

Pleiotropic Syndromes with Resonance in the Oral Sphere

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ABSTRACT: This research paper aims to highlight the significance of understanding the genetic phenomenon of pleiotropy for oral health specialists. It presents the latest information regarding the definition and classification of pleiotropy, accompanied by exemplifications of the most representative genetic syndromes, Marfan, Treacher-Collins and Bardet-Biedl syndrome with resonance in the oral sphere. Early identification of these oral manifestations allows for proactive dental interventions, aiding in speech development, proper nutrition, and overall oral health management and multidisciplinary approaches involving dentists, geneticists, and specialists in craniofacial anomalies are fundamental in providing tailored care and improving the quality of life for individuals affected by these genetic syndromes.

KEYWORDS: Pleiotropy, Marfan Syndrome, Treacher-Collins Syndrome, Bardet-Biedl Syndrome, Oral Manifestations.

I. INTRODUCTION

In the classical conception of gene function, the "one gene - one trait" relationship is the fundamental axis of classical genetics, but the "one gene - one trait" relationship, which essentially reflects the "genotype-phenotype" relationship, is much more complex because:

- there are many polygenic/"multifactorial" traits, determined by several non-allelic genes and influenced by environmental factors;
- in some cases, a single gene determines several traits, a phenomenon called pleiotropy, and in other cases, several genes participate in the development of a single trait;
- there are numerous allelic, non-allelic and environmental interactions - influencing the effect of the gene, the timing or cell type in which a gene is expressed;

- mutations in different genes result in an identical/similar phenotype, a phenomenon called genetic heterogeneity [1, 2].

II. GENETIC PLEIOTROPY

Pleiotropy, as a definition, refers to the phenomenon whereby a single mutant (dominant) gene or a pair of mutant (recessive) genes produce diverse, multiple phenotypic effects (in multiple organ systems) [3].

Two types of pleiotropy are described: relational and non-relational pleiotropy [4].

III. RELATIONAL PLEIOTROPY

Relational pleiotropy is characterized by the existence of a pathogenic correlation (a common mechanism) between gene mutation and phenotypic effects.

Marfan syndrome and Treacher-Collins syndrome are two representative examples of relational pleiotropy (Figure 1).

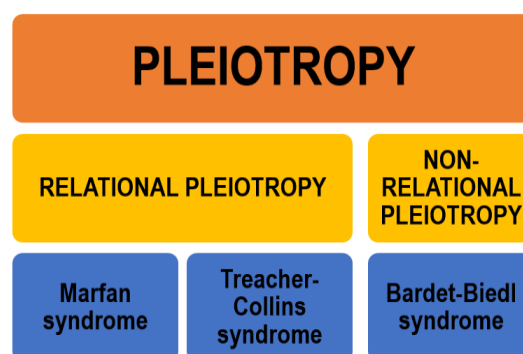


Figure 1. Pleiotropy: classification and clinical examples

Marfan syndrome

Marfan syndrome is a genetic disorder caused by a mutation in the FBN1 fibrillin gene,

which is transmitted through autosomal dominant inheritance.

The pathogenesis of this syndrome is characterized by abnormalities of fibrillin, the main component of connective tissue, leading to changes in the connective tissue of the osteoarticular system, the vascular wall, and the suspensory ligament of the lens [5].

The clinical diagnosis of Marfan syndrome is based on the identification of three main categories of signs and symptoms (Figure 2):

1. Ocular: subluxation or ectopia of the lens, myopia, hyperopia, megalocornea.
2. Skeletal: long limbs, thin and long fingers (arachnodactyly), joint hyperlaxity with risk of dislocation, spinal deformities such as kyphosis and scoliosis, and sternal deformities (pectus excavatum).
3. Cardiovascular: aortic aneurysms, mitral valve prolapse [6].

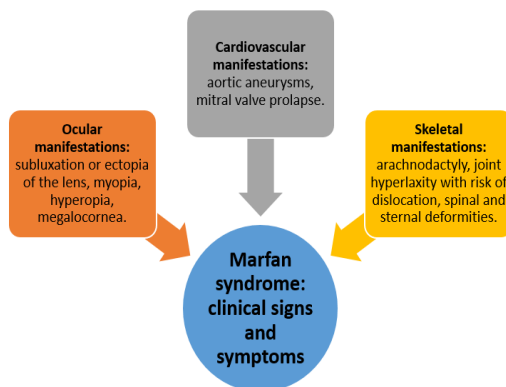


Figure 2. Signs and symptoms in Marfan syndrome

Oral Manifestations in Marfan syndrome

Dento-periodontal, oral, and maxillofacial manifestations of Marfan syndrome commonly include a high-arched palate, crowded teeth, and dental malocclusions [7].

These oro-dental characteristics often contribute to issues with bite alignment and dental crowding [8].

Additionally, individuals with Marfan syndrome might experience temporomandibular joint disorders, leading to jaw pain or dysfunction. Regular dental assessments and interventions are crucial to managing these oral manifestations and addressing potential complications that may arise due to the structural abnormalities associated with Marfan syndrome [9].

Understanding the genetic underpinnings and diverse phenotypic expressions of Marfan

syndrome is crucial for the management of this complex disorder.

Treacher-Collins syndrome

Treacher-Collins syndrome, also known as mandibulofacial dysostosis, is a genetic disorder largely attributed to mutations in the TCOF1, POLR1C, or POLR1D genes, affecting craniofacial development [10].

This syndrome disrupts the formation of facial bones and tissues, resulting in characteristic facial features such as underdeveloped cheekbones, downward-slanting eyes, notched lower eyelids, and a small jaw.

Individuals with Treacher-Collins syndrome often experience hearing loss due to malformations in the middle ear.

Furthermore, they might have respiratory and feeding difficulties at birth due to airway abnormalities.

Multidisciplinary care involving craniofacial surgeons, otolaryngologists, and speech therapists is essential for managing the varied clinical manifestations of this syndrome.

Oral Manifestations in Treacher Collins syndrome

Dento-periodontal, oral, and maxillofacial manifestations in Treacher-Collins syndrome primarily revolve around craniofacial abnormalities impacting oral health [11].

Dental anomalies such as missing or supernumerary teeth, crowding, malocclusions, and delayed dental development are common [12-14].

Moreover, individuals with this syndrome might exhibit high-arched palates, cleft palate, or other structural abnormalities affecting speech and feeding.

The maxillofacial region often presents with underdeveloped jawbones, leading to difficulties in chewing and swallowing [15].

Additionally, hearing loss, frequently associated with Treacher-Collins syndrome, can impact speech and language development.

Timely and comprehensive dental and craniofacial evaluations are essential to manage these oral and maxillofacial manifestations for individuals affected by this syndrome [16].

IV. NON-RELATIONAL PLEIOTROPY

Non-relational pleiotropy is the phenomenon in which, there is no pathogenic correlation between gene mutation and phenotypic effects.

The Moon-Bardet-Biedl syndrome is an illustrative example of non-relational pleiotropy (Figure 1).

Bardet-Biedl syndrome

Bardet-Biedl syndrome is a genetically heterogeneous disorder, primarily inherited in an autosomal recessive pattern, characterized by various clinical features and genetic complexities.

The syndrome is caused by mutations in multiple genes known as BBS genes, affecting ciliary function [17].

Bardet-Biedl syndrome exhibits considerable clinical variability, with common features including brachycephaly, retrognathia, and retinal dystrophy leading to vision impairment, obesity, polydactyly, cognitive impairment, kidney abnormalities, and genital anomalies [18, 19].

The multifaceted nature of Bardet-Biedl syndrome poses challenges in diagnosis and management, requiring comprehensive clinical evaluations and genetic testing to address the diverse spectrum of symptoms and provide appropriate care for affected individuals.

Oral Manifestations in Bardet-Biedl syndrome

Dento-periodontal, oral, and maxillofacial manifestations of Bardet-Biedl syndrome are not as extensively documented as other systemic features.

However, some individuals with Bardet-Biedl syndrome may present brachycephaly and oral abnormalities such as retrognathia, dental crowding, malocclusions, and, in some cases, cleft lip and palate [20].

Additionally, there might be reports of delayed eruption of teeth and abnormalities in tooth development, small teeth, hypoplastic enamel, and short dental roots [21, 22].

While oral manifestations in Bardet-Biedl syndrome are not as prominent as other systemic features, regular dental assessments and interventions remain crucial for managing potential oral health concerns in individuals affected by this complex syndrome.

V. CONCLUSION

Dental conditions within pleiotropic genetic syndromes such as Marfan syndrome, Treacher-Collins syndrome, and Bardet-Biedl syndrome often manifest as part of a broader spectrum of systemic effects.

These conditions showcase a diverse range of oral manifestations, including dental crowding,

malocclusions, craniofacial abnormalities, and palate irregularities.

Understanding the oral implications of these syndromes is paramount in providing holistic care for affected individuals [23, 24].

Early identification of these oral manifestations allows for proactive dental interventions, aiding in speech development, proper nutrition, and overall oral health management.

Multidisciplinary approaches involving dentists, geneticists, and specialists in craniofacial anomalies are fundamental in providing tailored care and improving the quality of life for individuals affected by these genetic syndromes [25].

Future perspectives revolve around advancing interdisciplinary collaborations between dentistry, genetics, and specialized medical fields.

This collaboration aims to enhance early detection through genetic screening, implement tailored dental interventions, and develop targeted therapies addressing the specific oral challenges presented by these syndromes. Such efforts will contribute not only to improved oral health but also to the overall well-being and quality of life for individuals impacted by these complex genetic conditions.

Disclosure of conflict of interest

The authors declare no conflict of interest.

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