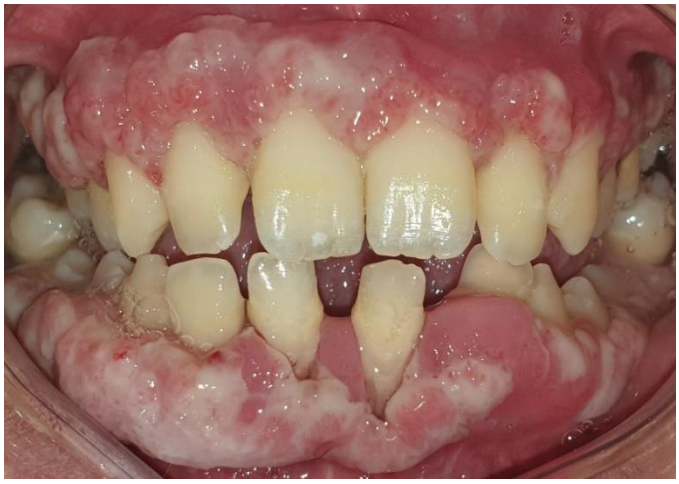

Figure 5. At the one-month follow-up session gingivectomy operation was performed on upper jaw. This picture shows the healing of gingiva one month after gingivectomy was performed on the upper jaw.

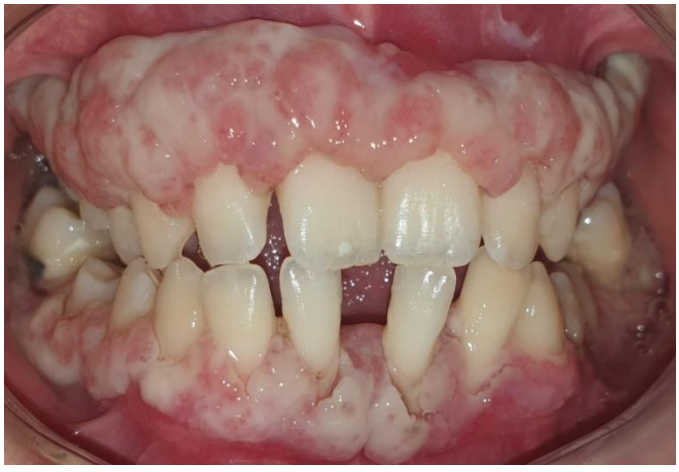

Figure 6. One month later from performing gingivectomy operation on upper jaw the same operation was made on the lower jaw. This picture shows the healing of gingiva one month after gingivectomy was performed on the lower jaw.

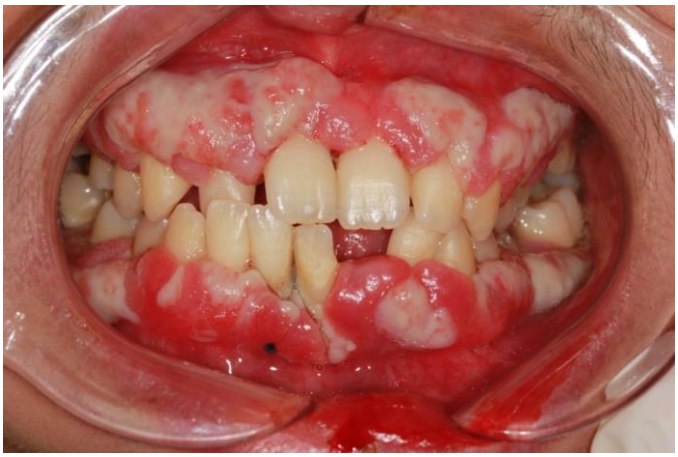

Figure 7. Three years after first visit. The picture reveals that in spite of moderate oral hygiene gingival enlargements remained stable.

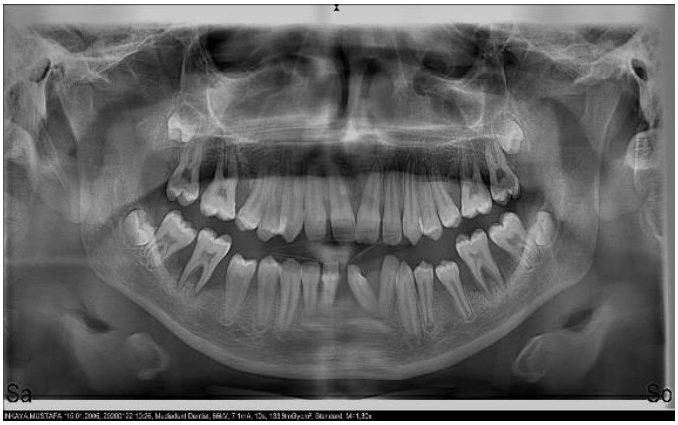

Figure 8. Three years after the initial radiograph in case 1. Notice that severe alveolar bone loss is present in the permanent dentition.

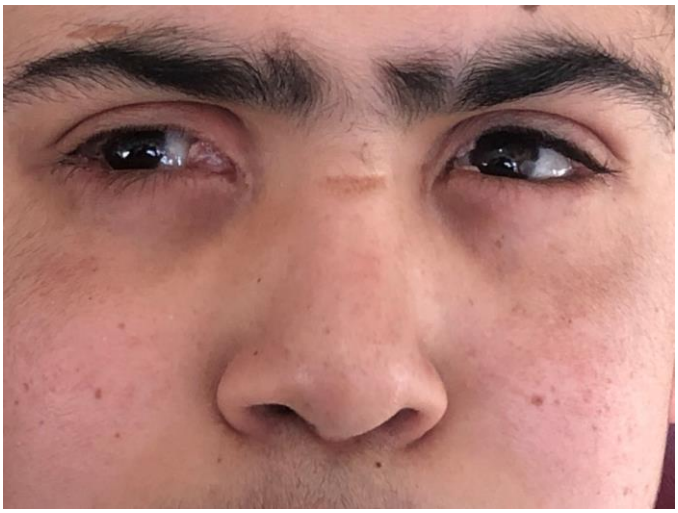

Figure 9. Appearance of eyes of case 1, three years after first visit.

Case Report 2

In a 14-year-old female patient, there was diffuse nodular gingival enlargement, together with spontaneous gingival bleeding around the maxillary and mandibular teeth (Figure 10). The teeth were almost covered with yellow-white pseudomembranous. Miller class-3 mobility was observed in the mandibular molar teeth. Radiographic examination revealed

progressive bone destruction at the molar tooth areas and migration of the teeth due to bone loss in the lower anterior region (Figure 11).

There was difficulty in closing the eyelids, increased tear secretion, and observed vision loss. The patient had undergone medical treatment for this reason.

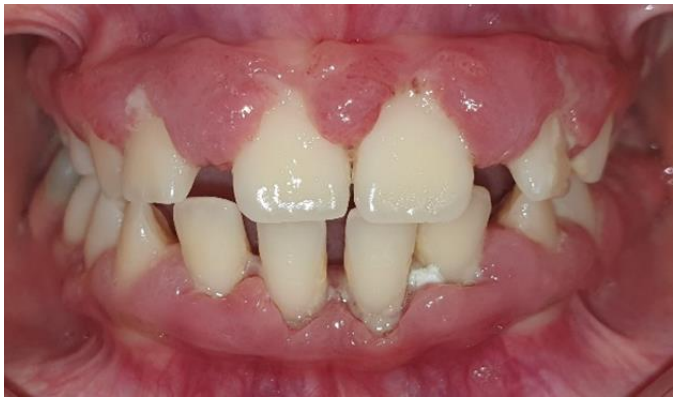

Figure 10. Before treatment, in case 2 there were diffuse nodular gingival enlargements and spontaneous gingival bleeding was observed in all teeth.

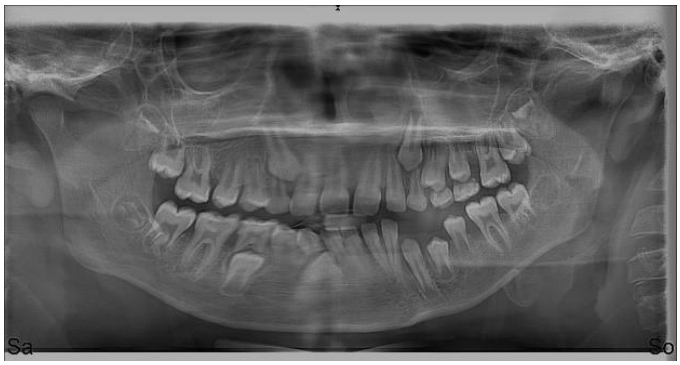

Figure 11. Radiograph of case 2 before treatment. Severe bone destruction at the molar tooth areas and migration of the teeth due to bone loss in the lower anterior region was detected.

Case 2 Management

Scaling and root planning were performed on all patient teeth under local anaesthesia. One month later, at the follow-up session, it was observed that gingival bleeding and complaints of the patient were reduced. Histological examination and gingivectomy were not performed because the gingival lesions were not as bad as her younger brother's (Figures 12, 13, 14, 15).

In case 2, the severity of gingival enlargement did not decrease. The patient was followed-up with periodic examinations for her periodontal condition (Figures 12, 13, 14).

HISTOLOGICAL RESULTS

The histological features of the lesions, which can involve various parts of the body, are similar. Two types of changes occur, and both might usually be identified within the same lesion.

Figure 12. Clinical appearance of case 2, one month after scaling and root planing. Gingival enlargements regressed and bleeding on probing or spontaneous gingival bleeding stopped.

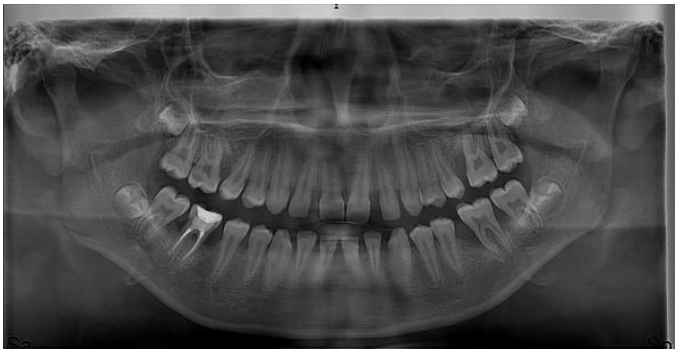

Figure 13. Radiograph of case 2. Two years after initial radiograph, mild alveolar bone loss was observed in permanent dentition.

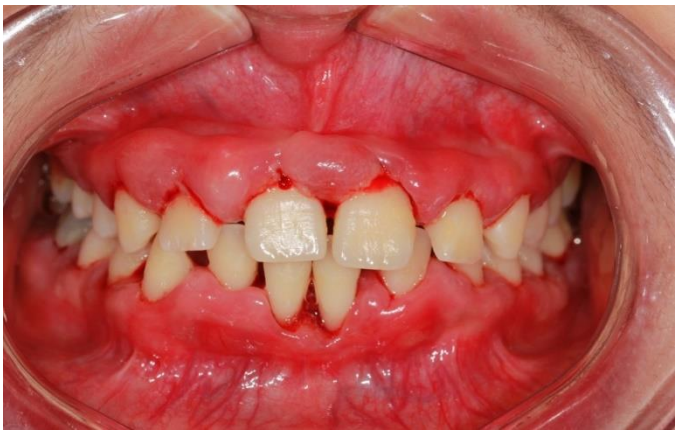

Figure 14. Three years after first visit. The picture reveals that in spite of moderate oral hygiene gingival enlargements remained stable.

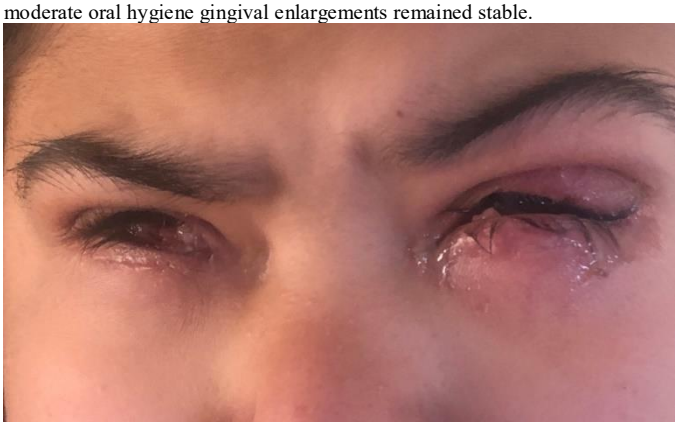

Figure 15. Appearance of eyes of case 1, three years after first visit.

Early histological changes are characterized by ulceration, intraepithelial edema, polymorphonuclear leukocyte-rich exudate, keratinocyte detachment, and fibrin deposition. In addition, the mucosal epithelium may show extensive down-growth. The main feature of late changes is the accumulation of subepithelial, nodular, amorphous, amyloid-like, eosinophilic material that cannot be stained as amyloid with Congo-Red stain. The overlying epithelium manifests hyperplastic changes around these depositions (Figure 4) (11).

In the histopathological examination of this study, Hematoxylin-Eosin stain was used under x100 magnification. In human tissues, various abnormal cellular products are resistant to degradation. The fibrillary structure of some of these might be integrated with typical tissue components. The depositions identified in colloid milium, lichen, and macular amyloidosis are of this type. Apoptosis of keratinocytes and filamentous degeneration of specific proteins are also crucial in the pathogenesis (11-13). A similar pathogenetic mechanism is possible in ligneous mucosal disease.

DISCUSSION

Inherited plasminogen deficiency is classified into two types: hypoplasminogenemia (Type-I) and dysplasminogenemia (Type-II). In Type-I, both the functional plasminogen level and plasminogen antigens are reduced, whereas, in Type-II, only the functional activity is reduced markedly.[10] Interestingly, only hypoplasminogenemia (Type-I) has been reported to be associated with the ligneous disease (2,4,10,14-19).

In patients with plasminogen deficiency Type-I, the functional activity of plasminogen ranged from 6% to 66% (2,14,17,20). Furthermore, specific homozygous or compound-heterozygous mutations in the plasminogen gene have been identified in patients with hypoplasminogenemia (2,10,15).

It seems that the severity of clinical symptoms depends mainly on the magnitude of functional residual plasminogen activity. Indeed, patients who show undetectable functional plasminogen activity (<5%, where the normal range is from 70% to 143%) usually manifest severe multi-system disease (2,10). Some authors have mentioned that the time of onset for symptoms of ligneous periodontitis might be the eruption time of primary molars due to the eruption of larger teeth triggering the formation of gingival pseudomembranous (6). The administration of topical plasminogen has revealed better results for the treatment of ligneous conjunctivitis (16). On the other hand, its efficacy regarding the treatment of oral lesions remains to be elucidated.

The topical application of plasminogen was considered as a possible therapy for keeping pseudomembrane growth under control, at least until a more aggressive approach would be thought about in adulthood. In this study we did not have any opportunity to apply topical plasminogen. Scully et al. reported that gingival lesions could be controlled by topical application of heparin or intravenously administered purified plasminogen (14). Günhan et al. (3) claimed that systemic fibrinolytic and antithrombotic agents might prove more beneficial than local treatments because the ligneous lesions tend to involve several mucosal areas.

Ligneous periodontitis is a rare disease and occurs in consequence of plasminogen deficiency and fibrin accumulation. This disease is manifested as pseudomembranous gingival lesions and can rarely affect the eyes and other organs.

Since dental professionals might help in diagnosing this disorder, which has significant morbidity often missed by medical professionals, they should be familiar with its manifestations. Nevertheless, it is not possible to cure ligneous periodontitis with our current knowledge. Maintaining oral hygiene procedures are crucial in the management of this disease.

Ethics Approval and Consent to Participate

A consent form is obtained from the patients. A written patient consent statement form had been read by patients and their parents. Also oral explanation was made. Thereafter the form including name and signature of the parents was received before treatments.

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Conflict of Interest

The authors declares no conflict of interest.

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