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AN AFFECTED CHILD LEADING TO THE DIAGNOSIS OF MATERNAL 22Q11.2 DELETION SYNDROME: A CASE REPORT

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ABSTRACT

DiGeorge syndrome (22q11.2 deletion syndrome) is a chromosomal microdeletion syndrome, characterized by marked clinical variability. While many affected individuals present during infancy, some adults remain undiagnosed until genetic evaluation is initiated following the diagnosis of an affected child. Pregnancy in women with 22q11.2 deletion syndrome poses significant challenges owing to the risk of vertical transmission and potential obstetric complications. A 29-year-old (G2P1L1) women at the gestational period of 33 weeks and 6 days was presented with her third episode of antepartum hemorrhage secondary to placenta previa. Her obstetric history included a preterm normal vaginal delivery at 36 weeks in 2023 of a 2.3-kg infant who was later evaluated for developmental delay and diagnosed with 22q11.2 deletion syndrome. Subsequent parental genetic testing revealed a normal maternal karyotype (46,XX) but MLPA confirmed a heterozygous deletion involving three probes within the 22q11.2 region, establishing maternal DiGeorge syndrome. During the current pregnancy, prenatal chromosomal microarray analysis following amniocentesis at 16 weeks showed no fetal chromosomal abnormality. The pregnancy was complicated by gestational thrombocytopenia and placenta previa. Owing to recurrent antepartum hemorrhage, she underwent emergency lower segment cesarean section with bilateral uterine artery ligation, delivering a late preterm female infant weighing 1.82 kg. The postoperative period was uneventful, and both mother and infant were discharged in stable condition. This case highlights the importance of parental genetic evaluation after the diagnosis of an affected child with DiGeorge syndrome. Molecular techniques such as MLPA are essential when conventional karyotyping is normal but clinical suspicion persists. Comprehensive genetic counselling, prenatal diagnosis, and multidisciplinary obstetric management are crucial for optimizing maternal and neonatal outcomes in pregnancies complicated by maternal 22q11.2 deletion syndrome.

KEYWORDS: 22q11.2 deletion syndrome, DiGeorge syndrome, Pregnancy, Placenta previa, Gestational thrombocytopenia, MLPA, Case report, Prenatal diagnosis.

INTRODUCTION

DiGeorge syndrome is a genetic condition caused by the loss of a small segment of chromosome 22. Its presentation is remarkably diverse. Some individuals are diagnosed early in life because of congenital heart disease, immune dysfunction, hypocalcaemia, or palatal abnormalities, while others have relatively mild manifestations and may not be recognized until adulthood. This wide clinical spectrum can make the diagnosis challenging, particularly in adults who have not previously undergone genetic evaluation. (1,2)

The reported frequency of 22q11.2DS varies between populations, partly because individuals with subtle manifestations may remain undiagnosed. (2,3) When a parent carries the deletion, there is a one-in-two chance of transmission during each pregnancy. However, inheritance of the deletion does not necessarily result in the same clinical features or severity in the child as observed in the parent. (1,4)

The deleted region contains several genes that are important for normal embryonic development, including TBX1. Disruption of these developmental pathways can affect multiple organ systems. Depending on the individual, this may result in congenital cardiac abnormalities, palatal defects, thymic dysfunction, hypoparathyroidism with hypocalcaemia, developmental delay, speech and learning difficulties, or neuropsychiatric manifestations. (5,6) The marked variability in presentation means that a parent carrying the deletion may have few recognizable features despite having the potential to pass the condition to a child.

The diagnosis is based on demonstrating the 22q11.2 deletion using molecular genetic techniques. Chromosomal microarray analysis is widely used for detecting copy-number abnormalities, while targeted methods such as multiplex ligation-dependent probe amplification (MLPA) can also identify deletions involving the 22q11.2 region. (7,8) Conventional karyotyping may remain normal because the deletion is generally too small to be detected by routine chromosome analysis. (1,4) Therefore, a normal karyotype does not exclude the diagnosis when there is a strong clinical or familial suspicion.

Once 22q11.2DS is identified in a child, evaluation of the parents can be particularly informative. Such testing helps determine whether the deletion occurred spontaneously or was inherited and provides important information for future pregnancies. In an affected woman, genetic counselling is especially important because of the 50% transmission risk. Prenatal diagnostic testing can subsequently be offered according to the family's circumstances and preferences. (4,9)

Management of 22q11.2DS is individualized because there is no treatment that removes the underlying chromosomal deletion. Care is directed toward the problems experienced by the

individual and may involve several specialties. Cardiac abnormalities, calcium disturbances, immune dysfunction, developmental difficulties, and behavioural or psychiatric manifestations require appropriate evaluation and treatment. [4,10] Pregnancy also requires individualized care, with attention to the mother's existing manifestations, genetic counselling, and assessment of the fetus when indicated. [9,11]

CASE PRESENTATION

A 29-year-old multigravida woman (G2P1L1) presented to the Department of Obstetrics and Gynecology, at 33 weeks and 6 days of gestation with a chief complaint of bleeding per vaginum for one hour. The bleeding was painless and represented the third episode of antepartum hemorrhage (APH) during the current pregnancy. She denied abdominal pain, leaking of liquor, or reduced fetal movements, and reported satisfactory fetal activity.

The pregnancy was conceived spontaneously. Her booking investigations, dating scan, and first-trimester nuchal translucency scan were normal. Because of a significant obstetric history, she was closely followed in a multidisciplinary high-risk pregnancy clinic.

The patient had one previous pregnancy resulting in a preterm full-term normal vaginal delivery (FTNVD) at 36 weeks of gestation in 2023, delivering a 2.3 kg infant. During infancy, the child demonstrated delayed developmental milestones, prompting further pediatric evaluation. Genetic analysis subsequently confirmed 22q11.2 deletion syndrome (DiGeorge syndrome).

Following the diagnosis in the child, both parents underwent genetic evaluation to determine the inheritance pattern.

Initial conventional cytogenetic analysis by G-banded karyotyping demonstrated a normal female karyotype (46,XX), excluding major chromosomal abnormalities.

However, because of the confirmed diagnosis of DiGeorge syndrome in the previous child, molecular testing using Multiplex Ligation-dependent Probe Amplification (MLPA) with the SALSA P245-B1 Microdeletion Syndromes Kit was performed at the Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad.

MLPA analysis demonstrated a heterozygous deletion involving three probes within the 22q11.2 (DiGeorge syndrome) region, confirming that the mother was a carrier of 22q11.2 deletion syndrome despite having no major congenital cardiac, craniofacial, or immunological abnormalities. This explained the familial occurrence of the syndrome in the first child.

Following genetic counselling, the patient conceived spontaneously again.

Considering the maternal carrier status, prenatal genetic diagnosis was offered. Amniocentesis was performed at 16 weeks of gestation, and chromosomal microarray analysis (CMA) revealed no chromosomal abnormality, indicating that the fetus had not inherited the maternal 22q11.2 deletion.

The fetal anomaly scan was normal. Nevertheless, serial ultrasound examinations performed during the third trimester demonstrated a small-for-gestational-age (SGA) fetus with an estimated fetal weight below the 10th percentile.

The pregnancy was additionally complicated by gestational thrombocytopenia, for which she remained under regular surveillance. She received routine antenatal supplementation with iron and calcium.

At admission, the patient was conscious, oriented, and hemodynamically stable. Abdominal examination was consistent with a singleton pregnancy of approximately 34 weeks' gestation. Uterine tone was normal, and fetal heart sounds were present. She continued to perceive adequate fetal movements.

Because of the known diagnosis of placenta previa and recurrent episodes of antepartum hemorrhage, vaginal examination was avoided.

During the admission laboratory investigations show; Hemoglobin: 11.5 g/dL,

Total leukocyte count: 9,570 cells/mm^3, Platelet count: 1.4 × 10^5/µL, Bleeding time: 1 minute 22 seconds, Clotting time: 4 minutes 18 seconds.

Based on the clinical presentation and investigations, the patient was diagnosed as G2P1L1 (Gravida 2, Para 1, Living 1), Singleton pregnancy at 33 weeks + 6 days, Placenta previa, Third episode of antepartum hemorrhage, Maternal heterozygous 22q11.2 deletion syndrome (DiGeorge syndrome), Gestational thrombocytopenia, Small-for-gestational-age fetus, Previous child affected with genetically confirmed 22q11.2 deletion syndrome

In view of the recurrent antepartum hemorrhage associated with placenta previa and the increased risk of significant maternal bleeding, an emergency lower segment cesarean section (LSCS) was planned.

The patient underwent emergency LSCS with bilateral uterine artery ligation on 29 April 2026 to achieve effective intraoperative hemostasis and reduce postpartum hemorrhage risk.

A late preterm female infant weighing 1.820 kg was delivered at 12:30 PM. The newborn cried immediately after birth and was transferred for routine neonatal evaluation and observation.

The postoperative period was uneventful. The patient received: Inj.ceftriaxone, Inj.metronidazole, Intravenous fluids, Analgesics, Supportive care, Iron and calcium supplementation

Her vital signs remained stable, vaginal bleeding was minimal, and no postoperative complications occurred. Platelet counts remained stable throughout hospitalization.

The patient was discharged in stable condition with oral medications including cefuroxime, pantoprazole, trypsin–chymotrypsin, ibuprofen, paracetamol, lactulose, iron, and calcium

supplementation. She was advised to attend the gynecology outpatient department for review after six weeks.

The neonate was discharged with advice for routine pediatric follow-up and developmental surveillance because of the family history of 22q11.2 deletion syndrome, despite normal prenatal chromosomal microarray findings

DISCUSSION

DiGeorge syndrome (22q11.2 deletion syndrome) is a chromosomal microdeletion syndrome, its clinical manifestations are highly variable. Individuals with mild phenotypes may remain undiagnosed until an affected child undergoes genetic evaluation. [1,2] This case highlights several clinically important aspects of 22q11.2 deletion syndrome (DiGeorge syndrome) in pregnancy. The mother's diagnosis was established only after her first child, born in 2023, was investigated for delayed developmental milestones and genetically confirmed to have DiGeorge syndrome. Subsequent molecular testing identified a heterozygous 22q11.2 deletion in the mother, emphasizing the importance of cascade genetic testing in families with an established diagnosis of 22q11.2 deletion syndrome. [4,9]

Unlike many patients with 22q11.2 deletion syndrome, this patient had no documented congenital cardiac anomalies, cleft palate, or clinically significant immunodeficiency. This finding is consistent with the recognized variable expressivity of 22q11.2 deletion syndrome, in which individuals carrying the same deletion can have substantially different clinical manifestations. [1,4,9] Such variability can contribute to delayed diagnosis, particularly among adults with relatively mild phenotypes. [2,6]

Because 22q11.2 deletion syndrome follows an autosomal dominant inheritance pattern, an affected parent has a 50% chance of transmitting the deletion to each offspring. [4,9] Following genetic counselling, prenatal diagnosis was performed in the current pregnancy using amniocentesis and chromosomal microarray analysis. No pathogenic copy-number abnormality was identified in the fetus. Chromosomal microarray is an established method for detecting clinically significant copy-number changes, and prenatal genetic testing has an important role in pregnancies at increased genetic risk. [7,8] The negative prenatal result provided reassurance regarding inheritance of the known familial deletion while allowing pregnancy management to continue with appropriate obstetric surveillance.

Yang et al. described a mother–fetus pair in which both carried the 22q11.2 deletion, with the fetus showing cardiac and urinary tract abnormalities. In contrast, in our case, the maternal deletion was identified only after her previous child was diagnosed with 22q11.2 deletion syndrome, while chromosomal microarray analysis of the fetus in the current pregnancy showed no evidence of the deletion. [12] Hicks et al. reported an unsuspected maternal 22q11.2 abnormality detected through prenatal cell-free DNA screening, involving mosaic deletion and duplication. Our patient, however, was found to have a heterozygous 22q11.2 deletion through cascade genetic testing, which was subsequently confirmed by

MLPA. [13] Pu et al. reported a pregnant woman whose diagnosis of 22q11.2 deletion syndrome was made in the setting of significant cardiac disease, particularly interrupted aortic arch. In comparison, our patient had no documented major cardiac or craniofacial abnormalities but experienced important obstetric complications, including placenta previa, recurrent antepartum hemorrhage, gestational thrombocytopenia, and fetal growth restriction. [14]

The current pregnancy was complicated by gestational thrombocytopenia, placenta previa, recurrent antepartum hemorrhage, and a small-for-gestational-age fetus. Gestational thrombocytopenia is the most common cause of thrombocytopenia during pregnancy and is generally mild and self-limiting. [15] In our patient, platelet counts remained above the level requiring platelet transfusion, and there was no documented significant coagulation abnormality. Nevertheless, the coexistence of thrombocytopenia with placenta previa was clinically important because the patient was already at increased risk of bleeding and therefore required careful hematological and perioperative assessment.

Placenta previa is an important cause of painless antepartum hemorrhage and is associated with an increased risk of preterm delivery and cesarean birth. [16] Our patient experienced three episodes of antepartum hemorrhage, with the third episode occurring at 33 weeks and 6 days of gestation. Because of recurrent bleeding in the setting of placenta previa, emergency lower segment cesarean section was performed. Bilateral uterine artery ligation was undertaken during the procedure to assist with control of uterine blood flow and minimize the risk of significant operative blood loss. The mother subsequently recovered without documented postoperative hemorrhagic complications.

The neonate was a late-preterm female infant weighing 1.820 kg. In this case, early delivery was primarily related to the obstetric complications rather than evidence of fetal 22q11.2 deletion, as prenatal chromosomal microarray did not demonstrate a pathogenic copy-number abnormality. Nevertheless, because of the family history, continued pediatric follow-up and developmental surveillance were advised. The clinical spectrum of 22q11.2 deletion syndrome includes developmental, learning, behavioural, and other manifestations that may become evident later in childhood. [2,6]

The case also demonstrates the importance of multidisciplinary care. Obstetricians, clinical geneticists, neonatologists, hematologists, anesthesiologists, and clinical pharmacists may each have an important role depending on the patient's clinical needs. Genetic counselling helped the family understand the inheritance pattern and recurrence risk, while prenatal testing provided information regarding the fetal genetic status. Obstetric management required balancing the risks associated with recurrent hemorrhage and prematurity, while hematological monitoring was important because of the coexisting thrombocytopenia. Management of individuals with 22q11.2 deletion syndrome is similarly recommended to be individualized and multidisciplinary because of the multisystem nature of the disorder. [4,10]

CONCLUSION

This case describes a 29-year-old woman with genetically confirmed maternal 22q11.2 deletion syndrome (DiGeorge syndrome), identified only after her first child was diagnosed with the same condition during evaluation for developmental delay. The subsequent pregnancy was complicated by gestational thrombocytopenia, placenta previa, recurrent antepartum hemorrhage, and a small-for-gestational-age fetus, concluded in an emergency lower segment cesarean section at 33 weeks and 6 days. Despite these challenges, comprehensive multidisciplinary care resulted in favorable maternal and neonatal outcomes.

This case emphasizes the importance of considering parental genetic evaluation after the diagnosis of an affected child, particularly in disorders with variable clinical expression such as 22q11.2 deletion syndrome. Molecular diagnostic techniques, including MLPA and chromosomal microarray analysis, play a pivotal role in confirming the diagnosis, assessing recurrence risk, and guiding prenatal management. Early recognition, genetic counselling, individualized obstetric care, and coordinated multidisciplinary management are essential to optimize outcomes in such high-risk pregnancies.

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