Neuroendocrinology Letters Volume 40 No. 1 2019
ISSN: 0172-780X; ISSN-L: 0172-780X; Electronic/Online ISSN: 2354-4716
Web of Knowledge / Web of Science: Neuroendocrinol Lett
Pub Med / Medline: Neuro Endocrinol Lett

Clinical attitude to the patient with Non-syndromic Pierre Robin Sequence with the cleft of soft palate and uvula – The necessity of fibroscopic investigation

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Submitted: 2019-03-03 Accepted: 2019-03-28 Published online: 2019-04-22

Key words: **Pierre Robin; non-syndromic sequence; palatal cleft; respiratory insufficiency**

Neuroendocrinol Lett 2019; **40**(1):5–9 **PMID:** 31184816 NEL400119C01

Abstract

Pierre Robin sequence is defined by a triplet of clinical signs in newborns: micrognathia, glossoptosis and tongue-based airway obstruction often accompanied by U-shaped cleft palate. The reported incidence is ranging from 1 to 8.500 to 30.000 newborns. Therapeutic management of Pierre Robin sequence is based on the degree of the airway obstruction. A priori management of such cases can be extremely challenging due to the phenotypic plethora of Pierre Robin Sequence. A ten-day male newborn diagnosed with Pierre Robin was referred to our department for investigation and management of severe airway obstruction. Oxygen support was administered immediately and further examination revealed micrognathia and tongue profusion through the U-shaped cleft palate resulting total obstruction in the rhinopharynx and the nasopharynx resulting in severe dyspnea. Clinical examination and as well further investigation did not reveal further congenital abnormalities. Fiberoptic nasotracheal investigation that confirmed total obstruction of the upper part of respiratory tract was followed by tracheostomy due to signs of persistent respiratory insufficiency. Our report describes the successful algorithm for management of Pierre Robin syndrome as well as highlights the importance of fiberoptic intubation in such rare case.

CASE REPORT

Abbreaviations:

O_2	- oxygen
Neo	- neonatal
PED	- pediatric
I. D.	- internal diameter
PRS	- Pierre Robin sequence
nsPRS	- non syndromic Pierre Robin sequence

INTRODUCTION

Pierre Robin sequence refers to heterogenic pathological entity, associated with micrognathia, glossoptosis and tongue-based airway obstruction highly associated with palatal cleft in a percentage of 66% to 90% (Cohen, 2017). The diagnosis between syndromic and non-syndromic form is of the utmost importance as most premature deaths occur with the syndromic form of Pierre Robin sequence (Bush & Williams, 1983). The epidemiological data reports an incidence fluctuating from 1 to 8,500 to 1 to 30,000 newborns (Lee *et al.* 2015, Printzlau & Andersen, 2004). To be specific, the great range is a result of studies conducted on different continents with various methodologies. The highest occurrence is reported in the United States of America, 1 per 3120 newborns whereas the lowest is found 1 out of 14,000 in Denmark (Côté *et al.* 2015, Printzlau & Andersen, 2004). To our knowledge, this is the first case from Slovak Republic reported in English literature.

CASE REPORT

The boy born at 40th weeks of gestational age (birth weight 3500g, birth length 50 cm, value of the Apgar score 9/9 points) by normal vaginal delivery in head position after uncomplicated pregnancy presented with severe dyspnea since delivery. No family history of congenital disorder was present. He was admitted to our department at the age of 10 days. The patient had micrognathia, cleft of the soft palate and his tongue protruded into the nasal cavity through a cleft of the posterior boarder of the hard palate, through the cleft of the soft palate and uvula. He was dyspneic also in pronate position, intermittently with the necessity of oxygen supply (O2 max 0,5 l/min). The rest clinical physical examination was normal. We did not confirm another congenital abnormality. Oropharyngeal intubation was impossible.

On the second day after admission, he had flexible fibroscopic investigation of the upper airways. Nasopharynx and oropharynx were totally obstructed with the root of the tongue. Hypopharynx was free and larynx had normal configuration without signs of laryngomalacia. The procedure was performed in supine position and the videoscope was propelled between the invaginated tongue and the pharyngeal wall. Tracheotomy was indicated. Introduction to anesthesia was complicated by difficult intubation (repeated failure with saturation drops up to 79%) for the underlying diagnosis. After tracheostomy, the child was dyspnoic, but without a stridor. Flexible bronchoscopy (wide 2.8 mm diameter) confirmed free subglottic area and did not found tracheomalacia. Tracheal tube Bivon 2.5 Neo was replaced for Bivon 2.5 PED with balloon (I. D. 2.5, length 38 mm). Due to dyspnea, the child was ventilated. After 15 hours, the mechanical ventilation was changed into noninvasive respiratory support for 24 hours. Using antiedematous therapy we could stopped the inhalation of oxygen (max. 30% O2) and respiratory support. Mild dyspnea was present due to abnormal shape of the thorax (pectus excavatum) and enormous salivation. Using respiratory physiotherapy (contact breathing, vibrating thoracic massage, elevated position of the thorax, regular airway cleaning, orofacial stimulation) we improved breathing mechanics. Serological investigations for herpes virus, rubella, cytomegalovirus were negative. We did not confirm any other congenital abnormalities.

The enteral feeding was complicated by frequent vomiting. Sonography of the stomach confirmed the presence of gastroesophageal reflux. A normal artificial milk formula was changed into antireflux one. The child was able to drink the whole amount of milk. In stable condition, the patient was release home. Multidisciplinary follow up after releasing home was indicated (otorhinolaryngologist, neonatologist, cleft out-patient department).

DISCUSSION

Pierre Robin sequence (PRS) is characterized by three related clinical findings which are micrognathatia, glossoptossis and tongue-based airway obstruction (Cohen, 2017). Whilst not necessary for diagnosis (Breugem *et al.* 2016), cleft palate is regularly found among newborns with PRS because the hypoplastic mandible prompts superior and retropositioning of the tongue, which may interrupt palatal shelf fusion.

Historically, Pierre Robin in 1923 was the first who recognized the triad in a cohort of newborns in 1923 and roughly a decade later emphasized the common association with the cleft palate (Breugem *et al.* 2016; Robin, 1934). Additionally, the definition of the Pierre Robin sequence was proposed roughly sixty years later. (Carey *et al.* 1982). Moreover, Breugem and Mink van der Molen in 2009 have described that the triplet by Pierre Robin is defined as an effective sequence of pathological events (Breugem & Mink, 2009). As highlighted by Breugem and Cohen, a patient with syndrome is characterized by a collection of abnormalities with one pathogenesis, as opposed to the patient with a sequence and many abnormalities, a number of them secondary to other existing anomalies (Breugem & Mink, 2009; Cohen, 1981).

A plethora of comorbidities is related with the PRS and the varying clinical finding can make the diagnosis quite troublesome. As, a heterogenic pathological entity, Pierre Robin can be distinguished as non syn-

dromic disease (nsPRS), or in relation with a concomitant syndrome or other dysmorphology (sPRS) such as velocardiofacial, teratogenic-related as well as Treacher Collins syndromes (Holder-Espinasse *et al.* 2001).

The pathogenesis of the PRS is subject of controversy as three distinct theories analyzed in literature. To begin with, mechanical theory suggests that due to pathological mandibular growth tongue remains high and in retroposed affecting the nasopharynx resulting feeding difficulties and respiratory issues. To be specific during the 11th week of development the abnormal position of the tongue hinders the palatal shelve fusion (Holder-Espinasse *et al.* 2001). The fact that mandibular growth relies on Meckel's cartilage lacks SOX9 gene to the hypothesis (Rathe, 2015). It is also hypothesised that the neuromuscular delay in the pharyngeal pillars, palate and the tongue hinders the mandibular growth and palatal shelve fusion (Abadie *et al.* 2002). Finally, the intrauterine mandible compression theory is suggested based on limited extension range of the flexed fetal head. Oligohydramnios, multigravid pregnancy and uterine anomalies are known also to hinder the mandibular growth (Bütow *et al.* 2016). In our patient we did not confirm neither the presence of oligohydramnios or multigravida pregnancy.

Even if non-syndromic Pierre Robin sequence is a heterogenic entity, current literature defines micrognathia as the principle feature relating to two other pathologies: glossoptosis and obstruction of upper airway (Breugem & Courtemanche, 2010). Micrognathic and retrognathic jaws display distinctive morphological features namely, reduced body length and mandibular branch height, greater mandibular angle and inclined chin posteriorly (Breugem, 2016). As regards, the mandibular growth in Pierre Robin, the latest publication by Abramson *et al.* in 2013 reached to the conclusion non-syndromic micrognathic cases can improve their clinical anomaly during postnatal growth and achieve favorable ventilation (Abramson, 2013). On the other hand, syndromic micrognathia should be managed surgically (Eriksen *et al.* 2006). Besides micrognathia, glosssoptosis is another distinctive clinical feature of Pierre Robin sequence. Glossoptosis defined by the displacement of the base of the tongue towards oropharynx and hypopharynx, increases the risk of developing sleep-related respiratory disorders (Suri *et al.* 2006). Disturbance in ventilatory dynamics in Pierre Robin patient include apnea, increase respiratory muscle activity, cyanosis and respiratory failure (MacLean *et al.* 2012). As a result growth curve could fall below standard as the patients energetic resources are utilized to perform vital functions (Daniel, 2013). The presence of U-shape cleft palate is associated with the clinical triplet by Pierre Robin, even though V-shape cleft palate can be found (Hanson & Smith, 1975). In addition to this cleft palate can hinder the speech development and the phonological skills (Morice, 2018). Lastly, nutrition-related conditions such as lengthily feeding time reduced oral feeding and additional respiratory deterioration in the course of the meals may be seen in cases with Pierre Robin sequence (de Vries *et al.* 2014).

Syndromic Pierre Robin sequence includes neurologic comorbidities (Filip, 2015) and cardiac anomalies (Pearl, 1982) in addition to micrognathia, glossoptosis and tongue based airway obstruction. Among the 34 conditions related to syndromic Pierre Robin, Stickler Sydrome is the most common (Snead & Yates, 1999). Rubinstein-Taybi syndrome, was part of the differential diagnosis of our patient, however serum TSH, fT3 and fT4 levels were physiological and no other characteristics of the syndrome were present (Zwierzchowski *et al.*, 2015) In similar fashion, congenital high airway obstruction syndrome (Hamid-Sowińska *et al.*, 2011) and Neonatal Marfan Syndrome were excluded as well (Jurko *et al.* 2017).

The primary therapeutic target is to sustain a viable upper airway in severe airway obstruction (Roy *et al.* 2009). Conservative treatment, such as positioning the patient in prone or lateral position (Poets & Bacher, 2011), inserting nasopharyngeal cannula (Côté *et al.* 2015) or utilizing mechanical positive pressure ventilation mask (Daniel, 2013) is preferred to Pierre Robin cases with periodic ventilation difficulties. In addition, a two stage orthodontic treatment can have prominent role in the conservative treatment protocols (Cohen, 2017). Nevertheless, the possible adverse effects of conservative treatments, such as increasing the risk of developing sudden infant death syndrome (Poets & Bacher, 2011) or aspirating gastric content (Daniel, 2013) are associated with conservative treatment should be mentioned.

As for the non-syndromic Pierre Robin sequence cases with significant airway obstruction or those cases who failed to respond to conservative treatment protocols surgical therapeutic options are available. On the contrary, syndromic Pierre Robin cases are more apt for surgical therapeutic procedures because of the various comorbidities and the reduced growth development (Lenstrup, 1925). To be specific, tongue-lip adhesion procedures and more common mandible distraction osteogenesis are invasive procedures that came unfortunately as well with risk of postoperative complications (Cascone, 2014; Shen *et al.* 2009). Furthermore, tracheostomy is considerate as another invasive procedure, although it is appropriate to highlight that is regarded as a short-lived treatment and should be reserved for severe airway obstruction or in patients where other measures failed (Amarillo *et al.* 2013). Tracheostomy comes with high rate of complication and fails to treat the pathophysiology of the Pierre Robin sequence subsequently; an additional treatment is required (Bangiyev *et al.* 2016).

As surgical treatments advance with the development of the technology, The Da Vinci Robotic System becomes more popular for paediatric tongue based masses cases. Rhbar *et al.* in 2007 was the first to treat

five paediatric patients with laryngeal clefts (Rahbar *et al.* 2007). Montevechii *et al.* as well as Thottam *et al.* performed transoral robotic tongue base resection in paediatric patients with obstructive sleep apnea syndrome (Montevecchi *et al.* 2017; Thottam *et al.* 2015). In both studies the patients did not required tracheostomy or nasogastric tube postoperatively and as significant drop in the obstructive apnea-hypopnea index value was observed (Montevecchi *et al.* 2017; Thottam *et al.* 2015). Utilisation of transoral robotic surgeries in paediatric population comes with a number of important advantages , minimally invasive approach, low morbidity, high quality endoscopic view and multiplanar movement (Hockstein, Weinstein, O'Malley Jr., 2005). However, the learning curve, as well as the high cost of trans oral surgeries remain major barriers.

Although there is a number of published treatment protocols to date there is no specific accepted guidelines (De Buys Roessingh *et al.* 2008). The fact that only 10% of non-syndromic Pierre Robin cases require invasive treatment as suggested by Bangiyev makes our case even more uncommon (Bangiyev *et al.* 2016).

CONCLUSION

The case of ten-day newborn with non-syndromic Pierre Robin sequence was present. We conclude that the severity of the airway obstruction even in non-syndromic PRS case requires the use of fiberoptic investigation for exclusion of added congenital abnormality as well as for local description of the degree of obstruction. The authors demonstrate that in case of non-syndromic Pierre Robin fiberoptic investigation and subsequently should be taken into consideration especially in combination with chest abnormality and problematic cleaning of the lower parts of a respiratory system.

CONFLICT OF INTEREST

None.

ETHICAL APPROVAL

All procedures were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

SOURCES OF FUNDING

None.

ACKNOWLEDGMENTS

None.

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