Root, Emily, Kaitlyn Nunnelly, Clare Batty, Vanessa Brown, Scott Duncan, Edward Miller, and Tiffany Tonismae. 2025. "Case Report: Trisomy 22 with 80% Mosaicism." *North American Proceedings in Gynecology & Obstetrics* 4 (1). https://doi.org/10.54053/001c.140821.

Case Report

Case Report: Trisomy 22 with 80% Mosaicism

Emily Root, MD[1], Kaitlyn Nunnelly, MD[2], Clare Batty, MD[3], Vanessa Brown, RDMS[4], Scott Duncan, MD, MHA, FAAP[3], Edward Miller, MD[5], Tiffany Tonismae, MD[5]

[1] Obstetrics, Gynecology and Women's Health, University of Louisville Hospital, [2] Obstetrics, Gynecology and Women's Health, University of Louisville, [3] Neonatal Medicine, University of Louisville, [4] Maternal Fetal Medicine, University of Louisville, [5] Maternal Fetal Medicine, University of Louisville Hospital

Keywords: Trisomy 22, pregnancy, aneuploidy, ultrasound

https://doi.org/10.54053/001c.140821

North American Proceedings in Gynecology & Obstetrics

Vol. 4, Issue 1, 2025

Background

Trisomy 22 is a rare aneuploidy with only a handful of case reports published in the literature. There is a paucity of cases that report neonatal outcomes and even fewer reports of ultrasound findings. The case reports that describe ultrasound findings are few and most are limited to cases of fetal demise or termination. In this case report and review of the literature we describe our ultrasound, physical exam and autopsy findings of a live born 47,XY +22 infant.

Case Presentation

A 41-year-old Gravida 3 Para 2002 presented for a routine anatomy scan at 20 weeks. Several anomalies were noted including an absent left kidney, right kidney with possible double collecting system, echogenic bowel, possible single atrium, abnormal 3 vessel view, abnormal left ventricle outflow tract, micrognathia, short nasal bone, hypertelorism, thickened nuchal fold, dilated 4th ventricle, single umbilical artery, and overall growth less than the 3rd percentile. Given these findings, an amniocentesis was performed. An abnormal male karyotype with Trisomy 22 (47, XY +22) was identified. A microarray was performed which detected mosaic gain, around 80%, of all markers on chromosome 22. Amniotic fluid alpha-fetoprotein was analyzed and found to be within normal range. Multiple fetal echocardiogram studies were performed which identified a complex congenital heart defect. The defects included a double outflow from the left ventricle with a large ventricular septal defect and a possible mispositioning of the great arteries, but no alterations to flow throughout the ventricles or the great vessels.

At 37 weeks and 0 days, the infant was delivered by a modified Ex-utero Intrapartum Treatment (EXIT) Procedure for palliative indications. The infant required emergent tracheostomy placement and positive pressure ventilation. His birth weight was 1730g (<1%ile) and APGARs were 1,2,2,2,2,5. On physical exam the neonate was noted to have microcephaly, micrognathia with retrognathia, cleft palate, absent left eye, low set ears with ear crease and pit, wide-set eyes, decreased breath sounds bilaterally, a holo-systolic III/VI murmur, pulses were strong in all extremities, no cry or response to tactile or noxious stimuli, hypertonicity in all extremities, there were no integumentary, abdominal or genitourinary anomalies. On abdominal ultrasound, there was no definite normal renal tissue identified, the right adrenal gland appeared normal, but the left was not visualized. The liver, gallbladder, pancreas, spleen, aorta, and inferior vena cava appeared normal. An initial bedside echocardiogram showed a large coronary sinus, 2 separate atrioventricular valves, severely depressed ejection fraction (15-20%), there was a double outlet right ventricle, a small anterior pericardial effusion, and moderate tricuspid regurgitation. Bilateral chest tubes were placed due to bilateral pneumothoraxes and a repeat echocardiogram was performed, which demonstrated the following additional findings: a hypoplastic ascending, and transverse aortic arch with possible interruption, as well as a large patent ductus arteriosus with right to left shunt. Ultimately on day of life 1 the parents elected to withdraw care.

An autopsy was performed demonstrating: microcephaly, cleft palate, micrognathia with retrognathia, left anopthalmos with absent ophthalmic nerve, absent corpus callosum,

low set ears, short bilateral radii and femurs, double outlet right ventricle with left ventricular hypoplasia and ventricular septal defect, a minuscule right kidney and an absent left kidney, Potter sequence with pulmonary hypoplasia and alveolar wall thickening. The placenta had diffuse distal villous dysmaturity, the umbilical cord had a single umbilical artery, a recent retroplacental hematoma was noted and <5% of the placenta had remote infarcts.

Conclusion

Our case describes ultrasound, physical exam and autopsy findings seen in a patient with a high level of mosaicism in Trisomy 22. With continued advanced ultrasound technique and genetic capabilities, it is critical that these cases are described so providers can better counsel their patients.

CASE

A 41-year-old Gravida 3 Para 2002 presented for a routine anatomical survey at 20 weeks. Several anomalies were noted: an absent cavum septum pellucidum (Figure 1A), micrognathia (Figure 1B), abnormal pericallosal artery (Figure 1C), hypertelorism (Figure 1D), nuchal fold thickening (Figure 1E), a complex cardiac defect (Figure 1F and 1G), and an absent left kidney (Figure 1H), Additional findings are listed in Table 1A. Amniocentesis revealed an abnormal male karyotype: Trisomy 22 (47, XY +22) (T22) (Table 1B). Microarray detected mosaic gain, around 80%, of all markers on chromosome 22 (Table 1B). Amniotic fluid alpha-fetoprotein was analyzed and found to be within normal range. Fetal echocardiogram identified a double outflow from the left ventricle, a large ventricular septal defect, and a possible mispositioning of the great arteries without alterations to flow throughout the ventricles or the great vessels.

At 37 weeks and 0 days, the infant was delivered by a modified Ex-utero Intrapartum Treatment Procedure for palliative indications. Multiple intubation attempts were made and ultimately, the infant required emergent tracheostomy placement and positive pressure ventilation. His birth weight was 1730g (<1st percentile), and APGARs were 1,2,2,2,2,5. On physical exam, the neonate had multiple anomalies (Table 1A). On auscultation of the chest, decreased breath sounds were noted bilaterally, a holo-systolic III/VI murmur was heard, pulses were strong in all extremities, no cry or response to tactile or noxious stimuli was elicited, and hypertonicity was noted in all extremities. On exam of the face and head, the following findings were noted: microcephaly, micrognathia with retrognathia, cleft palate, absent left eye, low-set ears with ear crease and pit, and wide-set eyes. No integumentary, abdominal, or genitourinary anomalies were noted.

An initial bedside echocardiogram showed a large coronary sinus, two separate atrioventricular valves, a severely depressed ejection fraction (15-20%), a double outlet right ventricle, a small pericardial effusion, and moderate tricuspid regurgitation. Bilateral chest tubes were placed due to bilateral pneumothoraxes, and a repeat echocardiogram was performed, which demonstrated the following additional findings: a hypoplastic ascending, and transverse aortic arch with possible interruption, as well as a large patent ductus arteriosus with right to left shunt. On abdominal ultrasound, no definite renal tissue was identified. The right adrenal gland appeared normal, but the left was not visualized. The liver, gallbladder, pancreas, spleen, aorta, and inferior vena cava appeared normal. On day of life one, the parents elected to withdraw care.

The placenta had diffuse distal villous dysmaturity, the umbilical cord had a single umbilical artery, a recent retroplacental hematoma was noted and <5% of the placenta had remote infarcts.

Autopsy identified microcephaly, cleft palate, micrognathia with retrognathia, left anopthalmos with absent ophthalmic nerve, absent corpus callosum, low set ears, short bilateral radii and femurs, double outlet right ventricle with left ventricular hypoplasia and ventricular septal defect, a minuscule right kidney and an absent left kidney, Potter sequence with pulmonary hypoplasia and alveolar wall thickening.

DISCUSSION

T22 is traditionally a lethal anomaly that results in in-utero demise. Due to the mosaic nature of this case, the fetus reached term gestational age and was able to be resuscitated. A recent systematic review of the literature has identified 25 postnatal and 18 prenatal cases reported in the literature (Trevisan, Meroni, Leoni, et al. 2024). There are few reports of liveborn infants with this condition, and fewer that describe liveborn infants with a high level of mosaicism (the highest reported in a liveborn neonate was 35%) (Trevisan, Meroni, Leoni, et al. 2024; Abdelgadir, Nowaczyk, and Li 2013; Wang et al. 2007; Basaran, Berkil, Ay, et al. 2001; Stiefmeier et al. 2004; Chen, Huang, Chern, et al. 2019). Our case report describes a liveborn infant with a high level of mosaicism (80%) and is the first to demonstrate anopthalmos with an absent ophthalmic nerve, absent corpus callosum, and renal agenesis.

AUTHORSHIP CONTRIBUTOR STATEMENT

ER: Direct patient care, literature review, manuscript writing; KN: literature review, direct patient care, CB: manuscript writing direct patient care; VB: direct patient care, figure development, manuscript editing; SD: direct patient care, manuscript editing, provided expert clinical guidance;

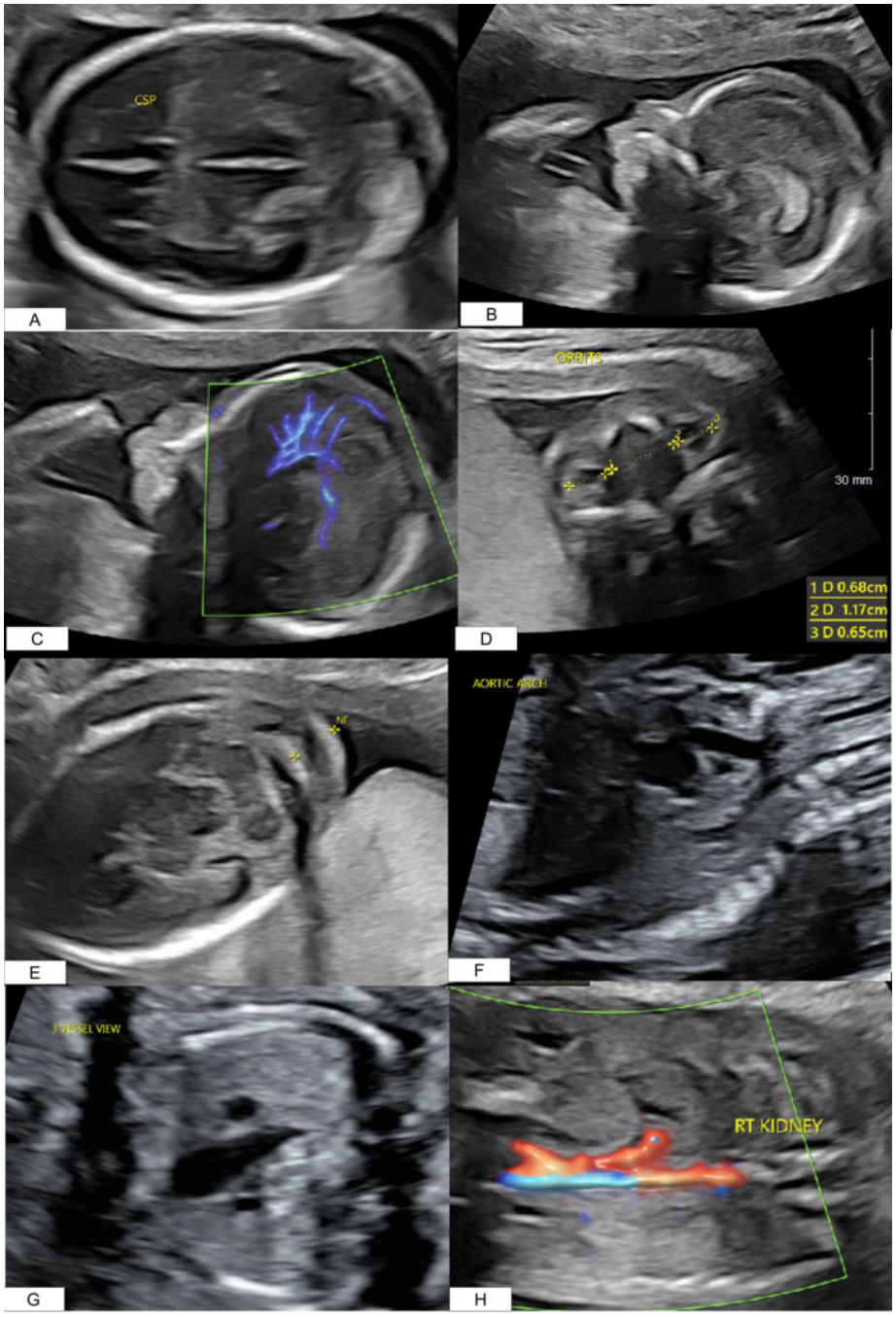

Figure 1. Ultrasound images from anatomy ultrasound at 20 weeks.

1A. Absent cavum septum pellucidum (CSP). 1B. Micrognathia. 1C. Abnormal pericallosal artery. 1D. Hypertelorism, interocular distance 1.17cm. 1E. Nuchal fold thickening measuring 8.04 mm. 1F. Abnormal Aortic Arch. 1G. Abnormal three-vessel view demonstrating bilateral superior vena cava, an enlarged pulmonary artery, and a possible right-sided aorta. 1H. Absent left kidney, blood flow is seen to the right kidney on Doppler imaging.

EM: direct patient care, manuscript editing, provided expert clinical guidance; TT: direct patient care, provided expert clinical guidance, reviewed final manuscript

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest in the conduct and reporting of this study.

FUNDING STATEMENT

No funding source was used in study design, analysis of data, interpretation of results, or writing of the report

The ethics approval statement is not applicable. Patient provided consent for publication of this case report regarding their

Data availability statement is not applicable.

Submitted: March 02, 2025 EDT. Accepted: May 26, 2025 EDT.
Published: June 11, 2025 EDT.

Table 1A. Clinical data

Case	Parental details			Gestation at diagnosis	Phenotypes (HPO terms)	Obstetric History	Family history	Outcome
1	Maternal	age	41	21 weeks, 1 day	Unilateral renal agenesis (HP: 0008678) Echogenic bowel (HP:0010943) Ventricular septal defect (HP: 0001629) Double outlet left ventricle (HP: 001581) Micrognathia (HP: 0000347) Hypoplastic nasal bone (HP: 0025707) Hypertelorism (HP:0000316) Thickened nuchal skin fold (HP:0000474) Dilated Fourth ventricle (HP: 0002198) Single umbilical artery (HP:0001195) Intrauterine growth retardation (HP:0001511)	G3P2002	Noncontributory	Term birth via modified EXIT procedure. Infant required emergent tracheostomy placement. Care was withdrawn on day of life 1.
		ethnicity	African American					
	Paternal	age	47					
		ethnicity	African American					

Table 1B. Genetic findings

Procedure (Gest Age)	Direct/ culture?	Performed test	Secondary confirma-tory test	Gene (name; REFSEQ)	Known disease (OMIM)	Vari-ant	ACMG classify-cation	Criteria applied	Inheritance & zygosity	Interpret-ation
Amniocen-tesis (21 weeks)	Direct	Microarray	Karyotype	NA	NA	NA	Patho-genic	NA	De novo	Patho-genic

REFERENCES

Abdelgadir, Dalal, Małgorzata J. M. Nowaczyk, and Chumei Li. 2013. "Trisomy 22 Mosaicism and Normal Developmental Outcome: Report of Two Patients and Review of the Literature" 161 (5): 1126–31. https://doi.org/10.1002/ajmg.a.35812.

Basaran, N., H. Berkil, N. Ay, et al. 2001. "A Rare Case: Mosaic Trisomy 22." *Annales de Génétique* 44 (4): 183–86. https://doi.org/10.1016/s0003-3995(01)01095-4.

Chen, C. P., M. C. Huang, S. R. Chern, et al. 2019. "Mosaic Trisomy 22 at Amniocentesis: Prenatal Diagnosis and Literature Review." *Taiwanese Journal of Obstetrics and Gynecology* 58 (5): 692–97. https://doi.org/10.1016/j.tjog.2019.07.020.

Stiefmeier, T., M. Parker, J.B.C. Tan, D.P. Duckett, and G. Woodruff. 2004. "Ocular Manifestations of Mosaic Trisomy 22: A Case Report and Review of the Literature." *Ophthalmic Genetics* 25 (1): 53–56. https://doi.org/10.1076/opge.25.1.53.29004.

Trevisan, V., A. Meroni, C. Leoni, et al. 2024. "Trisomy 22 Mosaicism from Prenatal to Postnatal Findings: A Case Series and Systematic Review of the Literature." *Genes* 15 (3): 346. https://doi.org/10.3390/genes15030346.

Wang, J. C., L. Dang, T. K. Mondal, and A. Khan. 2007. "Prenatally Diagnosed Mosaic Trisomy 22 in a Fetus with Left Ventricular Non-Compaction Cardiomyopathy." *American Journal of Medical Genetics Part A* 143A (22): 2744–46. https://doi.org/10.1002/ajmg.a.32004.