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Review Article

LIGNEOUS PERIODONTITIS: REVIEW OF LITERATURE

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ABSTRACT

Ligneous periodontitis is poorly defined, a rare form of periodontitis. It is characterized by pseudomembranous gingival lesion with accumulation of amyloid-like material and may or may not be associated with ligneous conjunctivitis. It is possibly due to type I plasminogen deficiency but the exact cause is unknown. This review describes ligneous periodontitis in detail with respect to etiology, clinical, histological features and treatment modality.

Keywords: Ligneous Periodontitis, Ligneous Conjunctivitis, Plasminogen Deficiency, Pseudomembranous Periodontitis.

INTRODUCTION

The term ligneous periodontitis was first used by Omer Gunhan et al[1] to describe a destructive membranous periodontal disease. It is poorly defined entity characterized by gingival enlargement and periodontal destruction due to accumulation of amyloid-like material. Accumulation of amyloid-like material lacks the classical histochemical and ultrastructural features of amyloid[2].

Most of the pseudomembranous gingival lesions have been reported in association with ligneous conjunctivitis. Therefore, finding suggests that both clinical manifestations are related. Ligneous conjunctivitis is rare form of chronic conjunctivitis that usually affects children, girls more often than boys in ratio of 3:1 but may occur at any age[3,4]. This condition is ocular manifestation of a systemic disease that might be accompanied by formation of pseudomembranes on mucosa of oral cavity (ligneous periodontitis)[1,5-7], respiratory tract-larynx, trachea[6,8-10], nasopharynx , female genital tract (ligneous vulvovaginitis or cervicitis)[6,10], middle ear[9,10], gastrointestinal tract the mastoid system[10].

ETIOLOGY

Etiology of this lesion is not clear. Among the possible causes Type I plasminogen deficiency, autoimmune reactions, trauma, hypersensitivity reaction, genetic disorders and secondary response to viral or bacterial infections have been suggested[5,6,11]. Mingers AM et al[12] and Schuster V et al[13] have reported homozygous mutations in plasminogen gene in ligneous conjunctivitis cases. It is suggested that plasminogen deficiency plays a central role in pathogenesis of this rare disease.

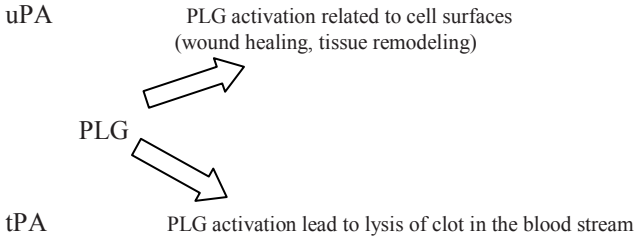
The fibrinolytic system plays an important role in hemostasis for controlled dissolution of fibrin clot. Two type of human plasminogen (PLG) deficiency exists[14]:

1) Hypoplasminogenemia / type I PLG deficiency:
   In which markedly decrease PLG antigen ≤ 1.9 mg/dl (normal range 6 to 25 mg/dl) and functional activity upto 33% (normal range 80% to 120%)
2) Dysplasminogenemia/ type II PLG deficiency:

There is reduced PLG activity, but normal or only slightly reduced PLG antigen levels[3].

Type I PLG deficiency was found to be associated with ligneous conjunctivitis (80%)[6] characterized by fibrin rich pseudomembranes mainly on tarsal conjunctivae and other pesudomembranous lesion such as ligneous gingivitis and periodontitis (34%)[3]. Autosomal-recessive inheritance of this disorder was confirmed.[13] In a large epidemiologic study in the United Kingdom, the prevalence of (heterozygous) type I PLG deficiency was reported to be 0.26% (25 of 9,611 subjects)[16]. The theoretically predicted prevalence of homozygote/ compound heterozygote was estimated to be in the range of 1.6 per 1 million people, at least in Europe.[3,8] Type II PLG deficiency patients, however, have never reported developing pseudomembranous lesion. PLG plays an important role in intravascular and extravascular fibrinolysis and wound healing. It is converted to plasmin by cleavage of the Arg561-Val562 peptide bond by either tissue-type PLG activator (tPA) or urokinase-type PLG activator (uPA).

Activation of PLG by tPA is the major pathway that leads to efficient lysis of fibrin clots in the blood stream, whereas activation of PLG by uPA seems to be mainly responsible for mediating PLG activation in association with cell surfaces (wound healing, tissue remodeling)[14].



The main substrate for plasmin is fibrin. Plasmin also has substrate specificities for several other components of the Extracellular matrix (ECM), including fibronectin, proteoglycans, and gelatin, indicating that plasmin also plays an important role in ECM remodeling.

Indirectly, plasmin also degrades additional components of the ECM via its ability to convert some promatrix MMPs (pro-MMPs) to active MMPs. During normal wound healing of the gingiva, significant fibrinolysis occurs by day 3 to 4 and is virtually complete by 1 week. Persistence of the fibrin matrix is associated with the induction of angiogenesis and formation of granulation tissue.[17]Mingers et al[12] were the first to show that plasma polymorphonuclear elastase protein levels were markedly elevated in patients with severe plasminogen deficiencies and more so in homozygous than in heterozygous patients. It is interesting to note that all patients with type I PLG deficiency have never been shown to have thrombophilia. In ligneous periodontitis, it is assumed that fibrin appearing during normal wound healing is persistent due to type I PLG deficiency.

Plasminogen is the precursor of plasmin, the main fibrinolytic enzyme which plays important roles in wound healing, keratinocyte division, migration, and differentiation. Central wound healing capacity with an arrest at the stage of granulation tissue formation and excessive fibrin deposition is possible cause of ligneous periodontitis.

Clinical features of ligneous periodontitis:

It is presented as generalized ulcerated, massive, nodular, waxy gingival enlargement can involve both maxilla and mandible[2]. Gingival swelling could be painless or painful. Enlargement is white-yellow to pinkish pseudomembranous covering teeth, with tendency to bleed. Accompanied by extensive bone loss may lead to loss of teeth[1].

Histological features:

Amyloid is a nonspecific histologic term for different chemical structures such as immunoglobulin light chain, serum amyloid fibril proteins, beta-2 microglobulin, transthyretin, keratin and some hormones[18]. All these materials look like homogeneous eosinophilic substances by routine histologic methods and show the same three-dimensional configuration.

There are two different phases of development[1]:

In the first, gingival epithelium showed extensive irregular down-ward proliferation. Severe acute inflammation of epithelium and underlying tissues with accumulation of homogenous eosinophilic fibrinous material around the vessels and beneath the epithelium. The inflammatory infiltrates included mostly plasma cells and polymorphonuclear leukocytes, with fewer lymphocytes and mast cells. Epithelium in acute phase showed edematous widening of intercellular spaces and contained numerous degenerated keratinocytes in the suprabasal layer in the form of hyaline apoptotic bodies. Subepithelial connective tissue is also edematous and contained numerous small dialated vessels and an amyloid like material.

In second phase, the epithelium showed slight acanthosis and parakeratosis without ulceration. Inflammatory cell infiltrate is not as heavy as in first stage. There is subepithelial amorphous, nodular, homogeneous, eosinophilic amyloid-like accumulation. The accumulated material did not show the typical apple green/ golden brown birefringence of amyloid with Congo-red stain.

Thioflavin-T fluorescence methods for demonstration of amyloid are also negative. Accumulation is reticulin poor and stained red with Masson's trichrome stain.

Immunostaining shows strongly positive for fibrinogen and weakly positive for immunoglobulins. Electron microscopy of gingiva shows fine filaments, approximately 10nm in diameter arranged in interweaving bundles resembling those seen in ligneous conjunctivitis. Within this network there are short bundles of thicker, darker filaments resembling epithelial tonofilaments and also fragments of cellular debris. No typical collagen fibers were found within this material[19]. The reason why the amyloid-like material in these cases failed to show all the tinctorial properties of amyloid can be explained by considering the process of amyloidogenesis. For materials like immunoglobulin light chain and keratins to acquire the typical properties of amyloid, a time-dependent series of events must occur consecutively[19]. Failure of one or more of these stages to take place may conceivably result in the formation of a material which shares only some of the features of amyloid. This half-amyloid, half-hyaline material (hyaline-amyloid) needs more filamentous degeneration of the deposited materials in order to stain as typical amyloid[19] (Table 1).

TREATMENT

Several treatment efforts such as subgingival curettage, gingivectomy, chlorhexidine rinsing and antibiotics were unsuccessful. Surgical excisions of gingival lesion are followed by rapid recurrence of membranous lesions. Extraction of most permanent teeth appears to be inevitable due to advanced alveolar bone loss and poor prognosis of this ligneous disease. Administration of topical plasminogen has shown good results for the treatment of ligneous conjunctivitis[20], whereas its efficacy for the treatment of oral lesion remains to be elucidated. It is expected, however that topical plasminogen together with periodontal therapy can postpone it until adulthood, when a more aggressive approach can be considered. In some cases gingival lesions become quiescent or disappear following tooth loss.[2] Frimodt- Moller[5] also noticed some regression in the eyelid lesion following tooth extraction. Different modalities of surgery, antibiotics, steroids, antiviral agents, beta and x-ray irradiation were found ineffective in the treatment[6].

Table 1: Lesions containing amyloid and amyloid-like hyaline substances (Adapted from Gunhan O et al[2]):

	Primary localized mucocutaneous amyloidosis	Juvenile colloid milium	Hyaline bodies of odontogenic cysts & tumor	Hyaline bodies of lichen planus	Lipoid proteinosis	Ligneous conjunctivitis	Ligneous periodontits
Clinical presentation	Yellowish pale nodules	Yellowish waxy papules	Odontogenic tumor or cyst	Whitish reticular papules & plaque	Yellowish waxy papules or nodules	Yellowish white membrane	Yellowish white nodules and membranes
Oral involvement	+	–	+	+	+	+	+
Other mucosal involvement	+	–	–	–	+	+	+
Cutaneous involvement	+	+	–	+	+	–	–
Genetic basis	uncertain	-	-	-	+	uncertain	-
PAS	+	+	+ or -	+	+	+	+
Masson's trichrome	green	red	red	Red	green	red	red
Congo Red	+	+/-	+/-	+/-	+/-	-	-
Electron microscopy	Filamentous masses	Filamentous masses	Homogenous lamellated, fibrillar	Filamentous Masses	Amorphous material, thick basal lamina	Filamentous masses	Fine filaments

Table 2: Review of ligneous periodontal cases (Adapted from Gunhan O 1999[1])

Reference	Age-gender-race	Oral presentation	Other diseases	Treatment of gingival lesion	Follow-ups
Frimodt- Moller[5]	14 months F	Recurrent mandibular epulis	Ligneous conjunctivitis	Surgical excisions	Eyelid lesion regressed with the excision of gingival mass & teeth extraction. No recurrence for 1 yr
Hidayat & Riddle[6]	7 F	Membranous gingival lesion	Ligneous conjunctivitis	Not reported	Not reported
Diamond et al[4]	25 F Caucasian	Tranexamic acid associated generalized gingival hyperplasia	Ligneous conjunctivitis	Discontinuation of drug resulted in resolution	Not reported
Nussgens & Roggenkamper[7]	12 F Turkish	gingival hyperplasia	Ligneous conjunctivitis since 2 yrs of age	Gingivoplasty	Eye-lid lesion recurred
Gunhan et al[2]	20 M Turkish	Membranous gingival enlargement more than 5 yrs	Ligneous conjunctivitis	Surgical excisions	recurred
Gunhan et al[2]	20 F Italian	Membranous gingival enlargement	Ligneous conjunctivitis	Surgical excisions	recurred
Baykara et al[15]	11 F Turkish	Membranous gingival enlargement	Ligneous conjunctivitis since 1yr of age	Gingivectomy	Not reported
Gokbuget et al[7]	24F Turkish	Gingival swelling	Ligneous conjunctivitis	Gingivectomy, oral hygiene care, tetracycline, topical chlorhexidine	Oral & conjunctival lesion recurred
Gokbuget et al[7]	15 M Turkish	Generalized ulcerated gingival swelling	Possible Ligneous conjunctivitis	Gingivectomy, oral hygiene care, tetracycline, topical chlorhexidine	Oral & conjunctival lesion recurred
Gokbuget et al[7]	10 M Turkish	Generalized ulcerated gingival swelling	Not reported	Gingivectomy, oral hygiene care, tetracycline, topical chlorhexidine	Oral lesion recurred
Gokbuget et al[7]	4 F Turkish	ulcerated gingival swelling	Iron deficiency anemia	Gingivectomy, oral hygiene care, tetracycline, topical chlorhexidine	Oral lesion recurred
Gokbuget et al[7]	10F Turkish	Generalized Gingival swelling	Ligneous conjunctivitis	Gingivectomy, oral hygiene care, tetracycline, topical chlorhexidine	Oral lesion recurred
Gunhan et al[1]	19 M Turkish	Membranous gingival enlargement	Ligneous conjunctivitis	Gingivectomy, Chlorhexidine rinsing, antibiotic therapy	Recurred within 1 yr
Gunhan et al[1]	18 F Turkish	Membranous gingival enlargement	Ligneous conjunctivitis	Gingivectomy, Chlorhexidine rinsing, antibiotic therapy	Recurred within 1 yr
Gunhan et al[1]	14 F Turkish	Membranous gingival enlargement	Ligneous conjunctivitis since 1yr of age	Gingivectomy, Chlorhexidine rinsing, antibiotic therapy	Recurred within 3 months

CONCLUSION

Ligneous periodontitis is atypical form of periodontitis, its etiology, clinical and histopathological features are distinct from classic periodontitis. Hence sound knowledge about ligneous periodontitis is important while diagnosing the disease. Since it is rare entity exact treatment modality is not yet established. There is need for further exploration of this entity.

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