

Pierre Robin Sequence: A Common Presentation

Tulika Shinghal, DMD; and Ted L. Tewfik, MD, FRCSC

Pierre Robin Sequence (PRS), a well-recognized presentation, is the association of the first branchial arch malformation. It presents with the classic triad of micrognathia, glossoptosis and u-shaped cleft palate. In 1923, a French physician, Pierre Robin introduced the term “glossoptosis” in association with micrognathia which resulted in grave upper airway obstruction in newborn infants. He subsequently reported an association with cleft palate in 1934. This constellation of findings was termed a syndrome until 1976 when Cohen introduced the word anomalad, defined as “a malformation together with its subsequent derived structural changes.” The term PRS is currently used. It reflects the developmental cascade of these anomalies with micrognathia being the primary anomaly that then causes the other two to occur.

Epidemiology

The prevalence is estimated to be one in every 8,500 live births. It is equally common in males and females. Nearly half of the patients have an underlying syndrome diagnosis. Developmental delays are more prevalent in these syndromic patients.

Etiology and pathogenesis

Three pathophysiological theories exist to explain the occurrence of micrognathia:

1. The mechanical theory is the most widely accepted. It has been postulated that the *in utero* constraint of mandibular growth results in failure of the tongue to descend. This prevents fusion of the palatal shelves resulting in a cleft palate.

Oligohydramnios can be a possible contributing factor. Decreased amniotic fluid causes reduced support for the fetal head with resultant downward flexion of the chin. Other causes of intrauterine constriction include multiple births, uterine abnormalities or abnormal zygotic implantation sites.

Numerous syndromes are associated with intrinsic hypoplasia

2. The neurological maturation theory is suggested by electromyography of the tongue musculature, pharyngeal pillars and palate.

The inability of the developing fetus to engage in mandibular exercise prevents the tongue from descending. The spontaneous correction with age supports this theory

3. The dysregulation theory or the motor and regulatory organization of the rhombocephalus is related to a major problem of ontogenesis

Chromosomal anomalies are often associated with PRS. It is classically associated with several Mendelian syndromes. Non-syndromic PRS may be etiologically related to dysregulation of both SOX9 and KCNJ2.

Clinical presentation

Micrognathia is obvious on the initial examination of the majority (91.7%) of these infants. It is characterized by the retraction of the mandible by 10 mm to 12 mm with respect to the maxilla. The mandible has a small body, an obtuse genial angle and the condyle is posteriorly located. The jaw index is defined as the alveolar overjet multiplied by the maxillary arch divided by the mandibular



Figure 1. Patient with Pierre Robin Sequence (PRS) demonstrating the small mandible (frontal view).



Figure 2. Patient with PRS demonstrating the small mandible and receding chin (lateral view).

arch. This index helps to objectify mandibular growth. The growth of the mandible usually catches up during the first year—the child attains a normal profile by approximately age five to six years.

Glossoptosis is another presenting abnormality which is seen in approximately 70% to 85% of the children. Macroglossia and ankyloglossia are relatively rare findings, which are reported in 10% to 15% of the cases. Palatal clefting can be u-shaped or v-shaped and can include the soft palate only or both the soft and hard palates. The incidence varies from 14% to 91%. Occasionally, it may present as a bifid or double uvula or as an occult submucosal cleft.

Respiratory problems at birth are often part of the sequence. Airway obstruction is most evident in the supine position, especially during sleep. Obstructive sleep apnea may also occur. The resultant hypoxia and hypercapnia can lead to right heart failure. PRS is associated with laryngomalacia in 10% of cases.

Feeding difficulties in these patients are characterized by low oral intake, feeding time usually of > 30 minutes, fatigue, coughing, gagging and vomiting during feeds. Upper airway obstruction leads to these problems by causing incoordination of sucking and swallowing. In addition, the cleft palate inhibits the creation of sufficient negative intraoral pressure necessary

to suck. Poor bolus propagation is another aggravating factor.

Failure to thrive (FTT) is common. Feeding difficulties, hypoxemia, respiratory distress with increased work of breathing, augmented caloric needs and prematurity are amongst the various contributing factors. In addition, associated pathologies such as gastroesophageal reflux and recurrent respiratory infections further exacerbate the FTT.

The speech of the patients with cleft palate is characterized by an abnormal nasal air emission due to velopharyngeal insufficiency (VPI). VPI decreases oral volume and leads to disarticulations.

The most common otic anomaly is otitis media, which occurs in 80% of the cases followed by auricular anomalies. Conductive hearing loss is found in approximately 60% of the patients with external auditory canal atresia in only 5% of the cases. Anomalies of the ossicles as well as defects of the inner ear, such as large vestibular aqueduct and aplasia of the lateral semicircular canals, can also be found. Dental and philtral anomalies are found in a third of the cases.

Ocular anomalies have been reported in a third of the cases, including esotropia and congenital glaucoma. CV findings such as benign

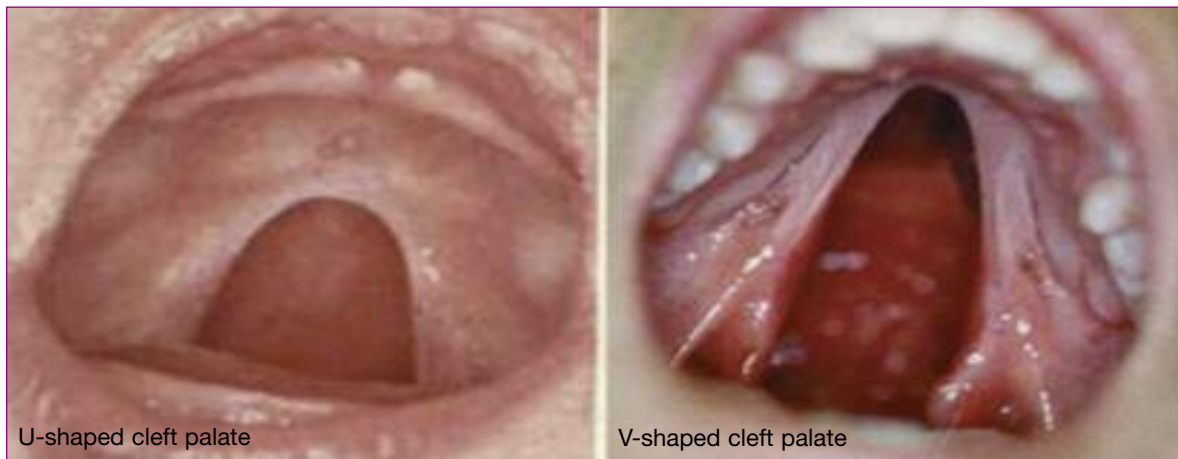


Figure 3. Inverted u-shaped and v-shaped cleft palate seen in patients with PRS.

murmurs, pulmonary stenosis, patent foramen ovale and ventricular septal defect have been documented. Musculoskeletal defects are the most frequent systemic manifestations which can affect the upper and lower limbs as well as the vertebral column. Some examples include syndactyly, hyperextensible joints, club feet, coxa varus or valgus, flexure contractures, scoliosis and sacral agenesis. Genitourinary conditions such as undescended testes are also associated with PRS.

Central nervous system defects are observed in 50% of the cases. Mental retardation has been seen in these children. A significant proportion of PRS children suffer from a coexisting syndrome, most frequently the Stickler and velocardiofacial (Shprintzen) syndrome.

Prenatal diagnosis

Prenatal ultrasonography can be used in the early identification of this sequence. The main sonographic findings are micrognathia, polyhydramnios

and cleft palate. In cases of polyhydramnios, it is recommended to further examine the facial profile and palate. Cardiac evaluation and karyotyping are also suggested. Prenatal telomeric screening is another test that is recommended.

Prognosis


After birth, there is a potential for rapid mandibular “catch-up” growth usually within the first year. However, this growth depends on the underlying cause of the underdevelopment. Despite initial feeding difficulties, most patients are able to tolerate an oral diet without airway distress by three-years-of-age. Successful decannulation for those who underwent tracheostomy is also achieved by this age.

Improved coordination of the velopharyngeal muscles results in a decrease in airway obstruction. The speech prognosis of PRS in non-syndromic patients appears to be similar to those with concomitant syndromes.

In general, death from PRS is thought to be the result of the poorly controlled combined effects of obstructive apnea and failure to thrive.

However, PRS is etiologically heterogeneous and the prognosis depends on the cause. Diagnostic subgroups based on associated syndromes help in evaluating the severity of the condition. Isolated PRS patients usually have a better prognosis.

	Dr. Shinghal is a Medical Student, Université de Montréal, Montreal, Quebec.
---	---

	Dr. Tewfik is a Professor of Otolaryngology, McGill University, Montreal, Quebec.
---	--

Conservative treatment

In the majority of patients, conservative management with close observation and follow-up is successful. Isolated PRS patients usually respond more favourably to the conservative approach.

Prone positional therapy has proved to be highly efficient in airway management. Oral airway placement, laryngeal mask, nasopharyngeal stenting and short-term intubation (less than two weeks) are other options in case positioning is inadequate. Intubation is often difficult due to the micrognathia and should be practiced by someone specialized in problematic pediatric airway management.

Feeding difficulties can be alleviated by upright feeding techniques, modification of the nipple for bottle feeding, temporary use of a nasogastric or orogastric feeding tube and the placement of a gastrostomy. Palatal plates such as the pre-epiglottic baton plate, which have a velar extension, pull the base of the tongue forward. This can be helpful in the relief of airway obstruction and it also facilitates the swallowing mechanism during feeds.

Surgical treatment

Operative intervention is reserved for those patients who fail to respond to non-operative treatment. Tongue-lip adhesion, subperiosteal release of the floor of the mouth, mandibular distraction and tracheotomy are different surgical options.

Conclusion

In conclusion, PRS is one of the most common congenital anomalies of the upper respiratory tract. It consists of micrognathia, glossoptosis and cleft palate which may result in airway problems and feeding difficulties. This sequence is often associated with syndromes such as the Stickler syndrome and velocardiofacial (Shprintzen) syndrome. Family history, cardiac and ophthalmologic examinations and

FISH (fluorescent *in-situ* hybridization) techniques should therefore be practiced in all children with PRS. The severity of the condition is variable with a more difficult course in the syndromic variant. As the mandible grows with age, the problem usually resolves. Conservative treatment is effective and the surgical options are reserved for more severe cases. Treatment modalities include prone/lateral positioning, nasopharyngeal and endotracheal intubation, glossopexy (including tongue-lip adhesion), tracheostomy and mandibular distraction osteogenesis. A multidisciplinary approach is essential in the management of these patients. Pediatricians, otolaryngologists, plastic surgeons, pedodontists, orthodontists, speech therapists, audiologists and social workers are all essential for a comprehensive and successful care plan.



Resources

1. Cohen MM Jr: Syndromes with Cleft Lip and Cleft Palate. *Cleft Palate J* 1978; 15(4):306-28.
2. Shprintzen RJ: The Implications of the Diagnosis of Robin Sequence. *Cleft Palate Craniofac J* 1992; 29(3):205-9.
3. Caouette-Laberge L, Plamondon C, Larocque Y: Subperiosteal Release of the Floor of the Mouth in Pierre Robin Sequence: Experience with 12 Cases. *Cleft Palate Craniofac J* 1996; 33(6):468-72.
4. Dionisopoulos T, Williams HB: Congenital Anomalies of the Mouth, Palate and Pharynx. In: Tewfik TL, Der Kaloustian VM, eds: *Congenital Anomalies of the Ear, Nose and Throat*. Oxford University Press, New York, NY, 1997, pp. 243-60.
5. Tewfik TL, Teebi AS, Der Kaloustian VM: Selected Syndromes and Conditions. In: Tewfik TL, Der Kaloustian VM, eds: *Congenital Anomalies of the Ear, Nose and Throat*. Oxford University Press, New York, NY, 1997, pp. 516-17.
6. Vegter F, Hage JJ, Mulder JW: Pierre Robin Syndrome: Mandibular Growth During the First Year of Life. *Ann Plast Surg* 1999; 42(2):154-7.
7. Hsieh YY, Chang CC, Tsai HD, et al: The Prenatal Diagnosis of Pierre-Robin Sequence. *Prenat Diagn* 1999; 19(6):567-9.
8. Nargozian C: The Airway in Patients with Craniofacial Abnormalities. *Paediatr Anaesth* 2004; 14(1):53-9.
9. Gruen PM, Carranza A, Karmody CS, et al: Anomalies of the Ear in the Pierre Robin Triad. *Ann Otol Rhinol Laryngol* 2005; 114(8):605-13.
10. Bronshtein M, Blazer S, Zalel Y, et al: Ultrasonographic Diagnosis of Glossoptosis in Fetuses with Pierre Robin Sequence in Early and Mid Pregnancy. *Am J Obstet Gynecol* 2005; 193(4):1561-4.
11. Evans AK, Rahbar R, Rogers GF, et al: Robin Sequence: A Retrospective Review of 115 Patients. *Int J Pediatr Otorhinolaryngol* 2006; 70(6):973-80. Epub 2006 Jan 26.
12. Lidsky ME, Lander TA, Sidman JD: Resolving Feeding Difficulties with Early Airway Intervention in Pierre Robin Sequence. *Laryngoscope* 2008; 118(1):120-3.