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CASE REPORT

Pierre Robin syndrome: A case report and review of literature and multidisciplinary approach in management updates

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Abstract

Pierre Robin sequence (PRS) is historically defined as a triad of small jaw, tongue retraction, and air passage hindrance, wherein infants often exhibit an immature mandible and respiration difficulties at birth. The small mandible drives the tongue backward, leading to PRS. In general, a cleft palate which is broad and U shaped is additionally related with this anomaly. PRS is not a syndrome alone, though instead various disorders, with single anomaly leading to another. Nevertheless, it is related to many other craniofacial abnormalities and may emerge together with a syndromic diagnosis, such as velocardiofacial and Stickler syndromes. PRS affected infants should be assessed by interdisciplinary unit to evaluate the skeletal findings, tracing the air passage hindrance origin, and address air passage and nourishment issues. Alignment resolves the air passage hindrance in 70% of cases, and most children are able to feed normally in the correct position. A nasopharyngeal tube placement is necessitated in case of baby persist with low oxygen blood concentration symptoms. Initial nutrition through a nasogastric tube may further lessen the proportion of energy required, facilitating early body mass. A fraction of PRS infants is unaffected by conservative measures and needs further medical mediation. The clinician should first exclude any sources of hindrance before opt for any surgical procedure, below the tongue base that would need a tracheotomy. The two generally accepted treatment procedures, surgical forward attachment of tongue to the lower lip and callus distraction of the mandible are explained.

Keywords: Airway obstruction, distraction osteogenesis, glossoptosis, micrognathia, Pierre Robin sequence

Introduction

The anomaly Pierre Robin has been described by a French stomatologist, Pierre Robin in 1923.[1-3] This was basically comprised extremely small sizes jaw (which he termed "mandibular hypotrophy") and glossoptosis[4] (an aberrant tongue retraction), leading to air passage hindrance and nourishment complications.[2,4] The smaller mandible is perceived to be as a result of hereditary issue or either a disfigurement issue with restrained intrauterine growth or altered mandible alignment. It is pertinent that Pierre Robin sequence (PRS) is a progression, wherein numerous aberration arising by a consecutive series of malformation, single following the others.[3] In PRS, the small jaw causes tongue retraction that further causes air passage obstruction and feeding inability.[3,4]

Hereditary Basis

The incidence of PRS is 1/8500–1/14,000 delivery.[3,5] This physical expression is due to myriad reasons and is exhibited in segregation or combination with a syndromic manifestation. A high incidence of twins with PRS has hereditary basis. Further, PRS affected infants family members have a greater occurrence of opening in the mouth roof and lip.[6] Opened mouth roof is related to removal on 2q and 4p and doubling on 3p, 3q, 7q, 78q, 10 p, 14q, 16p, and 22q. Small jaw[4] related to mutations in 4p, 4q, 6q, and 11q and osteogenesis doubling on 10q and 18q.[6] Izumi *et al.* assessed two groups of clinically detected PRS patients in novel approach [Figure 1]. Deletion sequencing leads to syndrome[7] and found that 40% segregated PRS and remaining 60% related to other anomalies, usually hereditary condition with distinctive

facial features, hearing loss, and joint issues and genetic condition with defective parathyroid, thymus, and conotruncal heart region syndromes[5] utilizing fluorescence *in situ* hybridization and array comparative genomic hybridization. Hereditary condition with distinctive facial features, hearing loss, and joint issues is related to variation in COL2A1, COL9A1, COL11A1, and COL11A2, while genetic condition with defective parathyroid, thymus, and conotruncal heart region is due to microdeletion of chromosome 22q11.2. Jakobsen *et al*. proposed that non-syndromic PRS is related to SOX9 and KCNJ2 impairment, together on chromosome 17, depending on independent set of PRS patients, one of them had a uniform shift among chromosomes 2 and 17.[3,8]

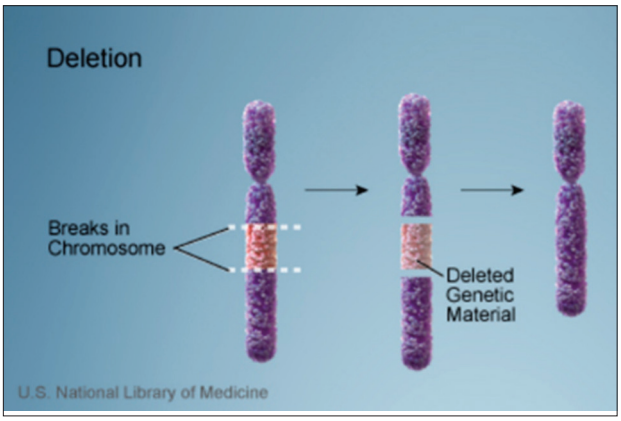

Figure 1: Deletion sequencing leads to syndrome

Clinical Presentation and Diagnostic Criteria

PRS is described as a classic triad of small jaw, retracted tongue, and air passage blockage. Microretrognathia [Figure 2] is at once detected at childbirth and is a characteristic diagnostic aspect. A female reported to our hospital emergency department in her full-term first pregnancy with labor pain, normal delivery was done under all aseptic protocol. She delivered a male child with respiratory distress; however, previous ultrasonography done did not show any sign of craniofacial anomaly. The patient was shifted to neonatal care for further management. Reference was sent to the department of craniofacial surgery and on further patient found pale, cyanosed with small mandible, retracted tongue,[4] and cleft palate which was diagnosed as PRS with no other congenital anomalies, was ruled out by pediatrician. Underdeveloped mandibles are small in both the perpendicular and parallel proportions that lead to front and back jaw protrusion and its resulting typical posteriorly placed jaw view. Other than small jaw, Randall reported remarkable finding of posteriorly placed chin, to describe the starting aberration in this set.[4] Glossoptosis[4] is described as an atypical posterior tongue alignment is the next typical aspect of PRS.[3] Tongue location is mainly established from mandibular proportion and position. Hypoplastic mandible has less anterior projection, following tongue moves backward forcing the tongue to adjust into a tighter space, which further worsens the posterior pharynx obstruction. Air passage blockage is an outcome of the aberrant tongue position, facilitating obstruction of naso-oropharynx on inspiration.[1,2] Blockage may end up in recurring low blood oxygen concentration, absence of breathing, and cyanosis.[9] For sustained breathing, a large amount of energy is utilized which is exhibited by inward movement of middle of skin neck above sternal level and the use of additional respiratory muscles. Based on the asperity of air passage hindrance, few child may manage air passage while awake, however, endure hindrance while asleep in supine position.[9] Infants often pose feeding complications[4] and strive to respire while consuming food. Acid reflux[4] and breathing in foreign object are usual end result of this procedure. The opening in mouth roof deters the unfavorable pressure within the mouth, necessitated to drink milk from the nipple or bottle; additionally, small jaw along with retracted tongue hinders

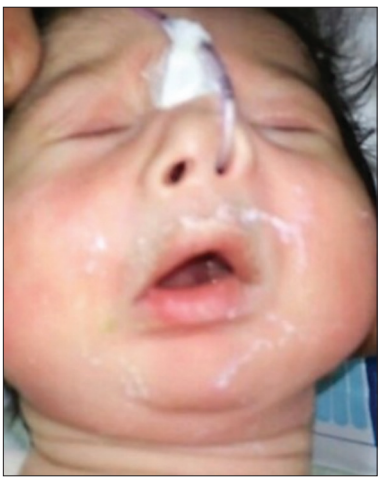

Figure 2: Microretrognathia in an infant with Pierre Robin sequence with cleft palate

physical aspiration.[10] Air passage hindrance and developing unfavorable intrapleural pressure have been recognized as determinant related to elevated acid backflow.[11] During early postnatal period, these infants frequently fail to live and gain weight due to undernourishment related to reflux and eating issues and high-energy expenditure related to high respiratory exertion. PRS is typically related with a broad U-form patent mouth roof; however, this is inessential to the clinical detection.[1] In extremely small jaw,[4] the tongue accommodates relatively large oropharyngeal space developing retracted tongue[4] in the small mandible scenario.[12] At the time of germinal growth, perpendicularly aligned palatal segments are assembled to a parallel position in the 8th week of growth. Various hypotheses suggested responsible for the presence of patent opening in the mouth roof in PRS. A remarkable hypothesis is that relatively huge tongue provides mechanical hindrance to this motion, emerging in a patent opening in the mouth roof.[12] Regardless of cleft palate absence in typical triad, it is still frequently related PRS anomaly. Further, 80% of PRS affected infants have other related aberrancies.[9]

Assessment

An evaluation must be done with PRS affected infants in a collaborative context to assay the skeletal outcome, outlining air passage hindrance origin, and address minimize hindrance[2] and nourishment issues to augment growth. A multifaceted approach is perfectly suitable for this task, comprises consultants from craniomaxillofacial surgeon, pediatric anesthesia, otolaryngology, pulmonologist, voices therapist, paramedical, and newborn specialist.[8] A genetic specialist should be consulted in case of latent syndrome or hereditary basis. In PRS, tongue retraction[3] may lead to upper air passage hindrance, though these patients can have various other causes for air passage breach due to syndromic reasons. These infants may also have insufficient epiglottis, laryngomalacia, and tracheal stenosis segments, all worsening air passage hindrance.[13,14] Airway passage assessment is crucial for PRS treatment decision-making. Significant investigations involve sleep supervision for uncontrolled low oxygen blood concentrations episodes, low oxygen blood concentrations while nourishment, sleep and sound production.[4,10] Endoscopic examination of velopharynx and endoscopic examination of lungs is helpful complements ascertaining air passage hindrance origin, as there could be more determinants of air passage breach apart from tongue basis, such as in congenital larynx tissue softening above vocal cord, partial tracheal collapse during increased airflow, or other lower larynx hindrances.[13,14] Partial evaluation will involve patient's assessment in various settings and how well this solves upper air passage hindrance.[10,13]

Management

A multidisciplinary team approach involving pediatrician, ENT, craniomaxillofacial surgeon, and anesthetist was taken, and after discussion, a conclusion was drawn that under fiber-optic intubation or tracheostomy was performed to correct the forward positioning of tongue to relieve the respiratory distress and tongue-lip adhesion procedure performed on 13-day-old newborn and the second stage surgery involving distraction of mandible was planned later nevertheless due to respiratory distress fiber-optic intubation performed; however, it was unsuccessful and condition of patient worsened, so we decided to do tracheotomy and performed our surgical procedure, and later on 4th post-operative day, tracheotomy tube was removed. Non-surgical sideways location will resolve the air passage hindrance in 70% PRS situations[2,10] by suitable posture, several of the babies are able to eat usually rendering additional therapy unnecessary. In case of sustained low oxygen blood concentrations manifestation, then it necessitates the nasopharyngeal or oropharyngeal tube placement [Figure 3] whose goal is to circumvent the site of upper air passage hindrance; however, in this case, after tongue-lip adhesion procedure was successfully performed and the newborn maintained the oxygen saturation level well enough.

Chang *et al*. have suggested methods of devising exclusive tube inserted into trachea through nose from specific tube inserted to trachea through mouth of the preferred length along diameter

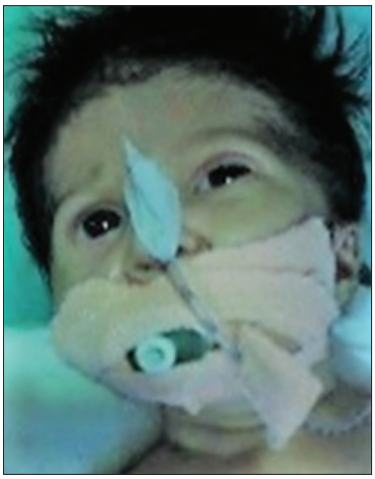

Figure 3: View showing oropharyngeal tube with nasogastric tube

in accordance with the infant's weight.[15-17] They demonstrated the favorable and secure use of a adjusted tube inserted into trachea through nose air passage as compared to traditional tube inserted into trachea through nose airway in easing air passage hindrance, thereby reducing surgical requirement. The adjusted tube inserted into trachea through nose air passage has minimal uninvolved inhaled air volume in gas exchange due to lessened size, thus facilitating concurrent usage of nasal hooks for additional oxygen.[15] Homecare of babies can be done by educating nursing staff and parent regarding cleaning and replacement of modified tube inserted into trachea through nose air passage.[16] Auxiliary air passage is usually required for 2–4 months for respiratory aid. Nourishment is considered as the second most significant determinant in treating PRS infants.[16,18] In the absence of respiratory distress also the infant's manifest active feeding mechanism issues due to related cleft palate. Earlier feeding through nasogastric tube [Figure 3] allows initial weight gain, thus minimizes the quantity of energy required[16] and yield of 20–30 g/d weight is considerable[18] Lately, it is advised that extremely affected PRS infants may have reduced urinary sodium.[19] The weight gain and survival rate propensity could be corrected by sodium supplement.[19] Although it should be noted that non-surgical treatment is more likely to succeed in syndromic patients as compared to syndromic patients.[16] There is a subdivision of PRS affected infants that are unaffected by traditional methods and needs additional mediation. Provisional methods such as additional oxygen, tube inserted into trachea through nose, and device keeping patent air passage while anesthesia and continuous ventilation tube insertion into trachea are insufficient with extreme breathing discomfort. The commonly accepted process for surgical execution of air passage hindrance is surgical forward attachment of tongue to lower lip, callus bone formation,[4] and tracheotomy.

Shukowsky, in 1911, explained surgical forward attachment of tongue to lower lip [Figure 4] later promoted by Douglas in the halfway - 20th century.[20] It is a method that helps to rectify the problem of tongue retraction[4] by stretching tongue base

anteriorly and joining it to the inferior labia. On recovery, the membranous scaffold facilitates by securing the tongue forward till the baby establishes a greater balanced air passage while development. It can only be planned on infants who have not grown any mandibular teeth, or else tear through repair negligently. Subsequently, when sufficient development has happened, the TLA should set free with a secondary method which is properly explained in the plastic surgery writings. A classical procedure is outlined here.[21]

Preceding intubation, a frank endoscopic examination of larynx and lungs should be performed to count out air passage aberrancies at above and below the larynx. Later, the child is subjected to flexible tube placement into trachea and aligned in a parallelly. A 3–0 polypropylene stitch is proceeded parallel over the tongue such as pulling stitch and vice versa similar membranous square folds are outlined on the inferior labial and inner tongue.[21] Local injectable medication causing absence of pain with epinephrine is injected into the cuts. The genioglossus is set free with a Cottle elevator through the inner lingual cut and raised toward tongue.[20] A 4–0 polypropylene stitch is driven circummandibularly and moved across tongue muscle and later tethered to the tooth socket rim in a concealed fashion like lingua is hauled onward with the pulling suture.[20]

The membranous folds sealed with 4–0 interrupted chromic and the muscle is fastened by 4–0 Vicryl. The lingual pulling suture is secured to the inferior lip and chin by adherent bands which can be stretched onward if required after operation. The posterior tongue button is linked to the inferior outer chin knobs through two stitches vertically crossing through TLA[21] [Figure 4].

These knobs and stitches ease the stress of lingual - labial folds while injury repairs. Rogers *et al*. suggested that crucial characteristics of this method are genioglossus and concealed circummandibular suture.[20] The lingual pulling stitches and knobs are taken out by 7–12 days post-surgery.[21,22] The tongue is set free, at the ages of 9 months–1 year.[22] Post-surgery complications include semi or complete healing rupture, repeated operation, pustules, unsatisfactory tongue basis disfigurement, and alteration to tracheal surgical incision for direct air passage.[22] Many authors described that TLA is an appropriate alternative for babies with air passage hindrance confined to tongue base and who persist with low oxygen blood concentration with supine positioning. Several reviews have assessed the effectiveness of TLA in preserving the PRS affected children air passage. Kirschner *et al*. described the outcome of 29 patients subjected to TLA with findings, 83.3% success in easing air passage hindrance and approximation in tube inserted into stomach through nose nourishment by 93.1% before operation to 72.4% after operation, with 62% of babies has been discouraged from all tube inserted into stomach through nose nourishment in 6 months.[23] Obstructive sleep apnea assessment of PRS affected infants, before and after TLA exhibits reduced obstructive apnea-hypopnea ratio (number of obstructive apneas and hypopneas divided by total sleep time), thereby depreciating the number of episodes to each hour, lowering the maximum carbon dioxide at the exhalation end pCO2 estimation and bettering the oxygen saturation.[24] However, suspended sleep interference is better in many scenario post-TLA, only 38% of patients exhibit thorough healing.[24] According to Denny *et al*., analysis of TLA confirms that despite there was huge early success proportion of air passage hindrance correction, still many cases with extreme breathing difficulties need an accessory medical mediation inside early life year, such as mandible aberration and tracheotomy for air passage regulation and gastric decompression tube insertion for nourishment aid[25] [Figure 5].

Distraction Osteogenesis (DO)

DO of the mandible or callus distraction[26] has become well known as the conclusive method for resolving PRS-related concerns to relieve air passage hindrance, fixing face beauty, and adjusting maligned teeth's.[27]

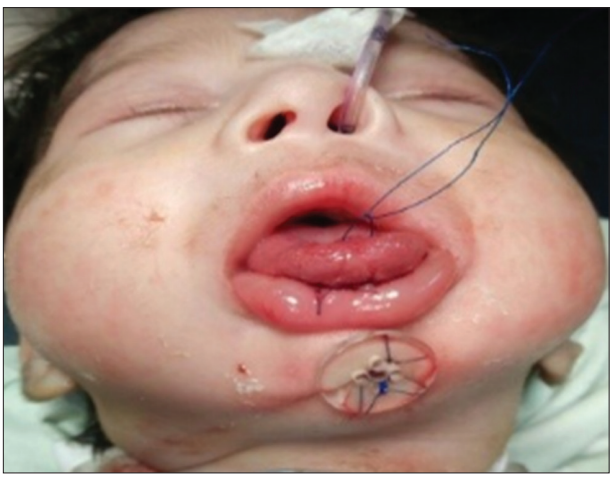

Figure 4: Tongue-lip adhesion procedure - chin button

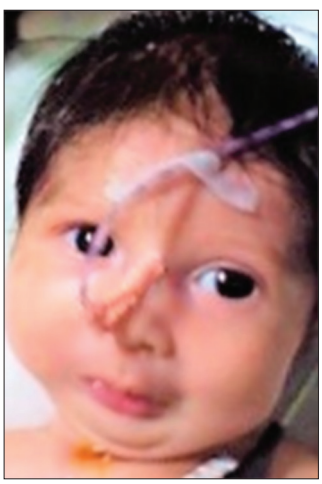

Figure 5: 18th post-operative day

Decision-Making in the Treatment of PRS

The therapy of PRS affected infants remains dubious which varies within organizations. We planned to commence with efforts at horizontal alignment to negate gravity impact on the lingual base. Constant blood oxygen saturation is performed on each case. If alignment was not favorable, accessory steps such as additional oxygen and adjusted tube inserted into trachea through nose were employed to circumvent lingual base hindrance. We found that sleep study[4] could be a significant means to record the obstructive apnea-hypopnea index and corroborate the absence of unknown central sleep apnea. Others main characteristic of therapy aims on eating and nourishment help. The patient was assessed carefully related to their feeding abilities by recognized voice specialist, specializing in nourishment. If required, prior feeding through special tube inserted to stomach through nose was started to augment mouth eating and boost body mass yield. Many babies treated favorably with conventional steps only. If these are unsuccessful in alleviating hindrance shown by poor polysomnography report[4] and poor body mass, then it necessitates surgical consideration. Pediatric otolaryngologist confirmed the non-existence of hindrance beneath the lingual base by frank endoscopic examination of larynx and lungs earlier to any operative intervention. Despite several breakthrough mentioned in the research related to invasive judgment, inconsistent general agreement presently exists. The probable benefit of single invasive method in contrast to different has not apparently been found out and not either process can be anticipated to render usual contacts between the teeth's while development. At our establishment, the pros versus cons of forward invasive attachment of tongue to lower lip and mandibular callus distraction were reviewed with the parents, and an interdisciplinary unit method was employed to reach the concluding invasive therapy method depending on the predicted span of breathing aid, unsuccessful conventional control, and the surgeon's analytical acumen. Tracheotomy[28] is still a benchmark for definitive air passage preservation and is the exclusive alternative for infants with related hindrance below the glottis[29] and partial hindrance of trachea during increased airflow.[30]

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