In utero diagnosis of micrognathia: A case report and review of the literature

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Abstract

Micrognathia is the presence of an abnormally small jaw and in most instances refers to the mandible. It is associated with many clinical syndromes, including the Pierre Robin Sequence (PRS). PRS features a triad of micrognathia, glossoptosis and airway obstruction. Syndromes such as PRS can have a large medical and psychological impact on the affected families. Specifically, micrognathia is associated with breathing and feeding issues that have been linked to impaired growth, development, and cognition. Prompt diagnosis, early monitoring, and multidisciplinary management of these patients is necessary for best possible outcomes. Ideally, early diagnosis of micrognathia or PRS would be made *in utero*. *In utero* diagnosis of micrognathia or PRS is rarely described in the literature. This report discusses such a case, allowing early planning for the post-natal period.

Introduction

Micrognathia is the presence of an abnormally small jaw and in most instances refers to the mandible. This is a craniofacial abnormality that can be associated with significant morbidity, including swallowing difficulty, airway obstruction, and feeding problems (1). Although it can occur alone, it is associated with as many as 274 syndromes, such as Turner syndrome and Cri du Chat syndrome (2). *In utero* diagnosis of micrognathia may, in some cases, lead to diagnosis of certain syndromes.

One presentation of micrognathia can be as part of Pierre Robin Sequence (PRS), a triad of micrognathia, glossoptosis (inferoposterior displacement of the tongue), and airway obstruction (3). PRS was initially described to include cleft lip and palate (CLP), but not all investigators now deem CLP to be necessary to the diagnosis. The incidence of PRS is estimated to be between 1:8,500 to 1:20,000 (4). Associated mortality has been reported to be between 2.2% and 30% (5).

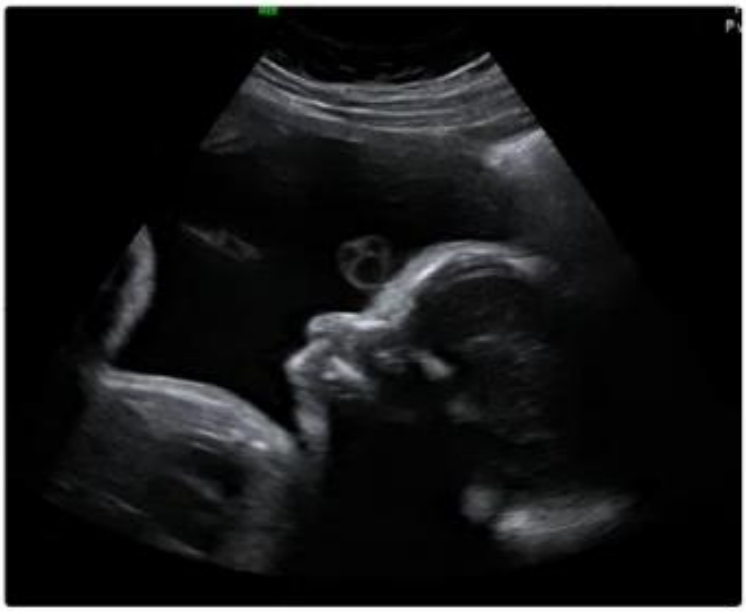

Figure 1 USS at 30 weeks confirms presence of small lower jaw.

In normal fetal development, there is a rostro-caudal delay of mandibular development compared with the maxilla. This results in the impression of a class II orthodontic skeletal relationship until early childhood when there is rapid growth of the mandible (6). Stunted growth of the mandible, however, can become apparent when there is increasing discrepancy between the upper and lower jaws. Lack of mandibular growth *in utero* can subsequently disrupt normal development of the tongue, palate, and associated structures. Consequently, micrognathia may be present in conjunction with other anatomical anomalies such as cleft lip and palate or natal teeth (7). In addition the tongue may have disrupted growth, or be displaced posteriorly. Displacement of the tongue before nine weeks gestation can disrupt palatal shelf fusion resulting in CLP (8). About 90% of PRS cases are associated with a cleft lip and palate (9).

Glossoptosis is believed to be responsible for the airway obstruction that may occur with micrognathia (3). It has been suggested that the posterior displacement of the tongue may allow it to rest on the epiglottis and act like a valve, closing off the airway during inspiration. Glossoptosis is usually diagnosed post-natally, where it can result in acute respiratory distress.

Airway compromise is worse when supine, or when there is disruption of pharyngeal tone such as during feeding and sleeping. This may be apparent as increased work of breathing, especially in the inspiratory phase, as well as apnoea and cyanosis.

Unlike other syndromes featuring micrognathia, pharyngeal motor problems are observed only in PRS (2). Pharyngeal muscle hypotonia may contribute to airway obstruction by allowing gastro-oesophageal reflux, which results in pharyngeal inflammation, further constricting the airway. These mechanisms result not only in airway difficulty, but poor feeding and problems with growth and weight gain in infancy.

Micrognathia is therefore an important feature in determining post-natal health. Early diagnosis, ideally , can aid in post-natal planning and optimisation of infant growth and development. In the available literature, only a few cases of *in utero* diagnosis of micrognathia have been published.

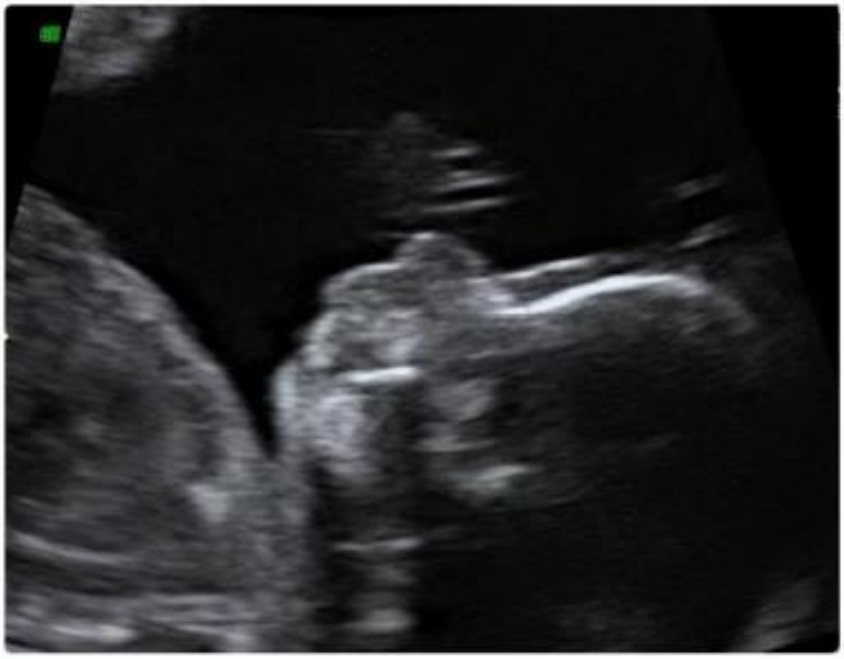

Figure 2 USS at 18 weeks shows micrognathia in sagittal section.

Case report

A 26 year old woman, Gravida 2 Para 1, was seen in the antenatal clinic. On anomaly ultrasound screening at 18 weeks gestation fetal micrognathia was detected (Figure 2). The possibility of low-set ears and a mid-palatal defect was also suspected. There was no known family history of PRS or isolated micrognathia.

An amniocentesis carried out at 19 weeks gestation revealed a normal fetal karyotyp (46XY). A fetal MRI was done at 20 weeks gestation that confirmed micrognathia (Figure 3). All other structures appeared normal. There was fluid in the stomach, indicating the fetus was swallowing.

At 25 weeks gestation the amniotic fluid index (AFI) was 19, with the largest pocket of fluid measuring 6cm. This was classified as the upper end of the normal range for gestation. At this stage fetal biometry placed the fetus between the 60th-80th centile. Estimated fetal weight was 1,250 +/- 185 grams. Further growth was monitored routinely via clinical examination and ultrasound (Figures 1 and 4).

The mother went into labour at 39 weeks gestation, and the neonate was delivered by rotational forceps due to persistent occipitoposterior (OP) positioning in the second stage of labour. The male neonate spontaneously ventilated on room air, and had Apgar scores of 8 and 9 at 1 and 5 minutes respectively. Venous and arterial cord gases were unremarkable. The birth weight of the neonate was 3,000 grams. He was noted to have micrognathia, retroglossia, and a cleft in the soft palate extending to the horizontal plates of the palatine bones (Figure 5 and 6).

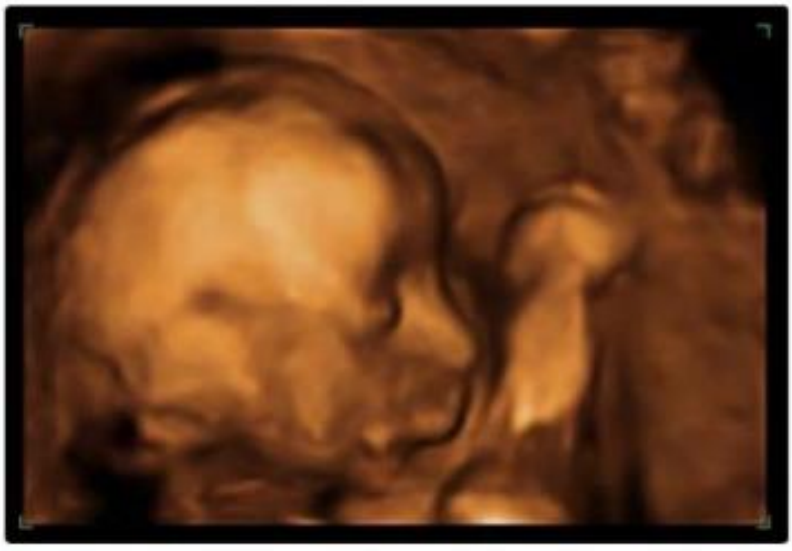

Figure 3 3D of USS at 18 weeks illustrating small lower jaw.

Although the neonate was crying spontaneously and did not seem to be in respiratory distress, he was initially transferred to the neonatal intensive care unit for observation. Here, he was found to have no problems breathing and no episodes of oxygen desaturation when lying down. Feeding was aided by a nasogastric tube (NGT).

As there were no breathing problems, a tracheostomy or mandibular distraction was not indicated. The patient was scheduled for surgical repair of his cleft palate at 2-3 months of age.

Comment

The craniofacial complex develops from the frontonasal prominence, and the paired lateral nasal, maxillary, and mandibular prominences. Growth

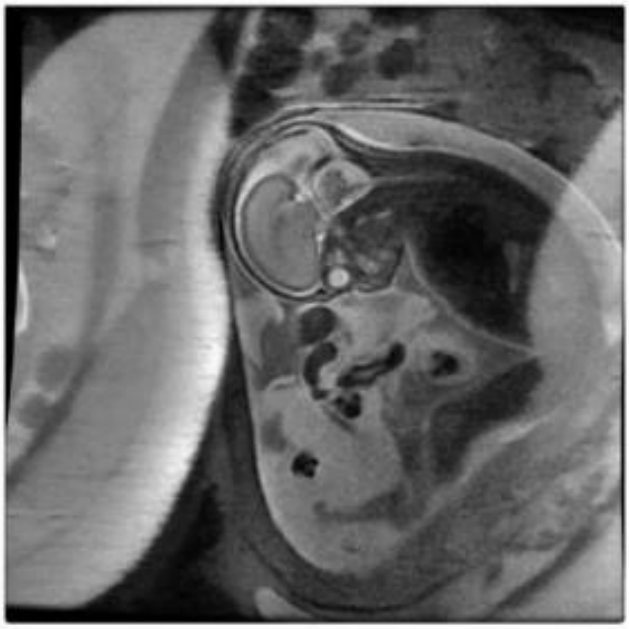

Figure 4a MRI at 20 weeks - sagittal section of fetus depicts micrognathia with other structures appearing normal.

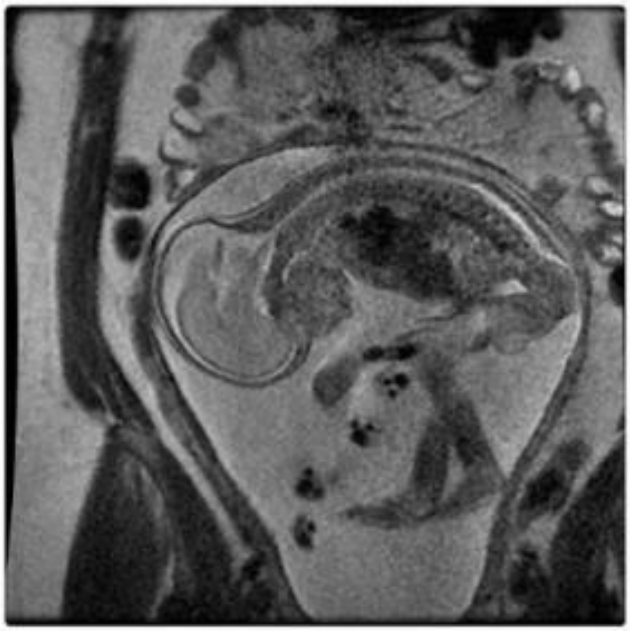

Figure 4b MRI at 20 weeks - sagittal section of fetus depicts micrognathia with other structures appearing normal.

and development of these prominences to form the craniofacial complex are affected by growth factors and chemotactic agents, as well as the pressure effects of neighboring structures. Specifically, proliferation and differentiation of neural crest cells in the facial structures are dictated by signalling pathways from the neighbouring endoderm and ectoderm. These signals occur at specific time-points during embryogenesis, and are dependent on formation of adjacent structures (10). Disruptions in these signalling pathways can result in malformation of the craniofacial structures, such as that seen in micrognathia.

Micrognathia can cause deformation of adjacent developing structures, such as the tongue and hard palate. Hard palate formation in embryogenesis involves fusion of the palatal shelves of the two maxillary processes. These shelves are initially oriented vertically. With mandibular growth the developing tongue is allowed to move anteriorly and inferiorly, providing space for the palatal shelves to elevate and fuse. Failure of mandibular growth can consequently prevent downward and forward movement of the tongue (resulting in glossoptosis), which in turn may prevent palatal shelf fusion (resulting in cleft palate) (5). Therefore, micrognathia can occur alone or in conjunction with glossoptosis with or without cleft palate (as seen in PRS).

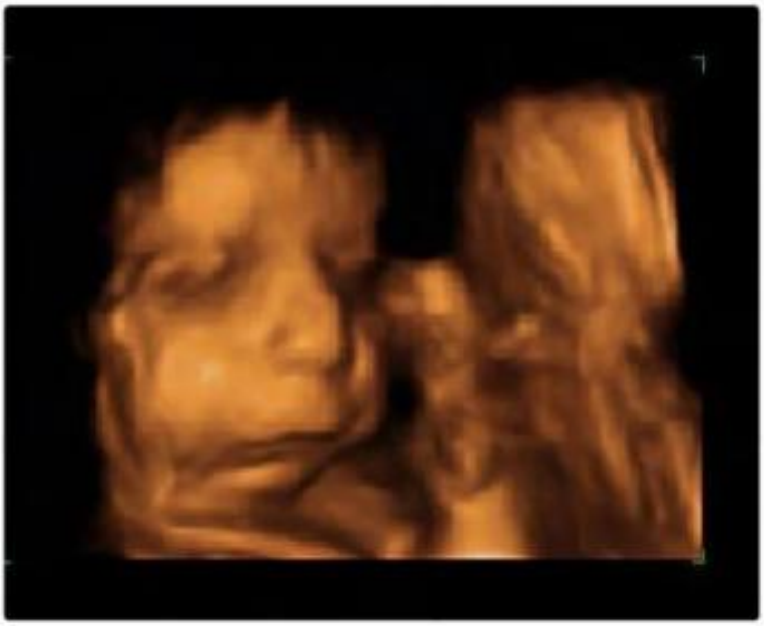

Figure 5 3D USS at 30 weeks showing oblique view of facial structures.

Development of these craniofacial anomalies can be due to both malformation (disruption of signaling pathways during embryogenesis) and deformation (disturbed growth due to adjacent structures).

The main acute issues associated with PRS are upper airway obstruction (UAO) and feeding problems (11). Together, these can lead to failure to thrive. Monitoring for these patients is based on oxygen saturation and weight gain. Some centres also describe the use of serial polysomnography (PSG) to monitor UAO (12).

Treatment options for PRS are aimed at widening the pharyngeal space and bridging the upper airway. Modes of widening the pharyngeal space include simple anecdotal measures such as prone positioning, but may extend to more invasive options such as glossopexy, mandibular traction, and mandibular

distraction osteogenesis (6). As this patient had a patent airway, none of these interventions were indicated. Bridging the upper airway aids both breathing and feeding. Breathing issues can be addressed via tracheostomy, nasopharyngeal airway, or positive pressure (11). Again, these were not considered in this patient as the airway was patent.

Feeding issues alone can be aided via a surgical repair of the cleft, or use of removable palatal plates, which may also improve tongue position and induce mandibular growth (11). The patient in this report was assessed to require a NGT for feeding until 2-3 months of age, at which stage he would have a surgical repair of his cleft palate.

The armamentarium of available treatment options for PRS illustrates the complex and dynamic nature of the condition. Ongoing feeding and breathing issues have been linked to the possibility of impaired cognition later in life, thus prompt diagnosis, early monitoring, and multidisciplinary management of these patients is mandatory for best possible outcomes (13).

Figure 6 Young male infant with Pierre Robin Sequence at 3 weeks of age.

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Declaration of Ethics Approval: The authors confirm that informed consent was gained from the patient prior to publication.

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