Review Article

Molar-Incisor Pattern Periodontitis: An Overview

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Abstract:

Molar incisor pattern periodontitis (MIPP) is a severe periodontal disease is that affects particular teeth with an early onset and rapid clinical attachment loss. It was previously referred as aggressive periodontitis and the term was revised in 2017 classification of periodontal and peri-implant conditions. Aggregatibacter actinomycetemcomitans (Aa), host susceptibility, familial aggregation and immunological aspects play a crucial role in the pathogenesis of the disease. A specific JP2 Genotype from serotype "b" of (Aa) is significantly associated with aggressive form of periodontal disease. Along with traditional mechanical therapy systemic antibiotics can be used as an adjunct in the management of MIPP. Surgical treatment includes open flap debridement. Guided tissue regeneration along with biologics like enamel matrix derivative (EMD), platelet rich fibrin etc. Antimicrobial Photodynamic therapy is another laser-based therapeutic procedure for treatment of MIPP. This review article provides an overview of recent concepts and treatment modalities for MIPP.

Keywords: Aggressive periodontitis, Familial aggregation, Guided tissue regeneration, Molar incisor pattern, Periodontitis.

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INTRODUCTION:

Periodontitis is a biofilm-dependant condition characterized by alterations in the resident microbiota, progressing to an enhanced host response to bacterial challenges. Because of this dysbiosis along with host's immune profile, the destruction of tooth-supporting apparatus takes place. It can be clinically identified in various forms and rate of progression. According to the 1999 classification of periodontal diseases and conditions, Localized Aggressive Periodontitis (LAP) was considered to be affecting systemically healthy individuals.[1] It appears at an early age with familial aggregation, limited deposition of biofilm, mild gingival inflammation, significant bone loss, rapid clinical attachment loss (CAL) development, specifically in the first molars and incisors.[2] Gunsolley et al. proposed that the aggressive form of the disease progresses from localized to generalised form when serum IgG or IgA levels are ineffective against target pathogens such as Aggregatibacter actinomycetemcomitans (Aa), allowing their overgrowth with time.[3]

TERMINOLOGIES

Destructive periodontal diseases affecting children, adolescents, and young adults have been recognized for many years, with various classifications and

terminologies proposed over the past decades (table 1). The 2017 World Workshop on the Classification of Periodontal Disease highlighted factors supporting aggressive periodontitis as a distinct term. In the 1999 classification, aggressive periodontitis was defined by 3 fundamental characteristics: rapid attachment loss, occurrence in systemically healthy individuals, and familial involvement. Due to the aggressive nature of the disease, defect localization, familial predisposition [4] and minimal subgingival biofilm, the terminology was updated to "molar-incisor pattern periodontitis" following the 2017 workshop on the classification of periodontal and peri-implant diseases and conditions. [5]

Table 1 – Terminologies

1923 Gottlieb B.	Described Aggressive Periodontits as Diffuse Alveolar atrophy
1942 Orban B and Weinman JP	Stayed term 'Periodontosis as non-inflammatory form of Aggressive Periodontitis
1966 American Academy of Periodontology	Dismissed Periodontosis as unique disease entity
1971 Baer PN	Promoted term Juvenile Periodontitis
1976 Newman MG et al	Aa associated with Juvenile Periodontitis
1976 Slots J	Aa associated with Juvenile Periodontitis
1976 Listgarten MA	Described thin biofilm on root surface of subjects with JP
1982 Goodson JM et al	Episodic nature of periodontal disease
1985 Moore et al	Challenged microbial disease specificity as related to Aa and JP
1985 Dewhirst FE et al	Highlighted importance of cytokines as related to bone loss
1991 Loe H and Brown LJ	Early onset periodontitis
1998 Socransky SS et al	Identified rate of progression in early onset periodontitis
1999 American Academy of Periodontology	Aggressive Periodontitis

EPIDEMIOLOGY

Epidemiological studies suggest that early onset aggressive periodontal disease differs by population, with African descendants having a greater prevalence (up to 6%) and Caucasians having the lowest (less than 1%).[6] The prevalence of the disease in South America varies from 0.3% to 5%, linked to the presence of mixed-race populations. This distribution shows a clear geographical distinction.

[7] This type of periodontitis can also affect primary dentition, often diagnosed late in advanced stages or through early exfoliation caused by greater bone loss around the teeth compared to the natural rate of physiological apical root resorption. Periodontal assessment is often neglected in pediatric dental examination so the actual onset of MIPP remains unknown.[2]

ETIOLOGY

The early sign of lesions in MIPP is marked by the emergence of highly virulent causative agents, increased individual susceptibility, or a combination of both. A. actinomycetemcomitans plays vital role in the pathogenesis of the disease. A specific JP2 Genotype from serotype "b" has been significantly linked with advanced forms of periodontal disease.[8] Aa can be detected in 90% of localised aggressive periodontitis and 30-50% adult periodontitis. It can produce virulence factors. The mechanisms by which Aa causes periodontal tissue destruction includes Leukotoxin (LtxA), Cytolethal distending toxin (CDT) and a toxin which is homologue of the Helicobacter pylori CagE. LtxA impacts human immune cells by inducing leukocyte killing, triggering neutrophil degranulation, and protecting bacteria from phagocytic destruction. A deformity in cementum formation maybe responsible for localization of the defects.[9]

A large number of studies established A. actinomycetemcomitans as the primary causative gram negative bacteria in molar-incisor pattern periodontitis. However, additional investigations

have also implicated other microorganisms, such as P. gingivalis, Fusobacterium, spirochetes, Eubacterium, and black- pigmented bacteroides.[9] Radiographically, periodontal lesions typically exhibit a characteristic pattern of intrabony defects on the interproximal surfaces of posterior teeth, often occurring bilaterally. In generalised patterns of disease, the bone loss may present as a horizontal pattern on radiographs.

Table 2 - Etiology and treatment modalities

	Molar incisor periodontitis	Periodontitis
Clinical characteristics	Rapid destruction Thin biofilm with minimal calculus Minimal inflammation Young population	Slower progression of disease Heavy biofilm with visible calculus Apparent inflammation Older population
Radiographic features	Mostly vertical defects Mirror image pattern bone loss	Horizontal defects
Etiological factors	Microbial dysbiosis Host response Diabetes mellitus Smoking Familial aggregation	Microbial dysbiosis Host response Diabetes mellitus Smoking
Non-surgical therapy	Scaling root planing	Scaling root planing
Surgical therapy	Open flap debridement, regenerative therapy	Open flap debridement, regenerative therapy

Features of MIPP

In addition to differences in age of onset, lesion location, and the rapid progression of tissue breakdown, MIPP exhibits several unique characteristics: increased activity of PMNs and macrophages, increased antibody response, particular bacterial subpopulations are more prevalent in specific areas and thin biofilm consisting gram negative bacteria have been seen on the roots of MIPP patients.[4]

Familial Aggregation

Genetic factors contribute more significantly to the pathogenesis of MIPP compared to chronic periodontitis. (table 3) Familial studies on individuals with MIPP gave an inheritance pattern indicative of a gene with a major influence. A specific JP2 Genotype from serotype "b" of (Aa) is highly associated with a aggrssive form of periodontal disease. In certain cases, the possibility of a sibling developing the condition was 50%. [10] An association between MIPP and Fanconi anemia has also been reported.[11]

Table -3 Syndromes associated with severe forms of periodontitis [11]

Syndrome	Mutated gene
Papillon–Lefevre	Cathepsin C (CTSC)
Chediak–Higashi	Lysosomal trafficking regulator CHS1/LYST
Hypophosphatasia	ALPL
Congenital and cyclic neutropenia	ELANE
Leukocyte adhesion deficiency type I	Beta-2 integrin chain
Leukocyte adhesion deficiency type II	GDP-fucose transporter-1
Glycogen storage disease	SLC37A4
Ehlers–Danlos	Collagen alpha-1(V) gene (COL5A1) or the collagen alpha-2(V) gene (COL5A2)

Generalized Versus Localized form of MIPP

The most severe and extensive form of periodontal disease and its greatest extent of heterogeneity is seen in the subtype known as Generalized MIPP (G-MIP). G-MIP exhibits different gingival tissue responses which are a severe, acutely inflamed tissue, proliferating, ulcerated, and fiery red. MIPP shows episodic pattern of periodontal tissue destruction, which includes periods of severe destruction followed by passive phase. The localized form is defined as a "first molar/incisor presentation," characterized by interproximal attachment loss on at least two permanent teeth one of which must be a first molar and affecting not more than two teeth other than the first molars and incisors. Bilaterally symmetrical patterns of bone loss

are observed in MIPP , referred as "mirror image pattern''[12]

Host Responce in MIPP

In MIPP, four key factors contribute to host susceptibility and disease manifestation: bacteria–host interactions, host defences in aggressive periodontitis, deficiencies in host defences, and familial predisposition. A statistically significant correlation between MIPP and the single nucleotide polymorphism rs1537415 was found by a genome-wide study. This single nucleotide polymorphism was detected on glycosyl transferase gene GLT6D1. Individual variations in response to bacterial plaque contributes to differences in host susceptibility. While certain individuals exhibit increased sensitivity and develop aggressive forms of periodontal disease at an early age, others demonstrate resistance and may never develop periodontitis.[13] Branco-de- Almeida et al. and Shaddox et al. found that the gingival crevicular fluid (GCF) from defect sites in MIPP patients contained significantly higher levels of IL- 12p40, TNF-α, IL-6, IL-12p70, IL-2, IFN-γ, and IL-1β compared to GCF from their healthy sites, healthy siblings, and unrelated healthy controls. Additionally, healthy siblings of MIPP individuals exhibited elevated levels of IFN-γ and OPG in their gingival crevicular fluid, despite showing no clinical signs of disease.[2] Therefore, it can be stated that in susceptible individuals, an inflammatory response may occur before bacterial dysbiosis.

Treatment of MIPP

Conventional scaling and root planing (SRP) is an efficient method for lowering microbial counts. However, it has limitations in completely eradicating microorganisms from anatomically complex areas like furcation sites, bony defects, the tongue, and tonsils. Along with mechanical debridement systemic antibiotics can be used as an adjunct in the management of MIPP. In a systematic review and meta-analysis conducted by Karrabi et al in 2022, the effectiveness of the dose and duration of Amoxicillin + metronidazole administration in the treatment of Stage II–III Grade C periodontitis was evaluated. A significant difference was observed in pocket depth reduction in moderate pockets treated with 250 mg metronidazole and 400–500 mg supporting the higher dosage.[14] Access flap surgery and root surface debridement are frequently performed surgical procedures for individuals with molar-incisor pattern periodontitis. The use of biologics as an adjunct with guided tissue regeneration is a suitable treatment for MIPP as intrabony defects related to MIPP are mostly vertical and containable. Guided tissue regeneration with GTR membrane is a treatment approach that can be utilized to treat MIPP, particularly when there are deep and narrow defects.

Biologics like enamel matrix derivative (EMD), platelet-rich plasma (PRP), and platelet-rich fibrin (PRF) can be used.[15] Artzi et al. (2019) studied the results of MIPP patients who underwent GTR or DBX with EMD, with a follow- up of 10 years. Both techniques used for periodontal regeneration showed significant reductions in probing depths and clinical attachment loss in both groups. However, no statistically significant differences were observed between the two groups.[16] Thorat et al. (2017), in a split-mouth study involving 15 patients with localized aggressive periodontitis, concluded that the use of platelet- rich fibrin (PRF) significantly improved both clinical and radiographic results of flap surgery. The study demonstrated a notable reduction in probing depth and an increase in clinical attachment level with the use of PRF. [17]

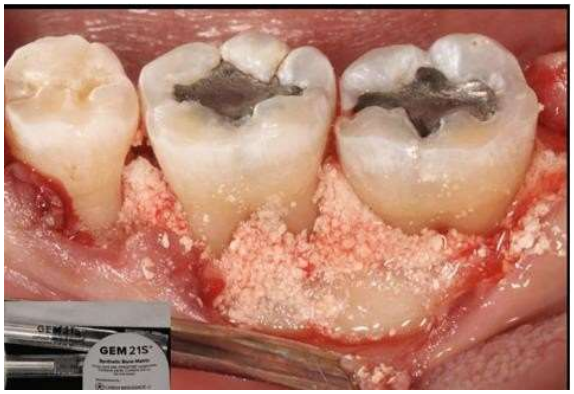

Fig 1 -GTR with placement of bone graft

Various types of dental lasers are used to manage periodontal disease. Several wavelengths can be

utilized as an adjunct with mechanical non-surgical procedures to remove pocket epithelium, incapacitate microorganisms, to eradicate subgingival calcification.[18] Antimicrobial photodynamic therapy (PDT) is another laser-based therapeutic procedure. In diseased areas, PDT is used to destruct bacteria by producing reactive oxygen species using a of laser light and photosensitizers. (fig- 2)

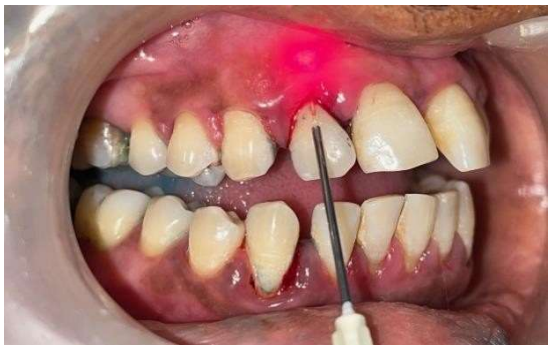

Fig 2-Antimicrobial photodynamic therapy

CONCLUSION:

In conclusion, MIPP is an aggressive periodontal condition characterized by rapid alveolar bone loss, minimal biofilm accumulation, familial aggregation, and increased inflammatory responses to bacterial colonization, particularly A. actinomycetemcomitans. Periodontal therapy, particularly scaling and root planing (SRP) combined with adjunctive antibiotics like amoxicillin and metronidazole, remains the gold standard for managing MIPP. Long-term periodontal maintenance is essential to sustain therapeutic success and minimize pathogen recolonization. Currently, there is no established set of inflammatory biomarkers to monitor the diagnosis, progression, and severity of the disease over time. A better understanding of biomarkers could provide valuable insights, enabling researchers and to adopt more effective strategies for managing the disease.

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