CLINICAL CASE REPORTS

Chromosomal discordance in monochorionic twins: clinical insights from a case series

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ABSTRACT

Monochorionic twin pregnancies are traditionally considered genetically identical due to their monozygotic origin. However, emerging evidence demonstrates that postzygotic chromosomal divergence may lead to significant karyotypic and phenotypic discordance.

We report two cases of monochorionic diamniotic twin pregnancies with discordant chromosomal abnormalities affecting only one fetus. In both cases the co-twin maintained a structurally and genetically normal profile. In the first case, one fetus presented mosaic monosomy X with severe hydrops, while the co-twin was structurally and genetically normal. Selective reduction was performed, followed by intrauterine demise of the co-twin. In the second case, one fetus had trisomy 13 with multiple structural anomalies, while the co-twin had a normal phenotype and favorable outcome after expectant management.

These two cases illustrate that chromosomal discordance may occur in monochorionic twin pregnancies and highlight the diagnostic challenges associated with discordant findings.

Keywords: karyotype; monochorionic twins; mosaicism; prenatal diagnosis; trisomy 13; turner syndrome; twin pregnancy

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INTRODUCTION

Monochorionic twin pregnancies, resulting from the division of a single zygote, are typically associated with genetic equivalence between the fetuses. Nevertheless, an increasing number of reports have documented discordant structural anomalies and chromosomal abnormalities in these pregnancies, challenging the assumption of genetically identical twins. Heterokaryotypia—the presence of distinct karyotypes in monozygotic twins—is a rare but clinically significant phenomenon that may result from postzygotic chromosomal events, including mitotic errors, confined placental mosaicism, or early embryonic aneuploidy rescue. These events may result in phenotypic discordance, complicating prenatal diagnosis and counseling.

In this study, we present two cases of monochorionic twin pregnancies with discordant ultrasound findings and karyotypes, highlighting the diagnostic challenges and the implications for clinical management. Through the analysis of clinical, cytogenetic, and imaging findings, we aim to discuss potential underlying mechanisms and contribute to the growing body of literature that redefines the genetic assumptions underlying monochorionic twinning.

METHODS

This study describes a retrospective case series of monochorionic diamniotic twin pregnancies with discordant chromosomal abnormalities managed at one tertiary center in Portugal between 2020 and 2025.

Cases were identified through review of fetal medicine and prenatal diagnosis records. Inclusion criteria were: confirmed monochorionic diamniotic twin pregnancy and discordant fetal chromosomal findings.

All cases identified during the study period meeting the inclusion criteria were included.

No additional similar cases were identified during the study period.

Clinical data, imaging findings, genetic results, and pregnancy outcomes were obtained from medical records meeting the inclusion criteria.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Case 1

A 36-year-old Caucasian woman, gravida 2, para 1, with no relevant medical history and a spontaneous monochorionic diamniotic twin pregnancy, was referred for routine first-trimester screening. At 13 weeks and three days of gestation, ultrasound revealed one twin with a markedly increased nuchal translucency (12.34 mm), while the co-twin appeared structurally normal with no evidence of first- trimester ultrasonographic markers of aneuploidy.

Combined first-trimester screening showed a high risk for trisomies 13 (>1:4), 18 (1:20), and 21 (1:47). A follow-up scan at 16 weeks confirmed progression to hydrops fetalis in the affected twin (**Figure 1**), with bilateral cervical cysts, generalized subcutaneous edema, and ascites. The co-twin continued to show normal growth and anatomy. Early fetal echocardiography performed at 14^{+4} weeks was normal for both. Fetal sex was suspected at this stage, with the affected twin presumed to be female and the healthy co-twin male (**Figure 2**).

The amniocentesis performed at 16^{+3} weeks revealed mosaic monosomy X (45,X/46,XY) in the hydropic twin having a higher proportion of 45,X cells (78.75%) compared to the 46,XY cells (21.25%). This result was confirmed by karyotype. The co-twin had a normal chromosomal microarray. Zygosity testing showed that both fetuses shared identical alleles at all 19 tested polymorphic markers, confirming monozygosity.

At 17^{+4} weeks, the affected twin continued to show signs of hydrops (**Figure 3**), while the other showed normal male phenotype and development.

The couple received multidisciplinary counseling, including detailed discussion of the poor prognosis of the affected fetus, potential risks to the co-twin related to shared placental circulation, including intrauterine demise and neurological injury, and available management options, including expectant management and selective reduction. The uncertainty and limitations associated with each approach were also addressed.

Given the poor prognosis, selective fetal reduction of the hydropic twin was performed at 19 weeks of gestation at a specialized fetal medicine center. Intrauterine demise of the structurally normal co-twin was diagnosed two days later.

The patient was admitted for labor induction at 20 weeks and delivered both fetuses vaginally.

Fetopathological evaluation revealed marked phenotypic differences between the monochorionic monozygotic twins. The affected fetus presented with severe hydrops, a large cystic hygroma, generalized edema, and multiple congenital anomalies, including renal and cardiovascular abnormalities, consistent with a classic Turner phenotype, later confirmed cytogenetically. Additional findings included craniofacial dysmorphism and limb abnormalities. The co-twin showed no relevant structural anomalies. Biometry and organ weight ratios were appropriate for gestational age (19+2 weeks). Histopathology demonstrated cortical neuronal necrosis and edema, with no infectious or metabolic pathology, supporting acute hypoxic-ischemic injury. A hemodynamic mechanism related to intertwin transfusion cannot be excluded; however, diagnostic criteria for twin anemia–polycythemia sequence were not fulfilled.

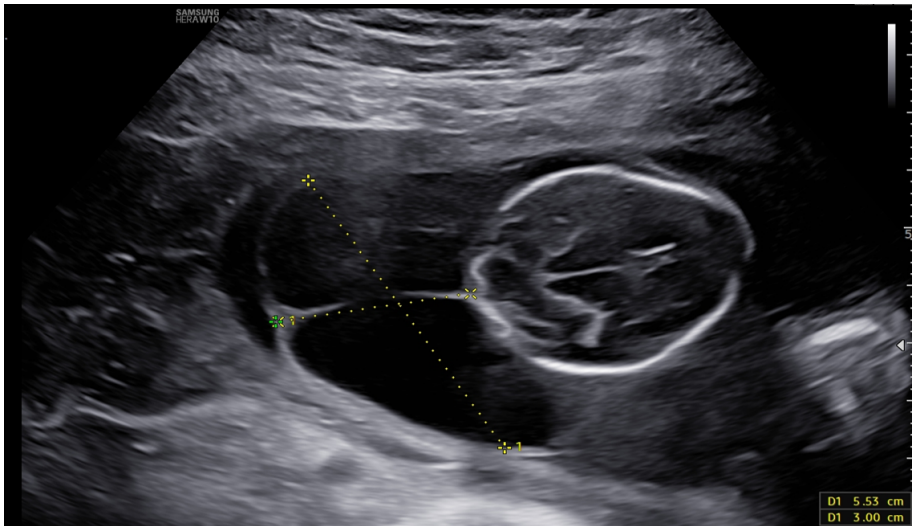

Figure 1 - Markedly enlarged nuchal translucency of the 45,X fetus at 16 weeks.

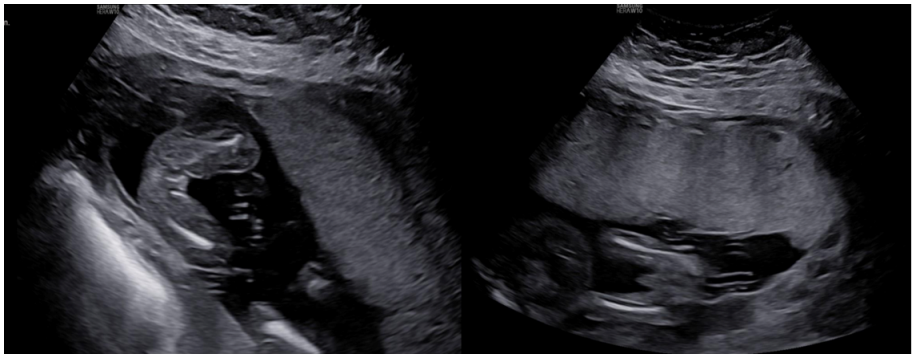

Figure 2 - Ultrasound images showing suspected fetal sex determination at 16 weeks: affected twin with female genital phenotype (left) and the healthy co-twin with male genital phenotype (right).

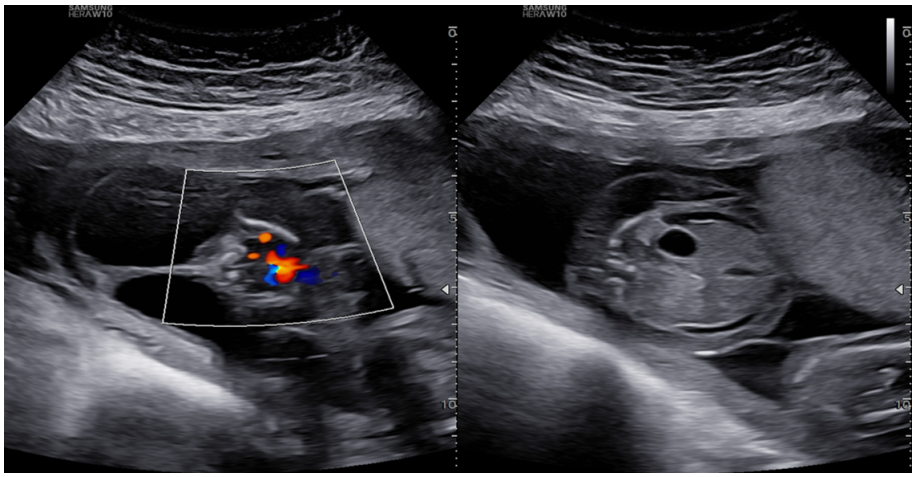

Figure 3 - Fetal thorax with color Doppler of the heart showing marked extension of the nuchal edema (left). Fetal abdomen demonstrating the stomach in normal position with associated ascites (right).

Case 2

A 32-year-old gravida 3, para 1 woman with no relevant medical history presented with a spontaneous monochorionic diamniotic twin pregnancy. First-trimester ultrasound at 12^{+2} weeks revealed discordant findings between the fetuses. One fetus showed increased nuchal translucency (6.4 mm) (**Figure 4**), absent nasal bone, and a non-visualized gastric chamber, while the co-twin appeared morphologically normal. Combined first-trimester screening indicated a high risk for chromosomal abnormalities, particularly trisomies 21 (1:9), 18 (1:10), and 13 (1:66), with 0.65 MoM of β-hCG and 1.03 MoM of PAPP-A.

An amniocentesis was performed at 16^{+1} weeks of gestation and the genetic testing confirmed that the affected twin had trisomy 13, while the co-twin had a 46,XX karyotype with 2.3% of the analyzed cells having a third signal for the chromosome 13, indicating marked karyotype discordance associated with a discordant phenotype in a monochorionic gestation. The detection of a low-level trisomy 13 signal raised the possibility of low-level mosaicism or technical artifact.

Additional analysis using fluorescence in situ hybridization (FISH) did not confirm trisomy 13 in the co-twin, supporting the interpretation of a likely technical artifact or true low-level fetal mosaicism. Although confined placental mosaicism cannot be completely excluded, it is less likely in this context, as the genetic material was obtained via amniocentesis, which predominantly reflects fetal cell lineage. Genetic counseling was provided to the couple, including discussion of the uncertain significance of this finding, potential risks to the co-twin related to shared placental circulation, and available management options, including expectant management and selective reduction, as well as the uncertainty associated with each approach. The couple opted not to pursue selective termination of pregnancy.

Subsequent imaging confirmed severe anomalies in the affected fetus, including cystic dilatation of the fourth ventricle, cerebellar hypoplasia, bilateral cleft lip and palate, retrognathia (**Figure 5**), echogenic and enlarged kidneys, and a ventricular septal defect.

Subsequent ultrasonographic evaluations demonstrated a gradual deceleration in growth of the fetus with trisomy 13, culminating in a diagnosis of fetal growth restriction.

Doppler studies during surveillance revealed progressively abnormal umbilical and ductus venosus flow patterns in the fetus with trisomy 13, although diastolic flow was mostly preserved. The pregnancy was followed with serial ultrasound and Doppler assessments initially on a weekly basis, and later, daily, given the worsening of the umbilical artery Doppler study. The co-twin remained morphologically and hemodynamically normal throughout follow-up, with no signs of twin-to-twin transfusion syndrome or twin anemia-polycythemia sequence.

After further counseling on possible outcomes—including the risk of intrauterine demise of the affected fetus and potential complications for the healthy fetus — the patient chose expectant management and not pursuing the option of selective termination of the affected fetus.

At 33 weeks of gestation, due to progressive deterioration in ductus venosus flow (IP > 95th percentile), intermittent end-diastolic flow in the umbilical artery, and concern for impending fetal decompensation, a cesarean section was performed.

Two female neonates were delivered. The twin with trisomy 13 weighed 1815 g, had Apgar scores of 5/6/6, presented visible dysmorphic features and passed away shortly after birth. An autopsy of the affected newborn was not performed because parental consent was not granted. The co-twin, weighing 1795 g with Apgar scores of 8/8/8, had a normal neonatal course and was discharged in good condition.

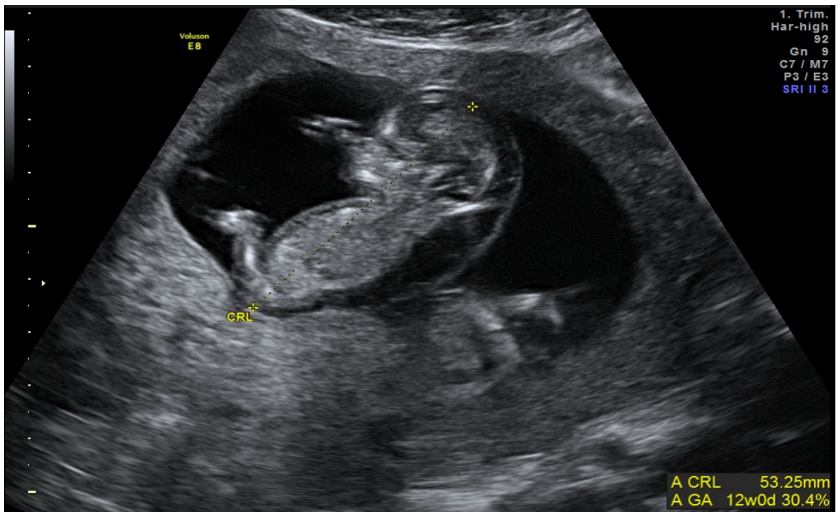

Figure 4 - Ultrasound image of the affected twin showing crown–rump length (CRL) measurement highlighting the markedly increased nuchal translucency at 12 weeks.

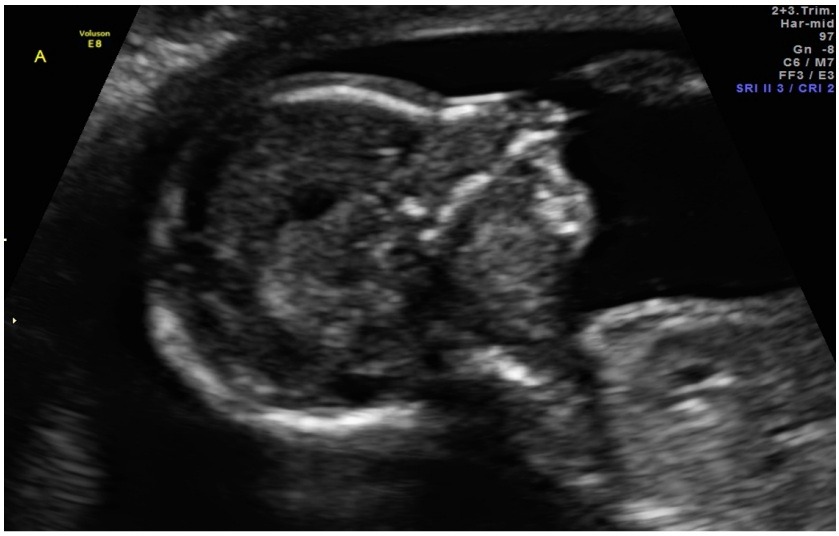

Figure 5 - Ultrasound evaluation of the affected fetus's face profile at 18 weeks of gestation, evidencing an apparent retrognathia.

DISCUSSION

These two cases illustrate the diagnostic and clinical challenges associated with karyotypic discordance in monochorionic twin pregnancies. Although monochorionic twins are generally assumed to be genetically identical due to their monozygotic origin, increasing evidence demonstrates that discordant chromosomal and phenotypic findings may occur, even in the presence of confirmed monozygosity. Similar cases have been described in the literature, highlighting that monochorionicity does not preclude genetic divergence and supporting the importance of genetic evaluation when discordant anomalies are identified.[1–4]

Several biological mechanisms have been proposed to explain postzygotic chromosomal divergence in monochorionic monozygotic twins. These include early mitotic errors after fertilization, such as mitotic nondisjunction or anaphase lag, occurring before or around the time of embryonic splitting, potentially resulting in the formation of distinct embryonic cell lineages.[5,6] Additional suggested mechanisms such as trisomy rescue or monosomy rescue are also considered, whereby an initially aneuploid conceptus undergoes partial correction in one embryonic lineage, leading to discordant karyotypes between twins.[7,8] Furthermore, unequal allocation of mosaic cell lines during early embryogenesis may contribute to phenotypic variability, while confined placental mosaicism may account for discrepancies between placental and fetal cytogenetic findings.[9,10,11] However, these mechanisms remain hypothetical and cannot be confirmed in the present cases.

In the first case, mosaic Turner syndrome was identified in only one fetus, while the co-twin had a normal chromosomal profile despite confirmed monozygosity. This finding is consistent with previously reported cases of heterokaryotypic monochorionic twins and may reflect a postzygotic event affecting a single embryonic lineage.[5] The subsequent intrauterine demise of the co-twin occurred shortly after selective reduction; however, a causal relationship cannot be established.

The second case involved trisomy 13 affecting a single fetus, while the co-twin remained phenotypically normal. Similar cases of monochorionic twins discordant for trisomy 13 and other aneuploidies have been reported, supporting the concept of postzygotic divergence.[2–4,12] In this case, the detection of a very low-level trisomy 13 signal (2.3%) in the co-twin raised several possible interpretations, including technical artifact or true low-level fetal mosaicism; confined placental mosaicism is less likely in this context given that the genetic material was obtained via amniocentesis. Additional analysis using fluorescence in situ hybridization did not confirm trisomy 13 in the co-twin, supporting a non-pathological interpretation of the finding, particularly in the absence of structural anomalies. Even if low-level fetal mosaicism were present, its clinical significance would likely be limited. The phenotypic expression of mosaic trisomy depends on both the proportion and tissue distribution of abnormal cells, and very low-level mosaicism has been reported in association with normal phenotypic outcomes.[6,9] Nevertheless, the possibility of tissue-specific mosaicism cannot be completely excluded, and the interpretation of such findings should be approached with caution, particularly in prenatal settings.

Management of monochorionic pregnancies with discordant anomalies remains complex and must be individualized. In previously reported cases, approaches have ranged from selective fetal reduction to expectant management, with variable outcomes.[3,4,12,13] In the present cases, different management strategies were adopted, reflecting differences in clinical presentation and parental

preferences. Genetic counseling was provided in both cases, addressing diagnostic uncertainty, potential risks for the co-twin, and available management options. These observations illustrate the challenges inherent to clinical decision-making in such scenarios but do not allow conclusions regarding optimal management strategies.

Collectively, these cases support the concept that chromosomal and phenotypic discordance may occur in monochorionic twin pregnancies and reinforce the importance of maintaining a high index of suspicion when discordant anomalies are detected. Additional reports of similar cases are needed to enhance understanding of the biological processes involved and to clarify their clinical significance.

CONCLUSIONS

This case series highlights that chromosomal and phenotypic discordance may occur in monochorionic twin pregnancies, despite their presumed monozygotic origin, as previously described in the literature.[1–4] These findings reinforce that monochorionicity does not necessarily imply genetic identity and that postzygotic chromosomal divergence may underlie discordant presentations.

In this context, the presence of discordant ultrasound findings should prompt consideration of genetic evaluation, as supported by prior reports of heterokaryotypic monochorionic twins.[1,2,12] The interpretation of discordant or low-level genetic findings may be challenging, particularly in the setting of potential mosaicism or confined placental mosaicism, requiring careful correlation with phenotypic assessment and available diagnostic techniques.[6,9,10]

Further accumulation of similar cases is necessary to improve understanding of the biological mechanisms involved and to better define their clinical implications.

AUTHORSHIP

Beatriz Sousa Ferreira - Conceptualization; Investigation; Project administration; Visualization; Writing – original draft; Writing – review & editing

Márcia Marinho - Conceptualization; Visualization; Validation; Writing - review & editing; Supervision

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Cristina Godinho - Validation; Project administration; Supervision

Conceição Brito - Validation; Supervision

REFERENCES

1. Rock KR, Millard S, Seravalli V, McShane C, Kearney J, Seitz E, Baschat AA, Miller JL. Discordant anomalies and karyotype in a monochorionic twin pregnancy: a call for comprehensive genetic evaluation. Ultrasound Obstet Gynecol. 2017 Apr;49(4):544-545. doi: 10.1002/uog.15985. Epub 2017 Feb 16. PMID: 27255445.
2. Sepulveda W, Wong AE, Ocaranza M. Heterokaryotypic pregnancy: monozygotic monochorionic twins discordant for trisomy 13. Fetal Diagn Ther. 2010;28(2):109-13. doi: 10.1159/000309175. Epub 2010 May 21. PMID: 20501972.
3. Ramsey KW, Slavin TP, Graham G, Hirata GI, Balaraman V, Seaver LH. Monozygotic twins discordant for trisomy 13. J Perinatol. 2012 Apr;32(4):306-8. doi: 10.1038/jp.2011.123. PMID: 22460600.
4. Chang YL, Yi WP, Chao AS, Chen KJ, Cheng PJ, Wang TH, Chang SD. Monozygotic twins discordant for trisomy 21: Discussion of etiological events involved. Taiwan J Obstet Gynecol. 2017 Oct;56(5):681-685. doi: 10.1016/j.tjog.2017.08.019. PMID: 29037558.
5. Machin GA. Some causes of genotypic and phenotypic discordance in monozygotic twin pairs. Am J Med Genet. 1996 Jan 22;61(3):216-28. doi: 10.1002/(SICI)1096-8628(19960122)61:3<216::AID-AJMG5>3.0.CO;2-S. PMID: 8741866.
6. Levy B, Hoffmann ER, McCoy RC, Grati FR. Chromosomal mosaicism: Origins and clinical implications in preimplantation and prenatal diagnosis. Prenat Diagn. 2021 Apr;41(5):631-641. doi: 10.1002/pd.5931. Epub 2021 Mar 22. PMID: 33720449; PMCID: PMC8176867.
7. Robinson WP. Mechanisms leading to uniparental disomy and their clinical consequences. Bioessays. 2000 May;22(5):452-9. doi: 10.1002/(SICI)1521-1878(200005)22:5<452::AID-BIES7>3.0.CO;2-K. PMID: 10797485.
8. Eggermann T, Perez de Nanclares G, Maher ER, Temple IK, Tümer Z, Monk D, Mackay DJ, Grønskov K, Riccio A, Linglart A, Netchine I. Imprinting disorders: a group of congenital disorders with overlapping patterns of molecular changes affecting imprinted loci. Clin Epigenetics. 2015 Nov 14;7:123. doi: 10.1186/s13148-015-0143-8. Erratum in: Clin Epigenetics. 2016 Mar 07;8:27. doi: 10.1186/s13148-016-0194-5. PMID: 26583054; PMCID: PMC4650860.
9. Grati FR. Chromosomal Mosaicism in Human Feto-Placental Development: Implications for Prenatal Diagnosis. J Clin Med. 2014 Jul 24;3(3):809-37. doi: 10.3390/jcm3030809. PMID: 26237479; PMCID: PMC4449651.
10. Kalousek DK. Confined placental mosaicism and intrauterine development. Pediatr Pathol. 1990;10(1-2):69-77. doi: 10.3109/15513819009067097. PMID: 2315234.
11. Wu X, Huang B, Xie X, Cai M, Chen Y, Liang B, Shen Q, Guo D, Lin N, Su L, Xu L. Genetic evaluation for twin pregnancies using karyotyping and single nucleotide polymorphism array analysis. Gene. 2024 Feb 15;895:148005. doi: 10.1016/j.gene.2023.148005. Epub 2023 Nov 15. PMID:

37977315.
12. Labadini C, Lohmann L, Ville Y, Quarello E. Monochorionic twins with discordant trisomy 21, another case to remind this uncommon condition and how to deal with. J Gynecol Obstet Hum Reprod. 2023 Sep;52(7):102620. doi: 10.1016/j.jogoh.2023.102620. Epub 2023 Jun 8. PMID: 37295772.
13. Shi X, Liu Q, He W, Liu Y, Rao T, Fang L, Wu J. Prenatal and perinatal outcomes of twin pregnancy discordant for one fetus with nuchal translucency above the 95th percentile. J Matern Fetal Neonatal Med. 2022 Aug;35(16):3152-3157. doi: 10.1080/14767058.2020.1814242. Epub 2020 Sep 9. PMID: 32907415.

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