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Mosaic Trisomy 9 With Severe Fetal Growth Restriction, Diaphragmatic Eventration, and Pulmonary Artery Hypoplasia With Peripheral Stenosis in a Preterm Infant: A Case Report

Alaa Hamdan [1, 2], Esra Fadelelmolla [1], Asante Boateng [3], Alexander Rodriguez [4]

1. Pediatrics, New York City (NYC) Health + Hospitals/Woodhull, New York City, USA 2. Research, Larkin Community Hospital, South Miami, USA 3. Pediatrics and Child Health, New York City (NYC) Health + Hospitals/Woodhull, New York City, USA 4. Neonatology, New York City (NYC) Health + Hospitals/Woodhull, New York City, USA

Corresponding author: Alaa Hamdan, alaahassan28121993@gmail.com

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Abstract

Mosaic trisomy 9 (T9M) is a rare chromosomal disorder characterized by the presence of an additional chromosome 9 in a proportion of somatic cells. The clinical manifestations can vary considerably, which is thought to be related, at least in part, to the proportion and distribution of trisomic cells across different tissues. Prognosis is similarly variable and remains difficult to predict. Although earlier reports suggested that greater proportions of trisomic cells may be associated with more severe clinical manifestations, this relationship is not consistent, likely because the degree of mosaicism can differ substantially between tissues and other genetic and clinical factors may also influence the phenotype.

In this report, we describe a preterm infant with significant fetal growth restriction and multiple dysmorphic features whose hospital course was complicated by respiratory distress and feeding difficulties. While prematurity was likely an important contributor to his respiratory symptoms, diaphragmatic eventration and an underlying pulmonary artery stenosis were also considered as potential contributing factors. Pulmonary artery stenosis is not commonly emphasized among the cardiac abnormalities described in T9M and may further highlight the broad phenotypic spectrum of this condition. The infant also experienced significant feeding difficulties that ultimately required enteral tube support. This case adds to the growing clinical spectrum of T9M and illustrates the challenges of relating the observed phenotype to the degree of mosaicism in an individual patient.

Categories: Pediatrics
Keywords: diaphragmatic eventration, fetal growth restriction (fgr), mosaic trisomy 9, pulmonary artery stenosis, t9m

Introduction

Mosaic trisomy 9 (T9M) is an uncommon chromosomal disorder in which an extra chromosome 9 is present in only a proportion of somatic cells. The clinical phenotype can vary widely, likely reflecting differences in both the proportion of trisomic cells and their distribution among affected tissues. Reported manifestations include fetal growth restriction (FGR), craniofacial abnormalities, congenital heart defects, developmental delay, hypotonia, and feeding difficulties [1-3]. Larger case series have similarly demonstrated substantial variability in cardiorespiratory morbidities, feeding, developmental, and other multisystem manifestations among patients with T9M [4-6]. This marked clinical heterogeneity can make the severity and combination of organ system involvement difficult to anticipate in an individual patient.

The clinical course of T9M also differs from that of complete trisomy 9. Complete trisomy 9 is typically associated with multiple severe congenital abnormalities and a high risk of perinatal mortality, whereas some individuals with T9M survive well beyond the neonatal period and into childhood or adulthood [1,2,7,8]. FGR has been reported as an important prenatal manifestation of T9M, and prenatal series have described an association between severe growth restriction and adverse perinatal outcomes [1,9]. Cardiac abnormalities are also well documented in T9M, with reported phenotypes ranging from septal defects to other structural cardiac abnormalities [1,2,4,6,10].

Because T9M is rare and there are no established standardized management guidelines, individual case reports remain important in documenting the range of clinical findings and identifying features that may not yet be well recognized. Li et al. reported 16 additional cases, noting that more than 100 individuals with T9M had been described in the literature overall. Their study expanded the recognized clinical phenotype and identified diaphragmatic eventration as a novel or less commonly reported feature [1]. Respiratory, growth, and feeding problems were also prominent among the prenatal and perinatal manifestations described in their cohort [1].

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Our case involves a preterm male infant with T9M who presented with severe FGR and abnormal umbilical artery Doppler findings, followed by a neonatal course complicated by congenital cardiac abnormalities, diaphragmatic eventration, prolonged respiratory difficulties, and feeding problems. Although the individual manifestations have been reported within the spectrum of T9M [1-6,10], the coexistence of these findings represents a complex multisystem presentation that is less well characterized. Of particular interest in this case was the extent of multisystem involvement, as well as the evolution of cardiac findings over the course of follow-up. While pulmonary vascular abnormalities are less clearly characterized in the available literature, the present case does not imply that any single finding is unique to T9M; rather, it highlights the clinical significance of their co-occurrence and longitudinal evolution. The variable distribution of trisomic cells among different tissues may contribute to differences between prenatal and postnatal cytogenetic findings and may partly explain the marked phenotypic variability observed in T9M [11,12]. While this case illustrates the clinical heterogeneity of T9M and the difficulty of anticipating the clinical course based solely on the diagnosis of mosaicism, it also adds to the limited clinical literature by documenting the simultaneous occurrence and evolution of multisystem abnormalities in an infant with T9M.

Case Presentation

Pregnancy and prenatal course

We present the case of a male neonate born at 34 weeks and 1 day of gestation via elective cesarean section to a 29-year-old mother with a gravida 2, para 1-1-0-2 (G2P1102). Maternal serologic testing was normal. The pregnancy was complicated by progressive FGR with abnormal umbilical artery Doppler findings, including absent and intermittently reversed end-diastolic flow.

Fetal surveillance began at 15 weeks of gestation. Most biometric measurements were consistent with gestational age, although the estimated fetal weight was approximately at the seventh percentile. At 17 and 20 weeks, fetal ultrasounds demonstrated persistent mild growth restriction with otherwise normal early anatomic evaluation.

At 28 weeks, a repeat ultrasound demonstrated significant FGR, with an estimated fetal weight of 1,059 g (4.3rd percentile), borderline bilateral ventriculomegaly with lateral ventricular measurements of 11 mm, and an increased systolic-to-diastolic ratio in the umbilical artery. Serial ultrasounds from 30 to 33 weeks demonstrated persistent severe FGR with intermittent absent end-diastolic flow. At 33 weeks, the estimated fetal weight was 1,497 g (<1st percentile). The previously observed ventriculomegaly had improved, with lateral ventricular measurements of 8-10 mm. Biophysical profiles remained reassuring, with normal amniotic fluid, fetal movement, tone, and breathing (Table *1*).

Gestational age	Estimated fetal weight	Ultrasound findings	Doppler findings
15 weeks	~7th percentile	Early biometric assessment; no major structural abnormality	-
17 weeks	-	Mild FGR	-
20 weeks	-	Persistent mild FGR; early anatomy otherwise normal	-
28 weeks	1,059 g (4.3rd percentile)	Severe FGR; bilateral ventriculomegaly (11 mm)	Increased UA S/D ratio
30 weeks	-	Persistent severe FGR	Intermittent AEDF
33 weeks	1,497 g (<1st percentile)	Persistent severe FGR; ventricles improved to 8-10 mm	Intermittent AEDF
34+1 weeks	1,349 g at birth	Delivery by repeat cesarean section	-

TABLE 1: Prenatal ultrasound findings and progression of FGR

FGR: fetal growth restriction; UA: umbilical artery; S/D: systolic-to-diastolic ratio; AEDF: absent end-diastolic flow

Respiratory course

Shortly after delivery, the neonate developed mild respiratory distress with increased work of breathing and required positive-pressure ventilation before transfer to the neonatal intensive care unit (NICU). On the second day of life (DOL), respiratory status became more unstable, requiring mechanical ventilation with synchronized intermittent mandatory ventilation and administration of two doses of surfactant. Chest imaging demonstrated findings compatible with respiratory distress syndrome, including reticulonodular interstitial infiltrates, as well as elevation of the left hemidiaphragm consistent with diaphragmatic eventration (Figure *1*).

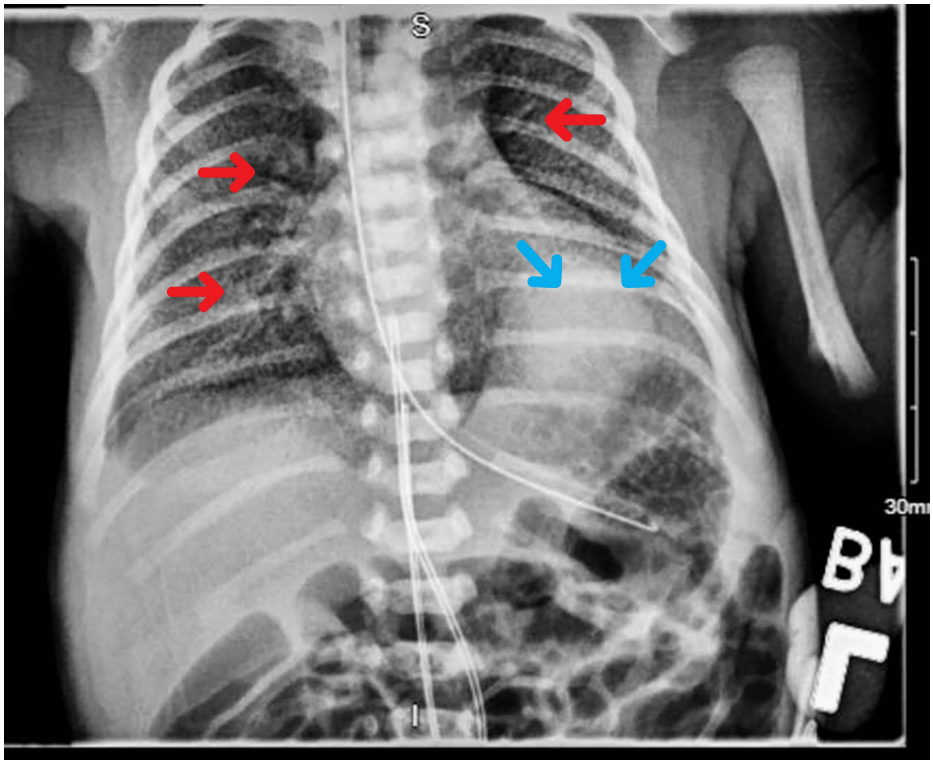


FIGURE 1: CXR showing left hemidiaphragm elevation consistent with mild to moderate eventration, along with reticulogranular changes reflecting RDS in prematurity

Chest radiograph (CXR) demonstrating left hemidiaphragmatic eventration (blue arrows) and bilateral diffuse reticulogranular pulmonary opacities (red arrows), consistent with respiratory distress syndrome (RDS).

He was subsequently weaned from mechanical ventilation to noninvasive respiratory support and then high-flow nasal cannula (HFNC). He was extubated to continuous positive airway pressure (CPAP) on DOL 7 and gradually weaned; however, on DOL 19, he developed recurrent oxygen desaturation and increased work of breathing requiring escalation of respiratory support. Repeat chest radiography did not demonstrate a new pulmonary process. He received a 20-day course of spironolactone and hydrochlorothiazide and subsequently improved, allowing weaning to room air.

After transfer to a tertiary care center at approximately two months of age for ongoing feeding management and gastrostomy tube placement, he again developed increased work of breathing and subcostal retractions and required nasal cannula support. Chest radiography continued to demonstrate mild hyperinflation and persistent elevation of the left hemidiaphragm. He received an additional course of chlorothiazide for persistent respiratory symptoms. Following a period of stability, recurrent oxygen desaturations required re-initiation of respiratory support. An attempted intubation for gastrostomy tube placement was unsuccessful, after which he required CPAP because of airway edema. Respiratory support was subsequently weaned through HFNC to room air.

Cardiovascular course

A grade II/VI systolic murmur was identified during the neonatal examination, and subtle dysmorphic features, including micrognathia and high-arched palate, were noted. The initial echocardiogram demonstrated a patent foramen ovale (PFO) with left-to-right shunting, moderate right ventricular dilation with low-normal systolic function, and low-normal left ventricular systolic function with a left ventricular ejection fraction (LVEF) of 54%. A mildly hypoplastic left pulmonary artery (LPA) with mild peripheral stenosis was also identified, with an LPA diameter of 0.23 cm (Z-score -1.91). A possible partial cleft of the posterior mitral valve leaflet was noted; however, there was no associated mitral stenosis or regurgitation. No patent ductus arteriosus was identified.

Follow-up echocardiography demonstrated interval improvement in cardiac function. The interatrial communication remained present but was characterized as a stretched PFO with mild left-to-right shunting; a small secundum atrial septal defect was considered as a differential diagnosis. Importantly, right ventricular size and systolic function had normalized, while left ventricular systolic function had improved

to normal, with an LVEF of 74%. The LPA remained mildly reduced in size but demonstrated an increase in measured diameter from 0.23 cm (Z-score -1.91) to 0.30 cm (Z-score -1.67), with persistent mild LPA stenosis. The previously suspected mitral valve cleft was not visualized in follow-up echocardiography, and the mitral valve appeared structurally normal without mitral regurgitation. Because the initial and follow-up studies may have differed in visualization, the absence of the cleft on follow-up should not be interpreted as definitive resolution of a congenital cleft. Overall, the follow-up study demonstrated improvement in biventricular systolic function and resolution of right ventricular dilation, with persistent but mild LPA hypoplasia/stenosis and a small interatrial communication (Table *2*). The patient remained hemodynamically stable throughout the hospitalization course.

Echocardiographic finding	Initial study	Follow-up study
PFO/interatrial communication	PFO, left-to-right shunt	Stretched PFO, mild L→R shunt; small secundum ASD considered
RV size	Moderately dilated	Normal
RV systolic function	Low-normal	Normal
LV systolic function	LVEF 54%	LVEF 74%
LPA diameter	0.23 cm	0.30 cm
LPA Z-score	-1.91	-1.67
LPA stenosis	Mild peripheral stenosis	Persistent mild stenosis
Mitral valve	Possible posterior leaflet cleft	Structurally normal; cleft no longer visualized
Mitral regurgitation	None	None
PDA	None	-

TABLE 2: Serial echocardiographic findings in an infant with mosaic trisomy 9

PFO: patent foramen ovale; L→R: left-to-right; ASD: atrial septal defect; RV: right ventricle; LV: left ventricle; LVEF: left ventricular ejection fraction; LPA: left pulmonary artery; PDA: patent ductus arteriosus

Feeding, swallowing, and surgical course

Because of prematurity and the need for respiratory support, enteral feeding was initially withheld, and total parenteral nutrition was provided. Trophic feeds with expressed breast milk were initiated on DOL 5 and progressively advanced as tolerated. The infant demonstrated poor oral coordination and weak suck, requiring prolonged feeding sessions and close monitoring. By DOL 9, enteral feeding volumes were progressively increased toward a target of 120 mL/kg/day, with fortification to 22 kcal/oz by DOL 10. Non-nutritive oral stimulation was implemented with speech-language pathology to improve suck-swallow-breathe coordination.

Following discharge from the NICU and transfer to a tertiary care hospital, the infant continued to have significant feeding difficulties. Oral feeding was limited by poor suck-swallow coordination and an inability to maintain safe and consistent oral intake. A modified barium swallow study was performed and demonstrated severe oropharyngeal dysphagia, with aspiration noted across all liquid consistencies tested.

During the oral phase, the infant had difficulty initiating nutritive sucking, with disorganized suck rhythm and poor control of the bolus during the suck-swallow sequence. The pharyngeal phase was notable for delayed initiation of swallowing, reduced laryngeal vestibule closure, and a diminished pharyngeal stripping wave. These abnormalities resulted in deep laryngeal penetration and recurrent trace silent aspiration of thin, slightly thickened, and mildly thickened liquids delivered through a Dr. Brown's Preemie nipple. There was also aspiration of pharyngeal residue after the swallow. Reflux of thin liquid into the oropharynx was observed and was subsequently aspirated.

Several compensatory approaches, including slower flow, changes in positioning, pacing, and increased liquid viscosity, did not result in meaningful improvement in swallow safety or physiologic stability. The study was therefore discontinued because of the persistent aspiration risk. Given the severity of the dysphagia and the inability to safely maintain adequate oral intake, the decision was made to proceed with gastrostomy tube placement. The infant subsequently became dependent on gastrostomy tube feeding for nutritional support at the age of three months.

Genetic workup

Whole-genome chromosomal microarray (CMA) analysis was performed on a peripheral blood sample using the CytoScan HD platform (Thermo Fisher Scientific, Waltham, Massachusetts, USA). The analysis demonstrated a mosaic gain of chromosome 9, reported as arr(9)x3[0.5], involving approximately 140.8 Mb of chromosome 9 material. The abnormality was detected in approximately 50% of the analyzed specimens and was classified as a pathogenic copy-number variant, consistent with T9M. No significant regions of homozygosity or evidence suggestive of uniparental isodisomy were identified.

The patient's clinical phenotype was consistent with several features previously reported in individuals with T9M. He demonstrated FGR, congenital heart disease, feeding difficulties requiring gastrostomy tube placement, diaphragmatic eventration, and subtle dysmorphic facial features, including micrognathia and a high-arched palate. The combination of growth restriction, congenital anomalies, feeding difficulties, and craniofacial features provides a clinically relevant correlation with the reported phenotypic spectrum of T9M.

Genetic counseling was done to discuss the clinical implications of mosaicism, limitations in predicting phenotype based on peripheral blood mosaic fraction, and future reproductive considerations.

Growth and development

The infant was born with severe FGR, with a birth weight of 1.349 kg (2 lb 15.6 oz), corresponding to a weight-for-age Z-score of -5.33 and below the 0.01st percentile on the WHO growth standards for boys aged 0-2 years. Despite nutritional supplementation with high-calorie formula, he remained significantly underweight during the early months of life.

Serial anthropometric measurements demonstrated progressive weight gain during infancy. Weight increased from 1.32 kg at four days of life to 1.48 kg at 16 days, 1.68 kg at 26 days, and 2.11 kg at 42 days. By seven months and two weeks of chronological age, weight had reached 6.75 kg, representing a cumulative gain of 5.43 kg (411.4%) from the earliest documented measurement. The average weight-gain velocity across this interval was 24.1 g/day, as reported by the electronic growth-chart comparison. At the final assessment, the chronological weight-for-age percentile was 2.01 (Z = -2.05), compared with the gestational-age-adjusted percentile of 6.26 (Z = -1.53). Although the infant demonstrated sustained absolute weight gain, his corrected weight-for-age remained below the 10th percentile, warranting continued monitoring of longitudinal growth and nutritional status (Figure *2*).

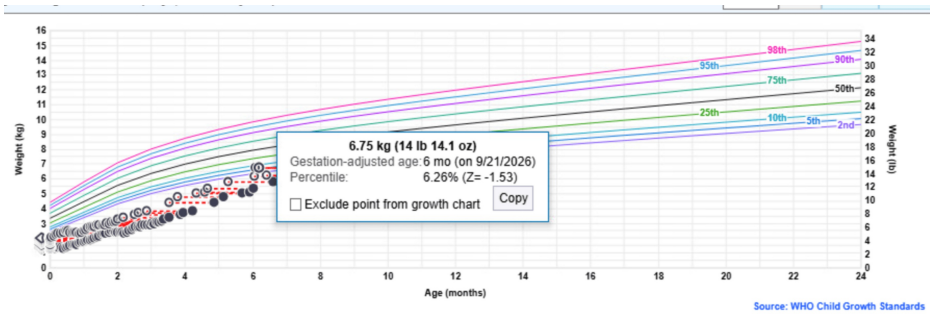


FIGURE 2: Weight trajectory from birth through seven months of age

Longitudinal weight trajectory adjusted for prematurity. WHO weight-for-age growth chart illustrating progressive weight gain in a male infant born at 34 weeks of gestation. Weight increased from 1.32 kg to 6.75 kg, representing a cumulative gain of 5.43 kg (411.4%). Solid circles represent chronological-age measurements, whereas hollow circles indicate gestational-age-adjusted measurements. At the latest assessment, the corrected weight-for-age percentile was 6.26 (Z-score -1.53), compared with the chronological-age percentile of 2.01 (Z-score -2.05), highlighting the importance of age correction when evaluating growth in preterm infants.

Longitudinal growth was also evaluated through serial measurement of recumbent length and head circumference using the WHO child growth standards, with adjustment for prematurity (Figures *3*, *4*).

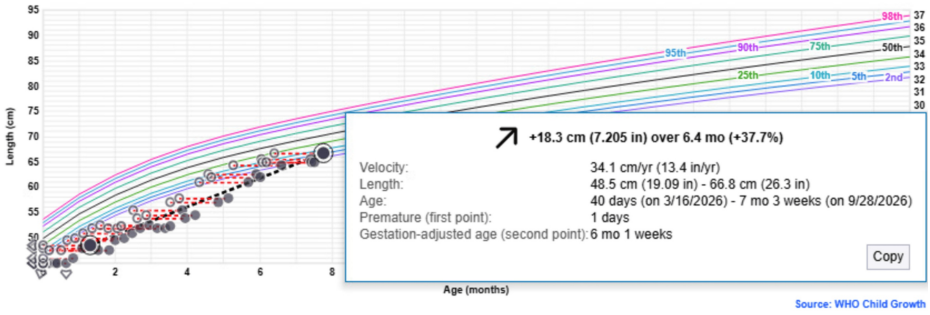


FIGURE 3: Length trajectory from birth through seven months of age

WHO length-for-age growth chart illustrating progressive linear growth in a male infant born at 34 weeks of gestation. Recumbent length increased as shown, representing a cumulative gain of 18.3 cm (37.7%), with an average growth velocity of 34.1 cm/year. At the latest assessment (seven months and three weeks chronological age), length-for-age was at the 5.84th percentile (Z = -1.57), compared with the 25.02nd percentile (Z = -0.67) at a corrected age of six months and one week. The chart illustrates longitudinal growth using both chronological and gestational-age-adjusted measurements.

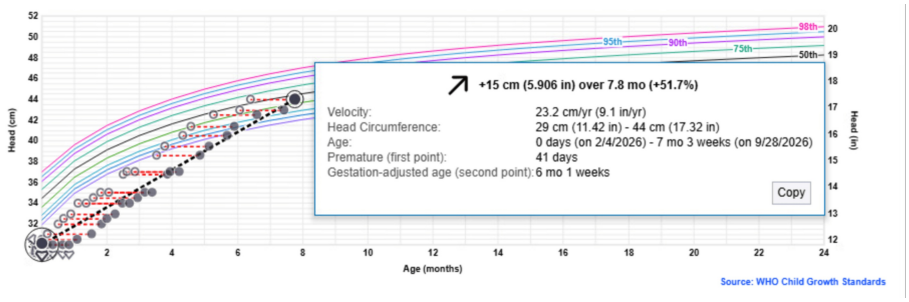


FIGURE 4: Head circumference trajectory from birth through seven months of age

Longitudinal head circumference growth adjusted for prematurity. WHO head circumference-for-age chart illustrating progressive cranial growth in a male infant born prematurely at approximately 34 weeks of gestation. Head circumference increased from 29 to 44 cm, representing a cumulative gain of 15 cm (51.7%) and an average growth velocity of 23.2 cm/year. At the latest assessment, head circumference was at the 37.55th percentile (Z = -0.32) by chronological age and the 62.97th percentile (Z = +0.33) after correction for prematurity, demonstrating the effect of gestational-age adjustment on growth interpretation.

Discussion

T9M is an uncommon chromosomal condition marked by the presence of an extra chromosome 9 in a fraction of cells. The clinical manifestations of this disorder are highly diverse, reflecting variations in the quantity and distribution of trisomic cells across different tissues. Over 100 cases of T9M have been documented in scientific literature; however, the infrequency of this disorder has hindered the establishment of formal diagnostic and treatment protocols [1]. Unlike complete trisomy 9, which is typically linked to severe congenital defects and elevated perinatal mortality rates, T9M can allow for extended survival, potentially into adulthood [1,2].

The clinical course of our patient demonstrates several features previously described in T9M, including severe FGR, cardiovascular abnormalities, feeding difficulties, and dysmorphic features. In addition, the patient had postnatally identified diaphragmatic eventration and mild peripheral pulmonary artery stenosis, which are less commonly reported findings and may add to the recognized cardiopulmonary phenotype.

Prenatal course

The prenatal course was notable for progressive severe FGR, abnormal umbilical artery Doppler findings, and transient borderline bilateral ventriculomegaly. FGR is a frequently reported prenatal manifestation of T9M, and small birth parameters are common among affected infants. However, long-term growth trajectories are highly variable [1,9].

In the study reported by Li et al., most patients had prenatal or perinatal complications, with growth,

respiratory, and feeding problems being particularly common [1]. The severe FGR observed in our patient, with an estimated fetal weight below the first percentile by 33 weeks, is therefore consistent with the previously described prenatal phenotype.

The transient ventriculomegaly observed at 28 weeks subsequently improved to 8-10 mm on serial examinations. Central nervous system abnormalities, including ventriculomegaly and other structural brain abnormalities, have been reported in T9M [1-3]. The absence of major structural brain abnormalities in our patient despite severe FGR illustrates the heterogeneous prenatal presentation of the condition.

Cardiovascular manifestations

Cardiovascular abnormalities are among the major organ-system manifestations reported in T9M. Previously described abnormalities include atrial and ventricular septal defects, patent ductus arteriosus, and other structural cardiac lesions [1,2,4-6,10].

Our patient's initial echocardiogram demonstrated a PFO with left-to-right shunting, moderate right ventricular dilation, low-normal right and left ventricular systolic function, mild LPA hypoplasia with peripheral stenosis, and a possible partial cleft of the posterior mitral valve leaflet.

The subsequent echocardiogram provided important longitudinal information. Right ventricular size and systolic function normalized, while left ventricular systolic function improved from an LVEF of 54% to 74%. The LPA also increased in diameter from 0.23 cm (Z-score -1.91) to 0.30 cm (Z-score -1.67), although mild stenosis persisted. In addition, the previously suspected mitral valve cleft was no longer visualized, and the mitral valve appeared structurally normal without regurgitation.

These findings demonstrate that some of the cardiovascular abnormalities identified during the neonatal period may be dynamic and influenced by the physiologic transition after birth, prematurity, and the infant's respiratory status. The initial right ventricular dilation and low-normal ventricular function may have reflected, at least in part, the cardiopulmonary effects of respiratory disease and altered pulmonary vascular resistance rather than fixed structural cardiac dysfunction. The subsequent normalization of right ventricular size and biventricular systolic function supports a dynamic component to the early cardiac findings.

Peripheral pulmonary artery stenosis is less frequently described than septal defects and other congenital cardiac abnormalities in T9M [1,4-6,10]. The persistent mild LPA hypoplasia and stenosis observed in our patient may therefore represent an additional cardiovascular feature associated with T9M. However, because of the limited number of reported cases, a definitive association cannot be established from a single case.

Diaphragmatic eventration and respiratory morbidity

A notable finding in our patient was left diaphragmatic eventration identified during the neonatal period. Diaphragmatic abnormalities have been reported in association with trisomy 9, although available reports are limited. Importantly, the comprehensive review by Li et al. identified diaphragmatic eventration as one of the less frequently reported characteristics found in individuals with T9M [1].

The occurrence of diaphragmatic eventration in our patient is particularly noteworthy as it manifested alongside severe FGR, respiratory distress, and various congenital anomalies. This condition can hinder diaphragmatic movement and diminish ventilatory efficiency, consequently escalating the effort required for breathing.

In our case, however, the respiratory complications were likely due to multiple factors. The infant was delivered at 34 weeks of gestation with significant FGR and subsequently developed respiratory distress syndrome, necessitating mechanical ventilation and surfactant treatment. The presence of diaphragmatic eventration may have further impaired respiratory mechanics. Additionally, the initial right ventricular dilation and peripheral pulmonary artery stenosis could have played a role in the abnormal adaptation of the cardiopulmonary system.

The prolonged respiratory course therefore likely resulted from the cumulative effects of prematurity, severe FGR, respiratory distress syndrome, diaphragmatic eventration, and cardiovascular abnormalities rather than from a single isolated pulmonary abnormality. The subsequent successful transition to room air demonstrates that these abnormalities did not result in persistent respiratory failure.

Feeding difficulties

Feeding difficulties are recognized manifestations of T9M and may be related to hypotonia, craniofacial abnormalities, impaired oral motor function, and developmental dysfunction [1-6]. In the cohort analyzed by Li et al., challenges related to respiration and feeding were identified as prevalent prenatal and perinatal issues [1].

Our patient exhibited a weak suck reflex and disrupted suck-swallow-breathe coordination, necessitating extended feeding sessions and intervention from speech-language pathology. The factors of prematurity and extended respiratory support likely played a role in exacerbating the feeding difficulties observed in this case. Early non-nutritive oral stimulation and multidisciplinary feeding support were associated with mild improvement in oral coordination. Ultimately, the infant needed G-tube placement to support his feeding.

Diagnostic considerations and mosaicism

Diagnosis of T9M can be challenging because the proportion of trisomic cells may vary substantially between tissues. Consequently, the percentage of trisomic cells detected in peripheral blood does not necessarily represent the mosaic fraction in other tissues or directly predict clinical severity [1,11,12].

In our patient, CMA analysis revealed a mosaic gain of chromosome 9 in about 50% of the examined cells, which is consistent with the diagnosis of mosaicism. The clinical observations corroborated this diagnosis and led to a comprehensive multidisciplinary assessment.

The extent of mosaicism identified in peripheral blood must therefore be interpreted with caution. Documented prenatal and postnatal cases have demonstrated discrepancies in the proportion of trisomic cells between tissues, highlighting the limitation of using peripheral blood mosaicism as a surrogate for overall tissue involvement [9,11,12]. Therefore, clinical phenotype and prognosis should not be predicted solely from the percentage of mosaic cells identified in peripheral blood.

When clinical suspicion remains high despite nondiagnostic peripheral blood testing, additional cytogenetic evaluation or analysis of another tissue may be considered. Genetic counseling is important to explain the variable phenotype, the limitations of mosaic fraction as a predictor of outcome, and the reproductive implications of the diagnosis.

Growth and development

Growth abnormalities are frequently described in children with T9M, although the pattern of growth after birth appears to vary considerably between individuals. In the review by Li et al., small birth parameters were common, and many of the children continued to have weight and length measurements below the 10th percentile during follow-up. At the same time, some children showed improvement in their growth over time, suggesting that severe growth restriction early in life does not necessarily predict the subsequent growth trajectory. The authors therefore emphasized the importance of longitudinal follow-up to better understand growth and other long-term outcomes in children with T9M [1].

The possibility of an underlying endocrine contribution to poor growth is less well established. There are currently no specific recommendations for routine growth hormone testing or growth hormone therapy in children with T9M. However, growth hormone deficiency has been reported in patients with trisomy 9p. In a small series of four patients with trisomy 9p and significant growth retardation, three were diagnosed with growth hormone deficiency and one with growth hormone neurosecretory dysfunction; the patients who received recombinant growth hormone showed a significant improvement in growth velocity [13]. Although these findings cannot be directly applied to T9M, they suggest that endocrine causes should remain part of the differential diagnosis when significant or persistent growth failure is present.

In our patient, severe FGR was followed by marked postnatal growth impairment despite nutritional supplementation, with weight remaining below the first percentile during the first several months of life. His weight subsequently improved after nutritional support and gastrostomy tube feeding, reaching approximately the sixth percentile by six months of corrected gestational age. This improvement suggests that his early growth failure was likely multifactorial, with contributions from his underlying chromosomal disorder, severe feeding dysfunction, congenital heart disease, and prolonged respiratory illness.

Nevertheless, given the limited information available regarding endocrine abnormalities in T9M, continued monitoring of weight, length, and head circumference is important. If poor linear growth or an inadequate height velocity persists despite adequate nutritional intake and stabilization of his other medical conditions, endocrine evaluation, including assessment of the growth hormone-IGF-1 axis, may be considered. Further longitudinal studies are needed to clarify whether growth hormone deficiency or other endocrine abnormalities occur more frequently in T9M and whether affected children may benefit from specific endocrine treatment.

Prognosis and longitudinal follow-up

Prognosis in T9M remains highly variable and difficult to predict. Earlier reports suggested that disease severity might correlate with the proportion of trisomic cells; however, the relationship between mosaic fraction and clinical severity is not straightforward because of tissue-specific mosaicism and other factors [1,2,4-8,10,14].

Arnold et al. emphasized the broad clinical manifestations among infants with trisomy 9 mosaicism,

including differences in congenital abnormalities and developmental outcomes, while Cantú et al. highlighted the importance of distinguishing nonmosaic vs T9M as the proportion of trisomic cells may vary between tissues [7,8]. These findings support careful prognostic counseling based on overall clinical phenotype rather than percentage of mosaicism alone.

The spectrum of neurodevelopmental outcomes is broad. Individuals with T9M have been reported with developmental outcomes ranging from significant intellectual and developmental disability to participation in educational settings alongside age-appropriate peers [1,4-6]. Long-term growth trajectories are also variable, making ongoing developmental and growth surveillance important [1,4].

Our patient's neonatal course was encouraging, with successful weaning from respiratory support, establishment of feeding, normalization of ventricular size and systolic function, and development appropriate for corrected gestational age at discharge. However, neonatal neurologic examination alone cannot predict long-term neurodevelopmental outcome in T9M. Continued developmental surveillance and early intervention are therefore important.

The improvement in cardiac function observed on follow-up echocardiography also highlights the importance of longitudinal assessment. While right ventricular dilation and ventricular dysfunction resolved, mild LPA hypoplasia/stenosis and the small interatrial communication persisted, supporting the need for continued cardiology follow-up.

Conclusions

This report illustrates the extensive and varied clinical spectrum of T9M, characterized in our patient by severe FGR, structural cardiac defects, diaphragmatic eventration, respiratory morbidity, and feeding difficulty. The clinical course demonstrates the multisystem nature of T9M and the interplay between prematurity and multisystem abnormalities in contributing to neonatal morbidity. The coexistence of diaphragmatic eventration and peripheral pulmonary artery stenosis is particularly noteworthy, highlighting the complexity of the cardiopulmonary findings observed in this patient and adding to the limited clinical literature describing the phenotypic variability of T9M. Importantly, prognosis cannot be reliably predicted from the degree of mosaicism in peripheral blood alone. Expanding case reporting and tracking longitudinal outcomes are essential steps toward better characterizing true genotype-phenotype relationships and establishing individualized management strategies.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Alaa Hamdan, Asante Boateng, Esra Fadelelmolla, Alexander Rodriguez

Acquisition, analysis, or interpretation of data: Alaa Hamdan, Asante Boateng, Esra Fadelelmolla, Alexander Rodriguez

Drafting of the manuscript: Alaa Hamdan, Asante Boateng, Esra Fadelelmolla, Alexander Rodriguez

Critical review of the manuscript for important intellectual content: Alaa Hamdan, Asante Boateng, Esra Fadelelmolla, Alexander Rodriguez

Supervision: Alaa Hamdan

Disclosures

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