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The Pierre Robin sequence: a focus on a rare congenital anomaly

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Abstract

The aim of this paper was to enlighten the peculiar findings of the Pierre Robin sequence, a rare congenital anomaly with important afterbirth comorbidities. The management of this pathology requires highly specialised centers and highly qualified specialists in order to offer the best therapeutic strategy to the affected child. Early diagnosis and parental counseling play a key role in the managing of PRS: an earlier activation of the treatment path helps to yield better outcomes and to prevent complications. A case of a newborn affected by PRS is presented, showing the steps of the treatment strategy and the final outcome.

KEYWORDS Mandibular Osteodistraction, Micrognathia, Pierre Robin Sequence, Congenital Anomalies.

Introduction

Pierre Robin sequence (PRS) is a rare (1:8,500–1:20,000) congenital anomaly characterised by the triad micrognathia, glossoptosis, and most of the time U-shape cleft palate [Papoff 2013] PRS is described as a sequence because the triad has a development order. Micrognathia is secondary to glossoptosis that reduces the functional stimulus responsible of the lower jaw development. The more superior positioning of the tongue, caused by the reduced oral cavity volume, limits the mandibular growth and creates a lack in the fusion among the two horizontal palatal shelves, with the result of a U-shaped cleft palate [Fontanari et al., 2020]. The sequence can occur isolated or as part of a craniofacial syndrome, such as Stickler syndrome, the most frequently associated, Larsen syndrome, Treacher Collins, and Nager syndrome [Cicchetti et al., 2012]. Ultrasounds (US) are the first-line examination of choice for prenatal diagnosis of PRS, visible from the 20th weeks of gestation [D'Ambrosio et al., 2020]. Magnetic resonance imaging should be used in case of doubts [Cascone et al., 2014]. Prenatal diagnosis is of fundamental importance: it prepares psychologically the parents and address the child birth in a hospital equipped with a paediatric intensive care unit, in order to be prepared to any possible respiratory complication after delivery [Cascone et al., 2014]. The major comorbidities associated to PRS are upper airway obstruction and feeding problems, due to the micrognathia, and glossoptosis: the tongue fall back into the pharynx obstructing the airway [Papoff et al., 2013]. In the past, mortality was very high due to respiratory comorbidities such as cerebral anoxia, pulmonary sepsis and malnutrition. In particular, prolonged hypoxia has also been reported as a high risk for permanent brain damage in PRS neonates [Cascone et al., 2014]. In 2008, Cole proposed a classification based on the severity of the infant's symptoms and signs on clinical examination [Cole, Lynch, and Slator 2008] as follows.

Grade 1: a newborn baby with the features of PRS but no obvious clinical signs of respiratory distress. Feeding assessment is satisfactory.

Grade 2: a newborn with the features of PRS and some intermittent signs of respiratory distress, such as inspiratory stridor. Feed precipitates respiratory distress.

Grade 3: a newborn with the features of PRS and clinical signs of respiratory distress. Oral feeding is impossible.

The majority of neonates with PRS with Grade 1 and part of Grade 2 can be treated with non-invasive treatments such as prone positioning and nasopharyngeal continuous positive airway pressure. However up to 23% of them may require a more invasive intervention [Papoff et al., 2013]. In the most severe cases, surgery becomes necessary and, in the past, the most valid option was represented by the tongue-lip adhesion and tracheostomy, while, more recently, the mandibular distraction osteogenesis (MDO) has became the treatment of choice [Cascone et al., 2015]. Mandibular distraction osteogenesis allows to lengthen the mandible, providing a more functional alternative method in airways management. In particular, this technique is based on the principle that tension stimulates histogenesis with bone formation [Ramieri et al., 2017]. The indications for mandibular distraction are represented by clinical criteria as respiratory distress and persistent feeding difficulties or on the distance from postpharyngeal wall to lingual root: if less than 3 mm in the preoperative radiological imaging, mandibular distraction could be required [Cicchetti et al., 2012].

The Importance of a Multidisciplinary Approach in the Treatment of Pierre Robin Sequence (PRS)

The great complexity of infants affected by Pierre Robin Sequence needs to be approached with a multidisciplinary modality: obtaining the correct diagnosis, managing the airway ob-

struction, optimising feeding, selecting the timing for the surgical treatment, and addressing the multisystemic abnormalities are the main steps to consider in the treatment planning [Hsieh and Woo, 2019].

I. Prenatal Screening

Prenatal diagnosis has become gradually more possible thanks to the great advances in radiology. The first-line exams is represented by ultrasound (US), and, in more recent years, nuclear magnetic resonance [Giudice et al., 2018]. US has a low sensitivity in intercepting micrognathia (72.7%), while the normalisation of the mandibular anteroposterior length by the biparietal skull width created a jaw index , which greatly improves US sensitivity to 100% and specificity to 98.1%. Another useful, but indirect, finding is represented by polyhydramnios, due to the impaired swallowing secondary to glossoptosis [Hsieh and Woo, 2019]. Regarding the clef palate, its detection is challenging. Adopting 2D US, the sensitivity is up to 65%, and 3D US yields better results [Boyd et al., 2021]. For these reasons, the most important findings to evaluate during mid-trimester examination are micrognathia and subsequent tongue posture, that can be defined as an indirect sign of cleft palate. Another important step in the prenatal diagnosis is the differential diagnosis between syndromic and non syndromic PRS [Giudice et al., 2018]. Prenatal screening makes families more conscious and prepared, optimises the care of the baby at birth because this ensure that delivery will occur in a hospital with a paediatric intensive care unit [D'Ambrosio et al., 2020].

II. Afterbirth first physical examination

Patients with positive prenatal screening or clinical features of PRS need to be evaluated right after birth for airway obstruction and feeding difficulties. Prolonged obstruction causes acute and chronic hypoxia, leading to a higher risk of pulmonary infections, cor pulmonale, heart failure and cerebral hypoxia with cognitive impairment [Hsieh and Woo, 2019]. Feeding difficulties as sucking and swallowing disorders, chocking or oxygen desaturation during feeding can have a great impact on growth and weight gain [Rathé et al., 2015]. The severity of PRS must be defined in accordance with the grading proposed by Cole following the three worsening grades [Cole, Lynch, and Slator 2008]. When signs of airway obstruction are present, the first step is evaluation by the paediatric intensivists and paediatric pulmonologist, in order to establish the degree of the obstruction. Also, a paediatric neurologist and a geneticist are necessary to evaluate syndromic PRS infants. Nasopharyngoscopy is often necessary to distinguish obstruction due to tongue position from other causes such as subglottic anomalies and tracheomalacia. Once airway obstruction is assessed, a surgical evaluation is performed by the maxillofacial surgeon to consider surgical treatment in patient with high Cole grade. Surgery is usually considered when non-invasive ventilation fails, or respiratory distress and feeding difficulties become prolonged [Papoff et al., 2013].

III. Airway obstruction and feeding difficulties management

The management of airway obstruction starts with non-invasive treatments like prone positioning and nasopharyngeal tube. But in quite 25% of patients these treatments are not enough and more invasive strategies such as intubation and tracheostomy are required. Although more invasive procedure can be considered life-saving, lengthen hospitalisation and increase healthcare costs. Another important issue is represented by home caring of tracheostomised patients outside the hospital [Rathé et al., 2015]. Feeding difficulties can be managed with a temporary nasogastric tube, at least as first intervention. When difficulties become prolonged and weight and growth are impacted, a gastrostomy tube represents a valid alternative [Hsieh and Woo, 2019]. Restoring the separation between oral cavity and nasal fossae with a palatal plate, improves the feeding difficulties and allows a partial competence in the sucking activity [Cicchetti et al., 2012]. Due to the great complexity of this kind of patients, the best strategy is to consider a gradual improvement in invasiveness of the chosen treatments, in order to find the most appropriated. Acute events of respiratory distress, apnea-hypopnea index, and average weight gain are the most used index to evaluate treatment strategy [Ramieri et al., 2017]. When Cole grade is high and non-invasive treatments does not reach the desired outcomes, surgery becomes mandatory and should be performed as soon as possible [Cascone et al., 2014].

IV. PRS surgical treatment

One of the first surgical options to be introduced was tongue-lip adhesion (TLA). This procedure, also described as glossopexy, consists in anchoring the tongue to the lower lip and the mandible, ensuring an anterior lingual position that alleviates the upper airway obstruction. Despite its immediate benefits, TLA can lead to serious complication as dehiscence, lacerations, and infections. It also requires secondary interventions to achieve complete airway patency and normal feeding [Papoff et al., 2013]. More recently, mandibular distraction osteogenesis (MDO) was introduced and considered as surgical technique to treat micrognathia and subsequent airways obstruction secondary to glossoptosis. Its principle is that tension stimulate histogenesis with bone formation, and was firstly performed by McCarthy [Cicchetti et al., 2012]. In PRS patients, the aim of MDO is to reduce the need for tracheotomy, allowing an improvement in oral volume to avoid events related to glossoptosis [Hsieh and Woo 2019]. The surgical protocol for mandibular distraction osteogenesis is composed by: bilateral jaw osteotomy, distractor device placement, postoperative mandibular distraction and consolidation. The approach is intraoral and the bone surface is reached by inferior vestibular incision. Two complete bicortical mandibular osteotomies are performed by piezosurgery. Once obtained a complete mobilisation of the segments, a mandibular distraction devices is inserted in each segment [Cascone et al., 2017]. An effective report of MDO in PRS patient, is represented by the Fast and Early Mandibular Ostedistraction (FEMOD) protocol, in which the distraction begins intraoperatively (2 mm or more) and then after 2 days with 2 mm or more per day. The osteodistraction can be considered concluded when a slight III class position is reached. The consolidation is then obtained after 4 weeks and it is followed by distraction device removal in outpatient if using the external fixation [Cascone et al., 2014]. In the long term evaluation, the FEMOD protocol showed no positional change in primary teeth with successful dental buds migration, no dental injuries, and no facial scaring if using the external fixation, as pin placement incisions are very short. As tooth agenesis or hypodontia are very common in patients with PRS, performing a surgical treatment that considers and



FIG. 1 A male newborn during acute respiratory distress.



FIG. 2 A: Clinical appearance of micrognathia in Pierre Robin Sequence. B: U-shaped cleft palate.



FIG. 3 A Preoperative CT scan showing airway obstruction. B: Tridimensional volumetric reconstruction of airways.

preserves the teeth normal development represents an optimal result [D'Apuzzo et al., 2019].

V. Report of a treated PRS case

The case presented report the steps adopted in the treatment of severe Pierre Robin Sequence. A newborn, with positive prenatal screening for PRS, was born and immediately admitted to the paediatric intensive care unit for respiratory distress (Fig. 1). The patient was intubated. During the maxillofacial consultation, the findings of micrognathia, tendency to glossoptosis and U-shape cleft palate were observed (Figs. 2 A-B). A nasograstric tube was positioned to ensure feeding. The radiological imaging showed a upper airway obstruction, confirmed by the tridimensional volumetric reconstruction of the airways (Figs. 3 A-B). Due to the severity of the respiratory system, the newborn was planned for mandibular distraction osteogenesis with FEMOD protocol. The distraction device was positioned after bilateral bicortical jaw osteotomy (Fig. 4 A). After surgical treatment, the newborn was kept intubated and strictly monitored for O2 and CO2 saturation (Fig. 4 B). In a secondary surgical step, the cleft palate was treated adopting the pushback technique. A CT scan was repeated right after surgery and compared with pre-operative imaging to evaluate the magnitude of the distraction. A second imaging examination was performed at the 2-year-follow-up: symmetrical and adequate mandibular growth and presence of all decidual teeth (Figs. 5 A-B-C). In a long term follow up, was possible to appreciate mandibular development (Fig. 6).

Conclusion

The multidisciplinary approach in the treatment of Pierre Robin Sequence offers reduced complications and optimal outcomes in the long term. When the PRS manifests with severity, the surgical treatment becomes mandatory and represents the first step for the complete resolution of respiratory and feeding difficulties. Mandibular distraction osteogenesis has become the gold standard in the surgical treatment of PRS. The adoption of distraction osteogenesis permits to preserve the integrity of future decidual teeth, granting a symmetrical and optimal mandibular development.

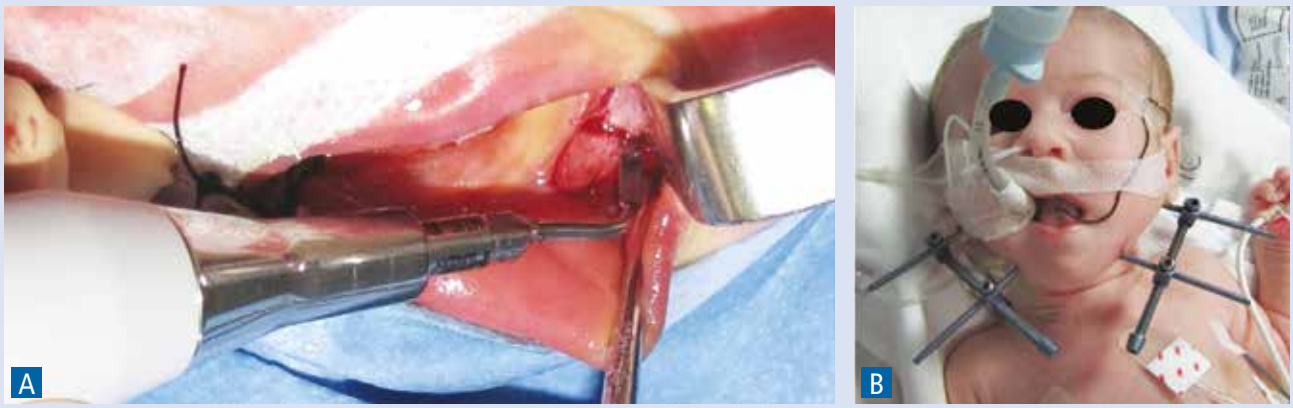


FIG. 4 A Jaw bicortical osteotomy during mandibular distraction osteogenesis. B: Postoperative phase with intubated patient and active mandibular distractor.

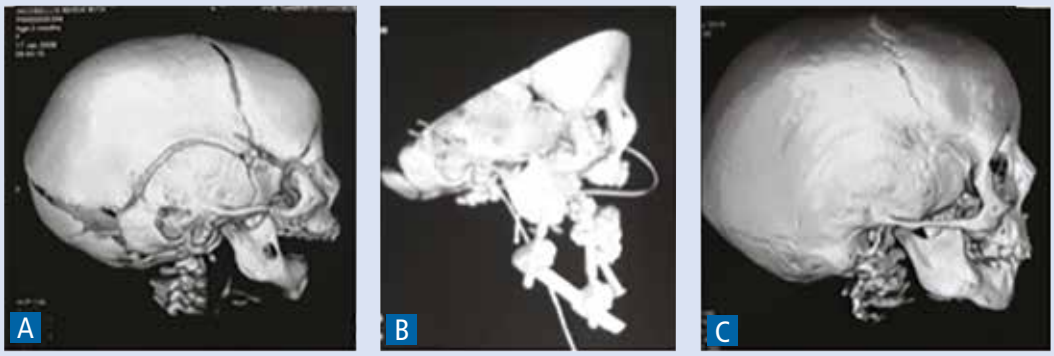


FIG. 5 A 3D reconstruction of preoperative micrognathia. B: Immediate 3D reconstruction of postoperative CT scan. C: 2 years follow up CT scan 3D reconstruction.



FIG. 6 Long-term follow-up showing the adequate mandibular development.

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