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Preterm Multigravida with Two Previous Cesarean Deliveries and a Fetus with Asymmetric IUGR and Cleft Lip and Palate: A Case Report

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Abstract

Cleft lip and palate and intrauterine growth restriction (IUGR) are common congenital conditions and may suggest subtle genetic abnormalities. When no chromosomal defects are detected through standard testing, this combination presents a diagnostic challenge in prenatal care. . This case report presents a 33-year-old multigravida woman at 34 weeks of gestation, referred for suspected fetal growth restriction and cleft palate. Serial ultrasound examinations confirmed asymmetric IUGR along with a complete cleft involving the lip, alveolus, and palate. Elective cesarean delivery of pregnancy was performed at 36 weeks of gestation via cesarean section, with the infant diagnosed with unilateral cleft lip and palate. This case underlines the importance of considering advanced genetic testing in non-syndromic cases of CLP with IUGR. This case highlighting a gap in standard prenatal diagnostics and emphasizing the need for a broader genetic approach in such cases. Clinicians should remain alert and pursue early, comprehensive evaluation and multidisciplinary planning to ensure accurate diagnosis, timely intervention, and better neonatal outcomes.

Keywords: Case Report, Cleft Lip and Palate, Intrauterine Growth Restriction

1. Introduction

Orofacial cleft is one of the most common congenital anomalies, encompassing cleft lip with or without cleft palate. A frequently encountered type of anomaly is *labiognatopalatoschisis*, also known as cleft lip and palate.[1,2] Cleft lip and palate occur in approximately 1% of every 700 live births worldwide.[3] The distribution of cleft lip and palate types consists of: cleft lip and palate (44.3%), cleft palate only (28.7%), and cleft lip only (21%). Unilateral clefts are nine times more common than bilateral clefts. In Indonesia, the incidence reaches 7,500 cases per year, with a national prevalence of cleft lip at 0.2%.[4]

Facial embryological development is a complex process that begins in the early fetal stage. This process requires coordination of cell migration, growth, differentiation, and apoptosis. Neural crest cells originating from the neural folds migrate through the mesenchymal tissue into the craniofacial area, which begins developing in the fourth week of gestation. These cells participate in the formation of the frontonasal, maxillary, and mandibular processes surrounding the oral cavity. Normal lip development occurs between the fifth and tenth weeks of gestation. Clefts may arise due to failure of mesodermal fusion with the medial nasal process. This condition is caused by the mesoderm failing to penetrate into the groove, preventing mesenchymal and epithelial fusion between the medial and lateral nasal processes, resulting in a cleft.[2,5]

Intrauterine Growth Restriction (IUGR) is defined as a fetus with a weight less than or equal to the 10th percentile, abdominal circumference (AC) ≤ 5th percentile, or a femur length/abdominal circumference (FL/AC) ratio > 24.[6] Approximately 2–10% of pregnancies affected by IUGR contribute to up to 20% of total stillbirths. Incidence rates vary, with 4–8% in developed countries and 6–30% in developing countries. In Indonesia, the prevalence is estimated at around 4.4%.[7] IUGR is classified into two types: symmetric and asymmetric. Symmetric IUGR occurs when fetal growth is proportionally restricted from an early stage, typically before 20 weeks of gestation, and is often associated with chromosomal abnormalities or infections. Asymmetric IUGR usually appears in the third trimester, where the fetus exhibits disproportionate body measurements, most commonly due to placental insufficiency. If symmetric growth shifts to asymmetric in late pregnancy, it is categorized as an intermediate type.[8] Contributing factors include decreased placental perfusion, chromosomal abnormalities, environmental influences, or infections.[6] IUGR may also be identified through ultrasound if biometric measurements do not increase significantly over a two-week period. To this day, IUGR remains one of the leading causes of perinatal morbidity and mortality.[6,7]

The concurrent presence of IUGR and cleft lip and palate may signal an underlying chromosomal abnormality, yet such associations are rarely reported and often under-investigated.[9] This case presents a combination of asymmetric IUGR and cleft lip and palate in a preterm multigravida with two previous cesarean deliveries. Although no chromosomal abnormality was identified, further genetic investigation remains essential, as anomalies may be subtle or undetectable with standard testing. This highlights a clinical gap in recognizing the potential genetic significance of coexisting IUGR and orofacial clefts in non-syndromic, high-risk pregnancies. This case report aims to deepen understanding, improve clinical perspective, and guide management of such conditions. The discussion outlines the clinical history, diagnostic approach, and emphasizes the need for thorough evaluation, including consideration of underlying genetic abnormalities.

2. Case Presentation

A 33-year-old multigravid woman was referred to the fetomaternal clinic at 34 weeks of gestation due to concerns of fetal growth restriction and suspected congenital malformation. Her obstetric history included one miscarriage at 10 weeks requiring curettage, and two previous cesarean sections. The current pregnancy was managed with regular antenatal care, with no known teratogenic exposures or family history of congenital anomalies. There was no history of hypertension, diabetes, trauma, or use of herbal medications. The patient had been taking folic acid, iron, and calcium supplements throughout pregnancy.

Serial ultrasonography revealed progressive growth restriction of the fetus with facial structural anomalies. On ultrasonography at 30 weeks of gestation (Fig. 1), the estimated fetal weight (EFW) was 1290 g, with biparietal diameter (BPD) of 7.51 cm, head circumference (HC) of 27.46 cm, abdominal circumference (AC) of 24.32 cm, and femur length (FL) of 5.40 cm. The ultrasonography confirmed the presence of a complete unilateral cleft lip and palate involving the upper lip, alveolar ridge, and primary palate.

Subsequent ultrasonography at 36 weeks (Fig. 2) showed asymmetric IUGR with EFW of 2485 g, BPD of 8.95 cm, HC of

32.44 cm, AC of 29.65 cm, and FL of 6.87 cm. The placenta was anterior at 30 and 34 weeks and posterior at 36 weeks. Amniotic fluid volume was within normal limits throughout (AFI ranged from 9.99 to 19.34 cm). Doppler velocimetry demonstrated normal pulsatility indices for the uterine arteries (PI Ute 1.02), middle cerebral artery (PI MCA 1.40), and umbilical artery (PI Umb 1.06), with no evidence of absent or reversed end-diastolic flow.Laboratory investigations including complete blood count, renal and liver function, coagulation profile, and screening for infectious diseases (HIV, hepatitis B, syphilis) were unremarkable. The decision to proceed with elective cesarean delivery of pregnancy had been made based on growth chart evaluation and coordination with the neonatal team due to potential risks of intra and extrauterine compromise requiring resuscitation and intubation. The baby was delivered via elective cesarean section at 36 weeks of gestation. Upon physical examination, a visible congenital malformation (Fig. 3) was noted in the form of a complete unilateral cleft involving the upper lip, alveolar ridge, and palate, consistent with the prenatal diagnosis of cleft lip and palate.

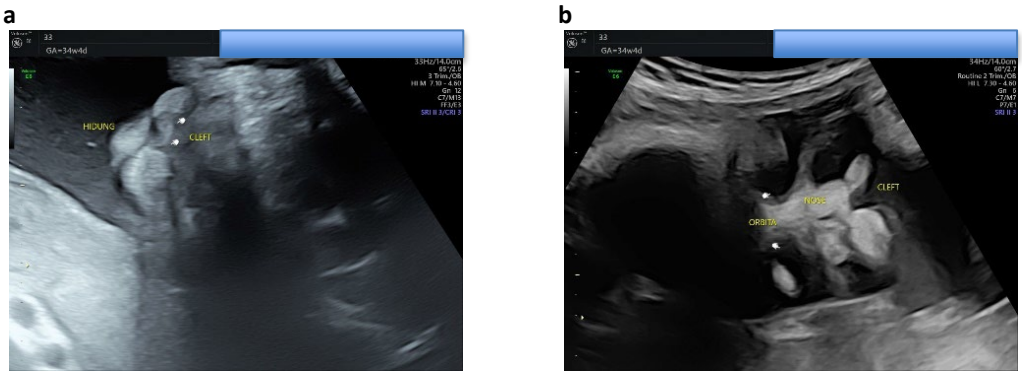

Figure 1. (a,b) Prenatal ultrasound at 30 weeks of gestation shows cleft lip and palate defect (between two white dots)

Figure 2. Prenatal ultrasound at 36 weeks of gestation shows asymmetric IUGR.

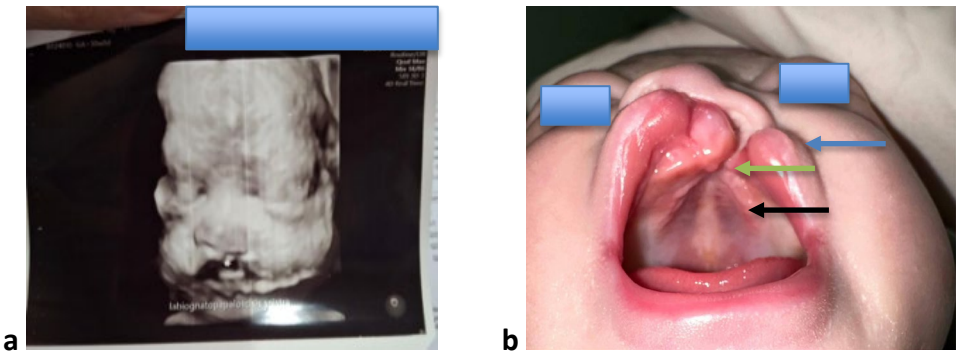

Figure 3. (a) Prenatal 3D ultrasound at 30 weeks of gestation shows unilateral cleft (b) Neonatal clinical shows unilateral cleft involving the upper lip (blue arrow), alveolar ridge (green arrow), and palate (black arrow)

Following the birth, a multidisciplinary conference was conducted to determine the comprehensive care plan. Psychiatric consultation was advised during follow-up visits to support maternal well-being. Neonatal dental assessment using a feeding plate was scheduled within the first week postnatally, with long-term orthodontic evaluation planned at approximately 8 years of age. Surgical correction of the cleft lip and alveolus was scheduled for age 3 months, followed by palatal repair between 6–10 months of age, depending on the child's body weight.

3. Discussion

Cleft lip and palate is one of the most frequently encountered congenital craniofacial anomalies and may occur as an isolated condition (non-syndromic) or as part of a more complex syndrome (syndromic).[1] This anomaly results from a failure of fusion between the medial nasal, lateral nasal, and maxillary processes during embryogenesis, which occurs between the 6th and 12th weeks of gestation.[10] In this case, the newborn was diagnosed with a complete cleft involving the lip, alveolus, and palate, accompanied by asymmetric IUGR, a form of fetal growth impairment caused by reduced placental perfusion or other conditions affecting body growth disproportionally.[11]

Asymmetric IUGR is characterized by head circumference and femur length that are relatively appropriate for gestational age, whereas the abdominal circumference and estimated fetal weight are smaller, as demonstrated by the serial ultrasound examinations in this case.[6,11] Several studies have identified the involvement of IRF6 and MSX1 genes in orofacial cleft, both in non-syndromic and syndromic forms, such as in Van der Woude syndrome or DiGeorge syndrome. This combination of these anomalies suggests further chromosomal investigations and genetic testing to confirm any underlying abnormalities.[12–15] A case involving 8q22.2–q23.3 deletion associated cleft lip and palate with IUGR, suggesting that such prenatal findings should prompt suspicion of subtle chromosomal abnormalities, even when standard testing is inconclusive.[9]

A large cohort study of prenatal clefts found that 21.5 % of fetuses with cleft lip/palate had chromosomal abnormalities. This highlight invasive genetic diagnosis should be considered in any case of cleft associated with additional anomalies.[16] Guidelines for evaluating dysmorphic infants recommend that chromosomal microarray is the first-line test in neonates showing dysmorphic features, even without a recognized syndrome.[17] Prior research on the genetic

etiology and diagnosis of fetal growth restriction states that chromosomal microarray analysis provides an additional 8–10% diagnostic yield over standard karyotyping, supporting its use as a first-line genetic test to detect subtle pathogenic variants.[18]

The management of cleft lip and palate anomalies requires a multidisciplinary approach due to its complex and varied nature, involving long-term care and the expertise of several healthcare professionals, including pediatricians, plastic surgeons, oral surgeons, pediatric dentists, orthodontists, prosthodontists, otolaryngologists, speech pathologists, geneticists, and psychiatrists or psychologists to address the psychosocial aspects of care.[1,13]

Surgical repair of cleft lip and palate is generally performed between 24 hours and 12 months of age. A commonly used guideline is the "rule of ten": surgery can be performed when the patient is at least 10 weeks old, weighs 10 pounds, and has a hemoglobin level of at least 10 g/dL.[13] The use of a feeding plate and early nutritional support are essential from birth to prevent failure to thrive and aspiration.[1] Speech ability is considered a primary outcome indicator in cleft management, and all children born with cleft anomalies should undergo speech therapy and receive surgical intervention according to the appropriate timeline to prevent speech development delays.[19]

4. Conclusion

This case highlights the co-occurrence of asymmetric intrauterine growth restriction and cleft lip and palate, while possibly isolated, may indicate an underlying genetic condition. Clinicians must conduct thorough antenatal evaluations and coordinate multidisciplinary care, not only to establish a clear diagnosis but also to distinguish between isolated anomalies and possible syndromic associations. This highlights the importance of considering genetic testing such as chromosomal microarray even in the absence of a confirmed syndrome. Early recognition and comprehensive evaluation allow timely intervention, accurate counseling, and better neonatal outcomes. For clinicians, this case underscores the need to treat seemingly isolated anomalies as potential indicators of broader syndromic patterns until proven otherwise.

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