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Cantù Syndrome: A Case Report With Orthodontic and Sleep Disorder Findings

Federica Guglielmi[1,2] | Anna Alessandri Bonetti[1,2] | Benedetta Nuzzo[1,2] | Patrizia Gallenzi[1,2]

[1]Institute of Dental Clinic, A. Gemelli University Policlinic IRCCS, Catholic University of Sacred Heart, Rome, Italy | [2]Postgraduate School of Orthodontics, Director: Prof. Massimo Cordaro, Catholic University of Sacred Heart, Rome, Italy

Correspondence: Federica Guglielmi (federica.guglielmi@unicatt.it)

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ABSTRACT

This case emphasizes the importance of comprehensive orthodontic and sleep evaluations in Cantù syndrome. Despite severe dento-skeletal malocclusions, the patient exhibited low risk of obstructive sleep apnea (PSQ score < 0.33), emphasizing that craniofacial anomalies do not uniformly predict respiratory compromise. Individualized assessment and awareness of behavioral and molecular factors are essential for optimal care.

1 | Introduction

Cantù syndrome (CS; OMIM #239850) is a rare autosomal dominant condition caused by pathogenic variants in ABCC9 or KCNJ8 genes, encoding subunit of the ATP-sensitive potassium channel [1]. The prevalence of CS is unknown; however, approximately 150 cases have been reported worldwide [2]. The syndrome was first described in 1982 by Cantù and colleagues and is inherited in an autosomal dominant pattern.

Clinical features associated with CS include cardiac and skeletal abnormalities such as enlarged heart, large patent ductus arteriosus, thickening of the calvaria, wide ribs, scoliosis, and flaring of the metaphyses [2]. Reported craniofacial features include high-arched/narrow palate, macroglossia, gingival hyperplasia, and anterior open bite [2]. Three-dimensional imaging further confirmed abnormal craniofacial morphology in CS patients [3].

Due to these craniofacial characteristics, patients may present with a high prevalence of malocclusions—such as transverse maxillary deficiency, anterior open bite, and Class II/III skeletal discrepancies—and sleep-disordered breathing (SDB), including obstructive sleep apnea (OSA). Recent data suggest that narrowed maxillae and mandibular retrognathia increase susceptibility to OSA [4].

Malocclusion is any deviation from ideal occlusion [5]—manifesting as irregular tooth alignment and/or abnormal inter-arch relationships in the sagittal, vertical, or transverse planes—beyond the range considered normal [5], and it is widely reported in systematic reviews as a prevalent, multifactorial condition with measurable impacts on oral health–related quality of life [6].

Sleep-disordered breathing ranges from primary snoring to OSA [7]. Childhood OSA is characterized by recurrent partial or complete obstruction of the upper airway during sleep, leading to hypoxia and sleep fragmentation [7]. Risk factors include adenotonsillar hypertrophy, obesity, craniofacial anomalies, prematurity, and asthma [8, 9]. Children with complex syndromes often present with multiple overlapping sleep disturbances [10].

To the best of our knowledge, there are no available data in the literature describing orthodontic features and OSA risk in patients with CS. This study aims to evaluate dental malocclusion

patterns, craniofacial features, and OSA risk in a patient with CS, providing insight into potential functional and molecular interactions affecting craniofacial development.

This is a clinical case reported according to the CARE (CAse REport) guidelines [11].

2 | Case History

The patient was eligible for inclusion in the study based on a confirmed molecular diagnosis of Cantù syndrome at the time of clinical evaluation. To ensure the reliability of the findings, certain exclusion criteria were applied: patients with a history of previous orthodontic treatment, the presence of other syndromic comorbidities potentially affecting the airway but unrelated to CS, or incomplete clinical documentation were not considered. This approach allowed us to focus specifically on the craniofacial and functional manifestations directly attributable to Cantù syndrome.

2.1 | Patient Information

A 12-year-old boy with CS was referred for clinical examination to the Pediatric Dental Unit of the A. Gemelli Policlinic IRCCS (Rome, Italy).

The diagnosis of CS was obtained following molecular analysis which revealed a mutation in heterozygotes of ABCC9.

With the patient's guardians' consent and according to the Helsinki Declaration, this patient was evaluated and a full set of orthodontic pictures was made (Figures 1 and 2).

3 | Methods (Differential Diagnosis, Investigations and Treatment)

3.1 | Orthodontic Evaluation

During the clinical examination, sagittal, transversal, and vertical parameters were systematically assessed. The type of malocclusion was recorded according to Angle's classification and categorized as Class I, Class II, or Class III [12]. Evaluation of maxillary transverse relationships included observation of the arch form and symmetry, palatal shape, predominant breathing mode (oral versus nasal), and buccal corridor width during smiling [13]. A transverse discrepancy was classified as a posterior crossbite when the buccal cusps of the upper molars contacted the central fossae of the lower molars [14], whereas a scissor bite was diagnosed when the palatal surface of the upper lingual cusp contacted or nearly contacted the buccal surface of the lower buccal cusp [15].

Sagittal discrepancies were evaluated by assessing the presence of anterior crossbite, defined as a negative horizontal overlap between the upper and lower incisors. This was measured from the facial surface of the upper incisors to the middle of the incisal edge of the lower incisors [16]. Vertical relationships were measured by calculating the degree of incisal overlap. An anterior deep bite was diagnosed when this overlap exceeded 4 mm [17], while an anterior open bite was defined as a negative vertical overlap [16].

Dental crowding was quantified using Little's Irregularity Index, which measures the discrepancy between available and required arch space [18]. The patient's facial profile was assessed clinically and classified as concave, straight, or convex following the criteria proposed by Arnett and Bergman [19].

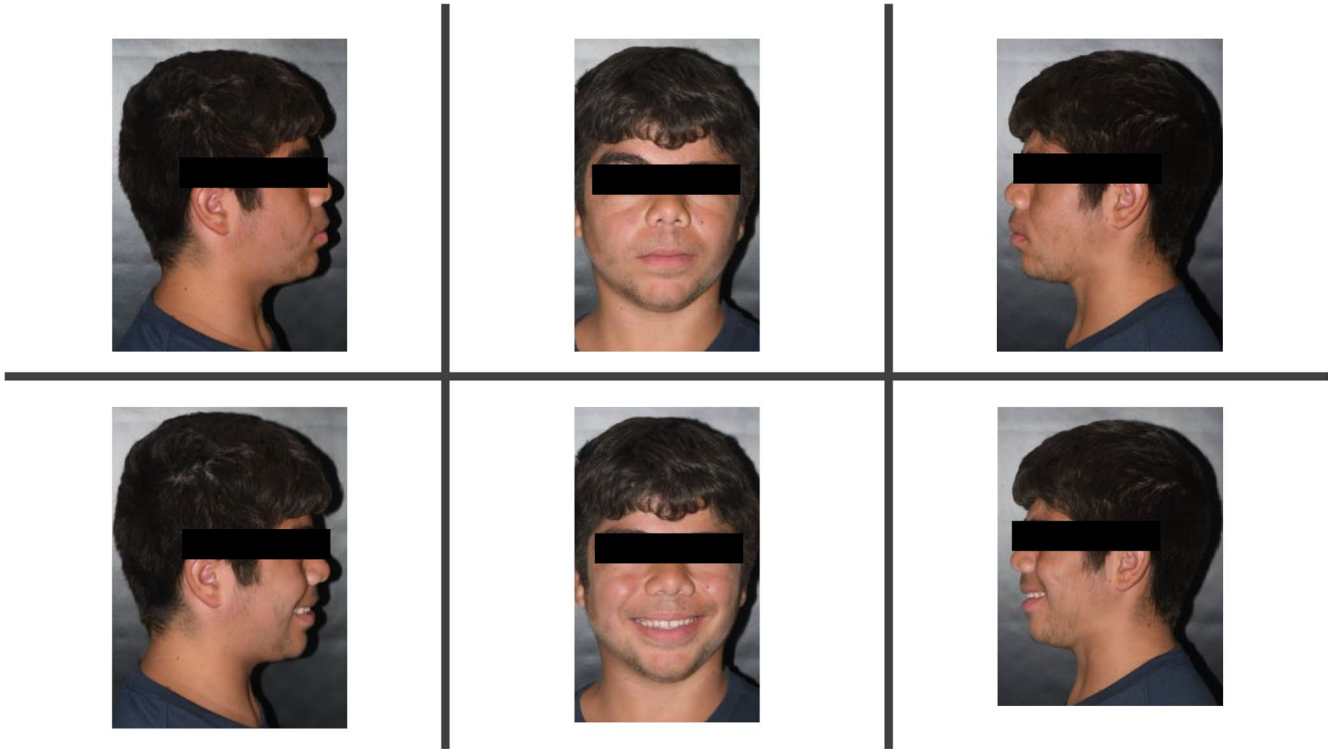

FIGURE 1 | Orthodontic extraoral pictures of CS patient.

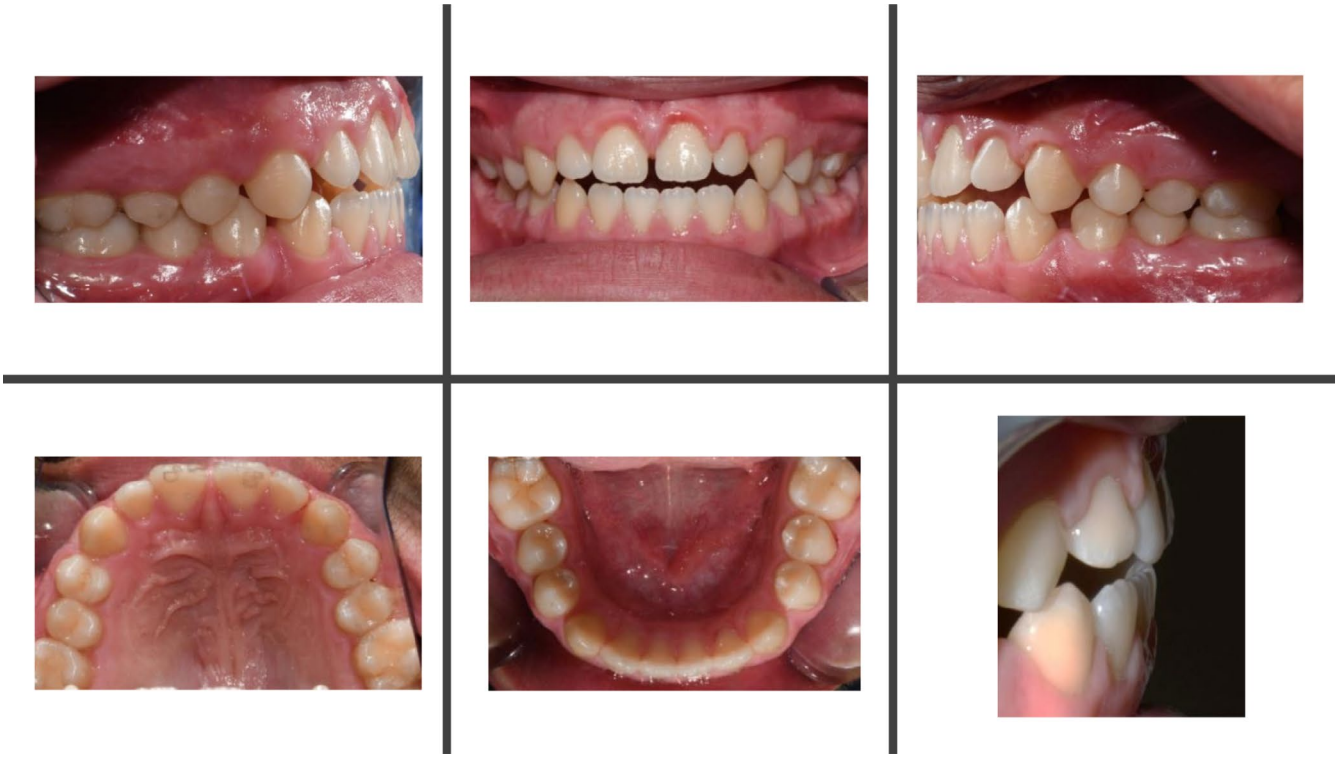

FIGURE 2 | Orthodontic intraoral pictures of CS patient.

In addition to the orthodontic assessment, a standardized periodontal evaluation was performed, including inspection of gingival phenotype, recording of probing pocket depths using a manual periodontal probe, assessment of bleeding on probing, presence of gingival inflammation or enlargement, and evaluation of clinical attachment levels. Periodontal status was classified according to current pediatric periodontal health criteria to ensure the absence of active disease or contraindications to orthodontic treatment [20].

The presence of probable sleep bruxism was investigated in accordance with the grading system proposed by the international consensus [21]. A diagnosis was established when a positive patient or guardian report was accompanied by at least one clinical sign, such as masticatory muscle hypertrophy, buccal linea alba, tongue or lip indentations, or tooth wear.

Finally, parafunctional habits were considered, including oral breathing, infantile swallowing, and non-nutritive sucking behaviors such as finger or pacifier use. Particular attention was given to atypical swallowing, defined as a deglutition pattern in which the tongue tip exerts pressure against the anterior teeth or the tongue base thrusts against the hard palate, often associated with contraction of the lower orbicularis oris and mentalis muscles. This functional disturbance typically results in the development of an anterior open bite [22].

3.2 | Pediatric Sleep Questionnaire for (PSQ)

In order to assess the risk of OSA, the patient's guardians were asked to complete the Italian version of the Pediatric Sleep Questionnaire (PSQ) [23, 24].

The PSQ was selected as a screening tool for pediatric OSA for its high sensitivity [25]. The scoring was performed according to Chervin and coll. Guidelines [23].

4 | Conclusion and Results

The orthodontic evaluation showed facial asymmetry and broad nasal bridge, a convex biprotrusive profile with thickening, concave curling of the lips and intraoral findings of anterior open bite, midlines asymmetries, dental diastemas and absence of dental crowding. Both arches appeared expanded and without clinically relevant maxillary transverse discrepancy. Sagittal evaluation showed bilateral molar and canine Class I with reduced overjet. Atypical swallowing was observed, likely secondary to macroglossia. Periodontal evaluation revealed a thick gingival phenotype with mild gingival enlargement consistent with previously reported gingival features in Cantù syndrome. Probing depths were within normal limits (2–3 mm) without clinical attachment loss. No bleeding on probing or signs of active periodontal inflammation were detected. The periodontal tissues appeared generally healthy, and no periodontal contraindications to orthodontic treatment were identified.

Based on caregiver report and on clinical findings, sleep bruxism was not supported. PSQ score was < 0.33 indicating low risk of OSA. Interestingly, behavioral subscales were positive, suggesting possible behavioral disturbances, consistent with recent literature reporting ADHD, autism spectrum disorder, and anxiety in up to 25% of CS patients [26].

When compared with previously published data on Cantù syndrome, our findings align with common dental and craniofacial

features such as anterior open bite and functional alterations secondary to macroglossia, both frequently reported in the literature [3] Conversely, the absence of a narrow, high-arched palate or transverse maxillary deficiency—which are often described—represents a less typical presentation [27]. With regard to sleep-disordered breathing, data from the International Cantù Syndrome Registry indicate that sleep apnea occurs in only a minority of patients (~14% of those with available data), typically requiring management such as adenoidectomy or adenotonsillectomy. Therefore, OSA should not be considered a constant feature of the syndrome [2] The low OSA risk observed in our patient is consistent with these findings and highlights the variability of respiratory involvement in Cantù syndrome.

In conclusion, while some craniofacial and occlusal features (open bite, macroglossia) appear common in Cantù syndrome, others (expanded arches, absence of transverse discrepancy) may represent individual variability. Obstructive sleep apnea, although described, is not prevalent in this syndrome, and our case reinforces the importance of individualized evaluation rather than assuming a systematic association between malocclusion and OSA.

5 | Discussion

This is the first reported case evaluating the orthodontic phenotype and OSA risk in Cantù syndrome. Malocclusions are highly prevalent in the general pediatric population (39%–93%), with variability due to ethnicity, age, and diagnostic criteria [28]. Our patient presented with anterior open bite and atypical swallowing, consistent with macroglossia, and a hallmark feature of CS.

The anterior open bite and parafunctional swallowing patterns align with findings from previous CS cases (Grange 2020) [1]. While these features are typically risk factors for OSA, our patient's PSQ indicated a low risk. This suggests that malocclusion alone does not predict OSA in CS, in line with broader evidence that OSA pathogenesis involves both structural and neuromuscular components [4].

With respect to treatment alternatives, several considerations arise in the management of patients with Cantù syndrome. Interceptive orthodontics—such as maxillary expansion, early open-bite correction, and habit interception—should be evaluated cautiously, particularly in the presence of macroglossia, which may compromise long-term stability [2, 22]. Myofunctional therapy may support the correction of atypical swallowing patterns, although current evidence remains limited in patients with syndromic macroglossia and complex craniofacial anomalies [29]. In cases presenting with more severe skeletal discrepancies, comprehensive orthodontic treatment using fixed appliances or aligner therapy during adolescence may be considered, taking into account growth potential, neuromuscular constraints, and the patient's overall medical profile [30, 31]. A multidisciplinary approach involving orthodontists, speech therapists, and medical specialists is often recommended to guide individualized treatment planning in syndromic patients [32].

Behavioral issues were flagged in the PSQ, consistent with recent reports of anxiety, ADHD, and autism spectrum disorders in up to 25% of CS patients [26]. Interestingly, in other pediatric populations, ADHD and bruxism have been linked to increased OSA risk [33], though this was not observed in our patient.

Recent evidence has highlighted the critical role of microRNAs (miRNA-7, −21, and −100) in regulating alveolar bone remodeling during orthodontic tooth movement in humans. These miRNAs modulate osteoblast and osteoclast activity, orchestrate the local inflammatory response, and facilitate adaptive changes in the periodontal ligament and alveolar bone under mechanical stress [34–37]. Specifically, miRNA-21 has been shown to promote osteoclastogenesis by modulating the RANKL/OPG balance, thereby facilitating controlled tooth movement [37]. Furthermore, studies have characterized a periodontal-inflammatory miRNA profile during multibracket orthodontic treatment in adolescents, identifying miRNAs as potential biomarkers for monitoring periodontal remodeling and cellular activity [36]. Recent reviews also highlight the potential of miRNA modulation as a novel diagnostic and personalized therapeutic strategy during orthodontic tooth movement [35]. In addition, a translational investigation demonstrated dynamic regulation of circulating and gingival crevicular miRNAs during active tooth movement, identifying specific signatures associated with osteoclastic activation and periodontal inflammation [38]. Similarly, a mechanistic study confirmed the central role of miRNAs in coordinating osteoblast–osteoclast signaling during mechanical loading, supporting their potential use as biomarkers for predicting orthodontic movement efficiency and periodontal response [39]. These findings collectively reinforce the emerging view of miRNAs as key regulatory elements in orthodontic biomechanics.

Understanding this molecular regulation may help explain the variability observed in dental and skeletal phenotypes and support the functional adaptation of craniofacial structures in patients with syndromic conditions, including Cantù syndrome. This is particularly relevant for malocclusion development, where molecular pathways and anatomical features interact to shape orthodontic outcomes. Comparisons with other syndromes are informative: in Treacher-Collins and Down syndrome, craniofacial malformations are strongly linked to high OSA prevalence (30%–50%) [9]. In CS, however, despite skeletal malocclusion, airway patency appears relatively preserved. Muscular factors such as hypotonia and impaired neuromuscular control may still contribute to OSA pathogenesis and warrant further investigation.

Overall, this case highlights that while malocclusions are present in CS, their direct association with OSA remains uncertain. Future cohort studies are needed to establish prevalence and clarify pathophysiological mechanisms.

Author Contributions

Federica Guglielmi: data curation, investigation, resources, writing – original draft. **Anna Alessandri Bonetti:** conceptualization, data curation, validation, writing – review and editing. **Benedetta**

Nuzzo: methodology, resources. **Patrizia Gallenzi:** conceptualization, project administration, supervision, writing – review and editing.

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Consent

A written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Data Availability Statement

The authors have nothing.

References

1. E. S. Apuril Velgara, M. Mariani, A. Torella, et al., "Cantù Syndrome: Report of a Patient With a Novel Variant in KCNJ8 and Revision of Literature," *American Journal of Medical Genetics. Part A* 188, no. 6 (2022): 1661–1666.

2. D. K. Grange, H. I. Roessler, C. McClenaghan, et al., "Cantu Syndrome: Findings From 74 Patients in the International Cantu Syndrome Registry," *Ameri- Can Journal of Medical Genetics Part C* 181, no. 4 (2019): 658–681, https://doi.org/10.1002/ajmg.c.31753.

3. H. I. Roessler, K. Shields, D. K. Grange, et al., "Three-Dimensional Facial Morphology in Cantú Syndrome," *American Journal of Medical Genetics. Part A* 182, no. 5 (2020): 1041–1052, https://doi.org/10.1002/ajmg.a.61517.

4. A. M. Paradowska-Stolarz, "Is Malocclusion a Risk Factor for Obstructive Sleep Apnea and Temporomandibular Disorders? An Orthodontic Point of View," *Dental and Medical Problems* 62, no. 2 (2025): 197–199, https://doi.org/10.17219/dmp/194232.

5. I. M. Alqahtan, R. A. Azizkhan, L. T. Alyawer, et al., "An Overview of Diagnosis and Management of Malocclusion: Literature Review," *Annals of Dental Specialty* 8, no. 4 (2020): 62–65.

6. G. Lombardo, F. Vena, P. Negri, et al., "Worldwide Prevalence of Malocclusion in the Different Stages of Dentition: A Systematic Review and Meta-Analysis," *European Journal of Paediatric Dentistry* 21, no. 2 (2020): 115–122, https://doi.org/10.23804/ejpd.2020.21.02.05.

7. A. C. Bitners and R. Arens, "Evaluation and Management of Children With Obstructive Sleep Apnea Syndrome," *Lung* 198, no. 2 (2020): 257–270.

8. Z. Xu, Y. Wu, J. Tai, et al., "Risk Factors of Obstructive Sleep Apnea Syndrome in Children," *Journal of Otolaryngology - Head & Neck Surgery* 49, no. 1 (2020): 11.

9. A. Lo Bue, A. Salvaggio, and G. Insalaco, "Obstructive Sleep Apnea in Developmental Age. A Narrative Review," *European Journal of Pediatrics* 179, no. 3 (2020): 357–365.

10. K. A. Waters, S. Suresh, and G. M. Nixon, "Sleep Disorders in Children," *Medical Journal of Australia* 199, no. 8 (2013): S31–S35.

11. J. J. Gagnier, G. Kienle, D. G. Altman, D. Moher, H. Sox, and D. Riley, "The CARE Guidelines: Consensus-Based Clinical Case Reporting Guideline Development," *Global Advances in Health and Medicine* 2, no. 5 (2013): 38–43.

12. L. W. Graber, R. L. Vanarsdall, K. W. L. Vig, and G. J. Huang, *Orthodontics: Current Principles and Techniques*, 6th ed. (Elsevier, 2017).

13. N. B. Dakhil and F. B. Salamah, "The Diagnosis Methods and Management Modalities of Maxillary Transverse Discrepancy," *Cureus* 13 (2021): e20482.

14. S. Mutinelli and M. Cozzani, "Rapid Maxillary Expansion in Early-Mixed Dentition: Effectiveness of Increasing Arch Dimension With Anchorage on Deciduous Teeth," *European Journal of Paediatric Dentistry* 16 (2015): 115–122.

15. J. W. King and J. C. Wallace, "Unilateral Brodie Bite Treatment With Distraction Osteogenesis," *American Journal of Orthodontics and Dentofacial Orthopedics* 125 (2004): 500–509.

16. F. Borrie and D. Bearn, "Early Correction of Anterior Crossbites: A Systematic Review," *Journal of Orthodontics* 38 (2011): 175–184.

17. G. J. Huang, S. B. Bates, A. A. Ehlert, D. P. Whiting, S. S. Chen, and A. M. Bollen, "Stability of Deep-Bite Correction: A Systematic Review," *Journal of the World Federation of Orthodontists* 1 (2012): e89–e96.

18. R. M. Little, "The Irregularity Index: A Quantitative Score of Mandibular Anterior Alignment," *American Journal of Orthodontics* 68 (1975): 554–563.

19. G. W. Arnett, J. S. Jelic, J. Kim, et al., "Soft Tissue Cephalometric Analysis: Diagnosis and Treatment Planning of Dentofacial Deformity," *American Journal of Orthodontics and Dentofacial Orthopedics* 116 (1999): 239–253.

20. T. Janssen and M. Borel, "Periodontal Assessment in Children and Adolescents: Clinical Parameters, Diagnostic Considerations, and Early Detection of Periodontal Pathology," *European Journal of Paediatric Dentistry* 22, no. 3 (2021): 210–216.

21. F. Lobbezoo, J. Ahlberg, K. G. Raphael, et al., "International Consensus on the Assessment of Bruxism: Report of a Work in Progress," *Journal of Oral Rehabilitation* 45 (2018): 837–844.

22. N. Cenzato, L. Iannotti, and C. Maspero, "Open Bite and Atypical Swallowing: Orthodontic Treatment, Speech Therapy or Both? A Literature Review," *European Journal of Paediatric Dentistry* 22, no. 4 (2021): 286–290.

23. R. D. Chervin, K. Hedger, J. E. Dillon, and K. J. Pituch, "Pediatric Sleep Questionnaire (PSQ): Validity and Reliability of Scales for Sleep-Disordered Breathing, Snoring, Sleepiness, and Behavioral Problems," *Sleep Medicine* 1, no. 1 (2000): 21–32.

24. G. Di Carlo, F. Zara, M. Rocchetti, et al., "Prevalence of Sleep-Disordered Breathing in Children Referring for First Dental Examination. A Multicenter Cross-Sectional Study Using Pediatric Sleep Questionnaire," *International Journal of Environmental Research and Public Health* 17, no. 22 (2020): 8460.

25. S. Incerti-Parenti, A. Fiordelli, M. L. Bartolucci, S. Martina, V. D'Antò, and G. Alessandri-Bonetti, "Diagnostic Accuracy of Screening Questionnaires for Obstructive Sleep Apnea in Children: A Systematic Review and Meta-Analysis," *Sleep Medicine Reviews* 57 (2021): 101464.

26. H. I. Roessler, L. M. van der Heuvel, K. Shields, et al., "Behavioral and Cognitive Functioning in Individuals With Cantú Syndrome," *American Journal of Medical Genetics, Part A* 185, no. 8 (2021): 2434–2444, https://doi.org/10.1002/ajmg.a.62348.

27. D. K. Grange, C. G. Nichols, and G. K. Singh, "Cantú Syndrome," in *GeneReviews*, ed. M. P. Adam, J. Feldman, G. M. Mirzaa, et al. (University of Washington, Seattle, 2014).

28. M. S. Alhammadi, E. Halboub, M. S. Fayed, A. Labib, and C. El-Saaidi, "Global Distribution of Malocclusion Traits: A Systematic Review," *Dental Press Journal of Orthodontics* 23, no. 6 (2018): 40.e1–40.e10, https://doi.org/10.1590/2177-6709.23.6.40.e1-10.onl.

29. M. P. Villa, M. Evangelisti, M. Barreto, M. Cecili, A. G. Kaditis, and M. Pavone, "Myofunctional Therapy in Pediatric Patients With Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis," *Sleep Medicine Reviews* 40 (2017): 142–152.

30. L. Lombardo, A. Carlucci, G. Maino, A. Colonna, and G. Siciliani, "Class II Subdivision Treatment Using Clear Aligners: A Case Report," *Journal of Orofacial Orthopedics* 78, no. 4 (2017): 331–338.

31. C. Maspero, C. Prevedello, L. Giannini, G. Galbiati, and G. Farronato, "A Systematic Review of Clear Aligner Therapy in the Growing Patient: Current Evidence and Future Perspectives," *European Journal of Paediatric Dentistry* 21, no. 1 (2020): 61–68.

32. K. A. Waters, S. Suresh, and G. M. Nixon, "Sleep Disorders in Children," *Medical Journal of Australia* 199, no. 8 (2013): S31–S35.

33. A. Alessandri-Bonetti, F. Guglielmi, G. Deledda, L. Sangalli, C. Brogna, and P. Gallenzi, "Malocclusions, Sleep Bruxism, and Obstructive Sleep Apnea Risk in Pediatric ADHD Patients: A Prospective Study," *Journal of Attention Disorders* 28, no. 6 (2024): 1017–1023, https://doi.org/10.1177/10870547231226139.

34. Z. Wang, J. Feng, Q. Wang, Y. Yang, and J. Xiao, "Analysis of the Correlation Between Malocclusion, Bad Oral Habits, and the Caries Rate in Adolescents," *Translational Pediatrics* 10, no. 12 (2021): 3291–3300, https://doi.org/10.21037/tp-21-531.

35. G. Cultrera, A. Lo Giudice, S. Santonocito, et al., "MicroRNA Modulation During Orthodontic Tooth Movement: A Promising Strategy for Novel Diagnostic and Personalized Therapeutic Interventions," *International Journal of Molecular Sciences* 23, no. 24 (2022): 15501, https://doi.org/10.3390/ijms232415501.

36. F. Rolfes, J. Heck, I. Riedel, C. Bär, and B. Schmitz, "Characterization of a Periodontal-Inflammatory microRNA Profile During Multibracket Orthodontic Treatment in Adolescents," *Scientific Reports* 15, no. 1 (2025): 19488, https://doi.org/10.1038/s41598-025-01794-6.

37. Y. Zhang, Y. Tian, X. Yang, Z. Zhao, C. Feng, and Y. Zhang, "MicroRNA-21 Serves an Important Role During PAOO-Facilitated Orthodontic Tooth Movement," *Molecular Medicine Reports* 22, no. 1 (2020): 474–482, https://doi.org/10.3892/mmr.2020.11107.

38. A. Polizzi, A. Alibrandi, A. Lo Giudice, et al., "Impact of Periodontal microRNAs Associated With Alveolar Bone Remodeling During Orthodontic Tooth Movement: A Randomized Clinical Trial," *Journal of Translational Medicine* 22 (2024): 1155, https://doi.org/10.1186/s12967-024-05933-x.

39. F. Huang, Y. Ren, Y. Hua, et al., "m6A-Dependent Mature miR-151-5p Accelerates the Malignant Process of HNSCC by Targeting LYPD3," *Molecular Biomedicine* 5, no. 1 (2024): 27, https://doi.org/10.1186/s43556-024-00189-9.