POSTER #

Managing a Dual Diagnosis of Pierre Robin Sequence and Stickler Syndrome: A Case Report

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ABSTRACT

Pierre Robin Sequence (PRS) and Stickler syndrome (SS) are two rare genetic conditions that can have notable effects on an individual's physical and facial development. PRS is characterized by a triad of clinical issues, which include micrognathia, glossoptosis, and upper airway obstruction. Feeding and respiratory issues, as well as dental issues like malocclusion and poor oral hygiene, may result from this. Cleft palate is frequently observed in individuals with PRS, but is not a requirement for diagnosis. PRS can be isolated or can occur as a larger syndrome, such as Stickler syndrome. Stickler syndrome is a disorder that affects the connective tissues in the body and is characterized by abnormalities of the head and face, eyes, ears, and skeleton. Enamel hypoplasia and other dental abnormalities may also be present in individuals with this condition.

Both PRS and Stickler syndrome can be treated with a range of medical interventions like surgery, speech therapy, and physical therapy. It is imperative for individuals with these conditions and their families to have access to specialized medical care and support services to help in managing the physical and emotional impacts of these conditions. This case study will explore the diagnosis and dental treatment of a 11-year-old patient with Pierre Robin Sequence and Stickler syndrome.

BACKGROUND

Pierre Robin Sequence (PRS)

- Rare craniofacial disease
  - Incidence: variable from 1 to 8500 to 1 to 30,000 newborns
- Triad of clinical signs: micrognathia, glossoptosis and upper airway obstruction
- Most often associated with cleft palate
- Heterogenic pathological entity-can be found as isolated disease or in association with other syndromes

Etiology

- Separated into isolated and syndromic PRS
- Non-syndromic associated with mutations on chromosomes 2, 4, 11, or 17
  - SOX9 or KCNJ2 mutations are on chromosome 17 and affect the development of facial structures and cartilage development
- Syndromic PRS accounts for 60% of PRS
  - 34 syndromes have been associated with PRS
  - Most common being ***Stickler syndrome***- 47% of syndromic PRS diagnosed with Stickler syndrome

Genetics

- Role of genes not completely understood still
- Genetic anomalies at chromosome 2, 11 or 17 identified and may be cause of PRS
- Presence of following mutated genes may be involved in isolated PRS etiology: SOX9, KCNJ2, KCNJ16, and MAP2K6
- SOX9 is critical chondrogenic regulator
  - Multiple roles during embryogenesis and is imperative for all cartilage development

Clinical Presentation

- Micrognathia: clinical diagnosis of underdeveloped mandible
  - Shorter mandibular length and a greater mandibular length
- Glossoptosis: displacement of base of tongue towards pharynx
  - Wide range of severity and therefore associated with respiratory distress
- Airway obstruction: clinical signs may include abnormal breathing sounds, increased respiratory accessory muscle use, desaturations, difficulty feeding/swallowing, reflux and aspiration
- Cleft palate: U-shaped cleft palate present in most cases
  - May be caused from tongue falling back, stopping palate from properly closing

Treatment

- Mild disease can be treated with conservative management without surgery (70% of cases)
  - Includes prone and lateral positioning to allow gravity to pull tongue anteriorly
- CPAP useful intervention but compliance is difficult
- Some studies have shown that isolated PRS may reach normal mandibular growth years following birth
- Severe cases of PRS require surgical intervention (10% of isolated PRS cases)
  - Tongue-lip adhesion, mandibular distraction, osteogenesis, and tracheostomy
- Mandibular distraction addresses issue of airway obstruction
  - Lengthens jaw in forward direction, which indirectly pulls tongue anteriorly
  - Reversal of PRS sequence= correct micrognathia, which improves glossoptosis, thereby relieving airway obstruction

Stickler Syndrome (SS)

- Multisystem connective tissue disorder
- Risk for severe ocular complications such as retinal detachment
- Serious skeletal, ear, and craniofacial structures may be involved as well
  - Micrognathia (alone or as part of ***Pierre Robin Sequence***), cleft palate, hearing loss, and/or early onset of osteoarthritis
  - SS is cause of 30 % of all PRS cases

Etiology

- 11 distinct phenotypic subgroups
- SS caused by mutations in the following genes encoding for collagen types II (*COL2A1*, 12q13.11), IX (*COL9A1*, 6q13; *COL9A2*, 1p34.2; *COL9A3*, 20q13.33), and XI (*COL11A1*, 1p21.1)

Genetics

- Most often inherited autosomal dominant (AD) but can be inherited in autosomal recessive (AR) manner as well
- Stickler Syndrome Type I (STL1) accounts for 80-90% of all cases
  - Heterozygous variants in COL2A1

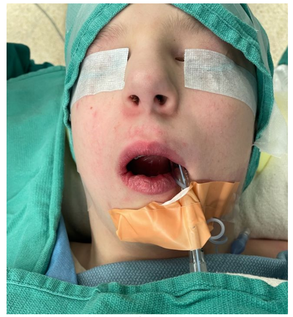
Clinical Presentation

- Common features: flat midface, epicanthal folds, retinal detachments, joint hypermobility and sensorineural hearing loss
- 50% of SS individuals have heart valve defect (mitral valve prolapse)

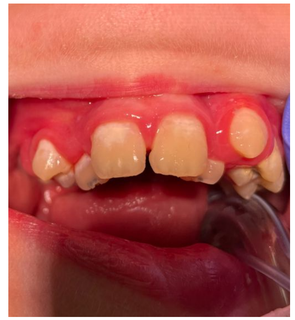
Treatment

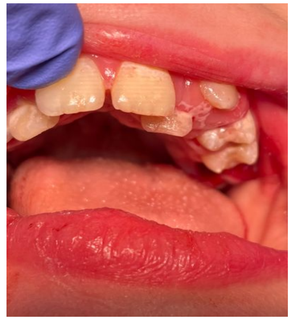
- Speech therapy, physical therapy, hearing aids, and/or special education may be necessary depending on severity
- Surgical interventions:
  - Tracheostomy- small jaw and displaced tongue causing breathing difficulties
  - Cleft palate repair
  - Eye surgeries including retinal reattachment and/or cataracts surgery to preserve vision
  - Other surgeries including jaw, ear tubes placement, and/or joint replacement

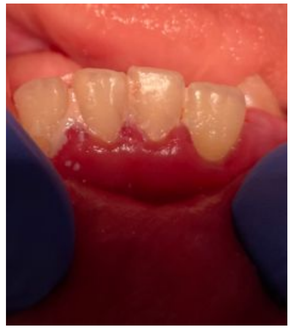
CASE REPORT

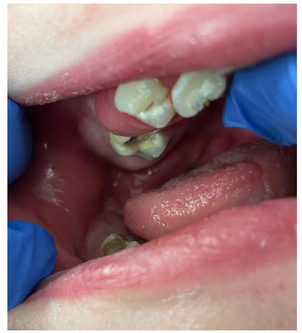


11y1m male patient

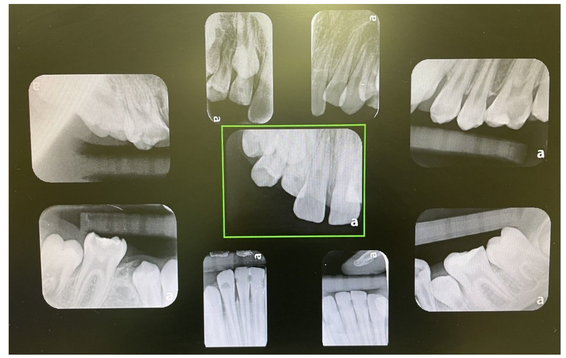








All images and radiographs from 2/2023 in OR at Mott's Children's Hospital for dental rehabilitation



CC: "One of his baby teeth was hurting before but it fell out so we are here for his routine dental check-up." -mother

Medical History

- Stickler syndrome
- Pierre Robin sequence
- Micrognathia (s/p mandibular distraction)
- Cleft palate (s/p 2014 and 2015)
- Epiphyseal dysplasia of femoral head
- Sensorineural hearing loss
- Global developmental delay
- High myopia of both eyes
- Eustachian tube dysfunction
- Feeding difficulty
- Cochlear implants in place

Current Medications:

- Melatonin

Allergies: No Known Drug Allergies

Clinical Findings:

- Micrognathia
- Evidence of cleft repair

Oral & Dental Findings:

- Permanent Dentition
- Severe generalized gingivitis, moderate generalized calculus
- Molar and canine classification, OB/OJ and midlines were not assessed due to oral intubation
- Severe crowding in both arches
- 2 mm diastema present between #8 and #9
- Gross caries

Past Dental History:

- 5/2018: seen at UM pediatric dental clinic for the first time
  - routed to OR for dental treatment under GA due to pt's complex medical history, obstructive behavior and extensive treatment needs
- 10/2018: 1st time dental treatment completed under GA in OR at Mott's Children's Hospital
  - Treatment completed: comprehensive exam, radiographs (4 PAs. 2 BW, and 2 occlusals), child prophylaxis, and dental treatment of 15 teeth
  - #H- L composite, #I- pulpotomy and SSC, #14- O composite, #19- O composite, #L- SSC, #30- O composite and extractions of #A, #B, #D, #E, #F, #G, #J, #K, #S
- 11/2022: recall exam completed in hospital dentistry at Mott's Children Hospital
  - Treatment completed: periodic exam, child prophylaxis, and topical fluoride management
  - Behavior management: protective stabilization
  - Gross clinical caries detected
  - Routed to OR for remaining dental treatment under GA

Recent Dental Treatment:

- 2/2022: Dental rehabilitation under general anesthesia due to complex medical history, obstructive behavior, and extensive treatment needs
- Oral intubation
- Complete intraoral exam, prophy, and topical fluoride varnish
- Full mouth radiographs: 8 PAs and 1 occlusal
- Treatment included 18 teeth:
  - #2: dental extraction, gelfoam
  - #3: dental extraction, gelfoam, 2-vicryl sutures
  - #5: O composite restoration
  - #7: IFL composite restoration
  - #26: MDF composite restoration
  - #25: MFDL composite restoration
  - #26: MFDL composite restoration
  - #10: DFL composite restoration
  - #12: O composite restoration
  - #13: O composite restoration
  - #14: dental extraction, Gelfoam
  - #15: O composite restoration
  - #18: O composite restoration
  - #19: OB composite restoration
  - #21: OB composite restoration
  - #M: dental extraction
  - #23: F composite restoration
  - #30: dental extraction, gelfoam

DISCUSSION

When initially brought to the dentistry clinic at C.S. Mott Children's Hospital, Ann Arbor, MI in November 2022, the patient's mother reported that her child was having pain that she suspected was from child losing some of his baby teeth . During the clinical examination, significant tooth decay was identified in several teeth. which may have been the cause of pain and discomfort. It was explained to the mother that the child had extensive dental needs that would need to be treated. Given the patient's dental condition and medical history, comprehensive dental treatment was carried out in the operating room. It was concluded that psychological and pharmacological behavior management options may not prove to be effective or ideal for the patient and thus necessitate a conservative surgical approach.

Upon entering the OR, the primary consideration was whether to use nasal or oral intubation. Generally, nasal intubation is the preferred approach when performing dental procedures under general anesthesia. However, in this particular case, oral intubation was deemed necessary because the patient had undergone cleft palate repair surgery in the past. Research has shown that surgical repair of a cleft palate can alter the anatomy of the nasopharynx, which could complicate future nasotracheal intubations. Furthermore, there is an increased risk of damaging the cleft repair with nasotracheal intubations. Given these factors, the anesthesiology team determined that oral intubation would be the safest choice. Although this posed difficulties for dental treatment, we managed to complete all necessary treatment.

There are numerous treatment options for the management of dental caries. However, in this case, a more aggressive approach was taken due to the patient's complex medical background and their difficulty in maintaining optimal oral hygiene at home. For example, non-surgical root canal treatment could have potentially saved teeth #2, #3, #14, and #30. Extraction, on the other hand, provides a definitive solution and eliminates the possibility of retreatment. Given the complexity of this patient's case, retreatment in a clinical setting would be challenging and would require another visit to the operating room.

Our intention was to give this patient the best possible care. It's critical to keep in mind that this patient's optimal may not be the optimal for everyone. To lessen the possibility of recurrent caries, more conclusive and vigorous treatment techniques were adopted. The possibility of extracting permanent teeth was discussed with the parent, and the advantages and disadvantages were weighed. The mother of the child had expressed concerns about maintaining the child's oral health and recognized why aggressive therapy may be required. When it comes to dental care for those with complicated medical histories and extensive dental caries, these discussions are essential. Realistic expectations must be set, and parents and providers should have a thorough discussion in regards to goals and outcomes.

REFERENCES

Baxter D, Shanks AL. Pierre Robin Syndrome. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

Bharati, S. J., & Chowdhury, T. (2013). Airway management for oral surgery in a patient with repaired cleft palate. *Saudi journal of anaesthesia*, *7*(4), 490. https://doi.org/10.4103/1658-354X.121072

Boothe, M., Morris, R., & Robin, N. (2020). Stickler Syndrome: A Review of Clinical Manifestations and the Genetics Evaluation. *Journal of personalized medicine*, *10*(3), 105. https://doi.org/10.3390/jpm10030105

Bowling EL, Brown MD, Trundle TV. The Stickler syndrome: case reports and literature review. Optometry. 2000 Mar;71(3):177-82. PMID: 10970261.

Giudice A, Barone S, Belhous K, Morice A, Soupre V, Bennardo F, Boddaert N, Vazquez MP, Abadie V, Picard A. Pierre Robin sequence: A comprehensive narrative review of the literature over time. J Stomatol Oral Maxillofac Surg. 2018 Nov;119(5):419-428. doi: 10.1016/j.jormas.2018.05.002. Epub 2018 May 17. PMID: 29777780.

Gómez OJ, Barón OI, Peñarredonda ML. Pierre Robin Sequence: An Evidence-Based Treatment Proposal. J Craniofac Surg. 2018 Mar;29(2):332-338. doi: 10.1097/SCS.0000000000004178. PMID: 29215441.

Mass, E, Segal S, Ariely Y, Zilberman U. Pierre Robin Sequence- Manifestation and Case Report. *Oral Health and Dental Studies*. 2018; 1(1):4. http://riverapublications.com/article/pierre-robin-sequence-manifestation-and-case-report

Snead M, Martin H, Bale P, et al. Therapeutic and diagnostic advances in Stickler syndrome. Therapeutic Advances in Rare Disease. 2020;1. doi:10.1177/2633004020978661

Varadarajan S, Balaji TM, Raj AT, Gupta AA, Patil S, Alhazmi TH, Alaqi HAA, Al Omar NEM, Almutaher SABA, Jafer AA, Hedad IA. Genetic Mutations Associated with Pierre Robin Syndrome/Sequence: A Systematic Review. Mol Syndromol. 2021 Apr;12(2):69-86. doi: 10.1159/000513217. Epub 2021 Mar 18. PMID: 34012376; PMCID: PMC8114067.