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# Heterokaryotypic Monochorionic Twin Pregnancy: New Perspective

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## Abstract

Monozygotic twins are thought to be identical since they are created from a single fertilized egg, yet there may be differences in their congenital defects, birth weight, and genetic makeup. Asymmetric X chromosome inactivation, unequal gene imprinting, and postzygotic mitotic mistakes including nondisjunction and anaphase lag can all result in heterokaryotypic monochorionic twins. We report a monochorionic twin pregnancy that exhibited stigmata associated with trisomy 18 on postnatal examination despite a low risk of common aneuploidy (trisomy 18) on noninvasive prenatal screening. Short tandem repeat markers were used for postnatal examination to confirm high-grade mosaicism. These markers indicated mosaic trisomy 18 in twin II and normal in twin I, ruling out uniparental disomy and establishing monozygosity in both fetuses. Twin sac amniocentesis is a prenatal diagnostic procedure that can be used to identify discrepant monochorionic twins because chorionic villus sampling, single sac amniocentesis, or cordocentesis may not be able to rule out aneuploidy in the second fetus and may yield a false-negative result. For prompt zygosity diagnosis, chromosomal complement, genetic counseling, and referral for selective fetal reduction, twin sac amniocentesis is recommended.

**Keywords**
- heterokaryotypic
- monozygotic twins
- mosaicism
- twin sac
- amniocentesis

## Introduction

A monochorionic twin pregnancy is a type of monozygotic pregnancy. They are nearly identical in appearance, genetic makeup, and even congenital abnormalities, if they have any. However, it does not mean that monochorionic twins are completely identical.[1]

Perinatal morbidity and mortality in monochorionic twin pregnancies is known to be significantly higher (3–6 times) than those in dichorionic twin pregnancies. Monochorionic twin pregnancies might suffer from specific complications such as twin-to-twin transfusion syndrome (TTTS), twin-reversed arterial perfusion sequence, conjoined twin, a significant risk for neurological morbidity, and increased risk of mortality in the co-surviving fetus in case of intrauterine demise of one fetus.[2] These complications develop due to intertwin vascular anastomoses within the placenta. Phenotypic discordance may occur because of

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structural fetal anomalies, which are three times more common in monozygotic twins as compared to dizygotic twins.[3,4]

Heterokaryotypic monochorionic twins with are rare and the karyotypic discordance may be caused by asymmetric X chromosome inactivation and differential gene imprinting postzygotic mitotic errors such as nondisjunction and anaphase lag.[5]

The most common etiology of this heterokaryotype is the nondisjunction of homologous chromosomes. According to the phase of zygote formation, when this nondisjunction occurs, the genetic abnormality might occur in all the fetuses or in only one of the fetuses. One of the fetuses may have a genetic abnormality with a normal second fetus if the nondisjunction occurs after zygote formation is completed.[6] Postzygotic mitotic nondisjunction and asymmetric X chromosome inactivation can result in the discordant karyotype.[7]

For prenatal diagnosis of discrepant genetic complement in monochorionic twins, chorionic villus sampling (CVS), amniocentesis, and cordocentesis may be considered. It is appropriate to perform amniocentesis in both amniotic sacs, as reported by Lewi et al to examine both amniotic sacs for genetic abnormality and to establish zygosity. CVS may have false-negative or false-positive results. Lewi et al documented the result of CVS on the cord insertion site of both twins; the karyotype of the aneuploid fetus was normal and the karyotype of the euploid fetus was abnormal.[8,9]

Cordocentesis showed an intrauterine exchange of lymphocytes through vessel anastomoses in monochorionic fetuses that can lead to false blood cord results.[10] After the demise of one of the monochorionic fetuses, around 15% of the remaining co-twin also dies; if the co-twin survives, it stands at high risk of significant neurological morbidity, which is a known complication.[11]

## Case Report

A 28-year-old primigravida, was seen in the department of fetal medicine at Artemis Hospital for evaluation of discordance in nuchal fold thickness at around 16 weeks. Ultrasound examination demonstrated a monochorionic-diamniotic pregnancy (MCDA) twins. The parents were counseled about the increased risk of congenital abnormalities, a TTTS, and growth restriction with discordant twin growth.

Increased NT in one twin (3.9 mm; ►**Table 1**) prompted us to offer and order noninvasive prenatal screening testing (NIPT) as monochorionic twins are presumed to have the same genetic makeup. The fetal fraction of the NIPT testing was 11.9% and the results showed a low risk of common aneuploidy with 96% sensitivity (►**Fig. 1**). The cell-free deoxyribonucleic acid (cfDNA) was extracted from the maternal peripheral whole blood and was sequenced using next-generation whole genome sequencing. The paired-end sequencing data were analyzed by the Illumina VeriSeqTM NIPT Assay Software. NIPT in MCDA twins suggested a low risk of aneuploidy of chromosomes 21, 18, and 13 with 95% sensitivity and 99% specificity (►**Table 2**).

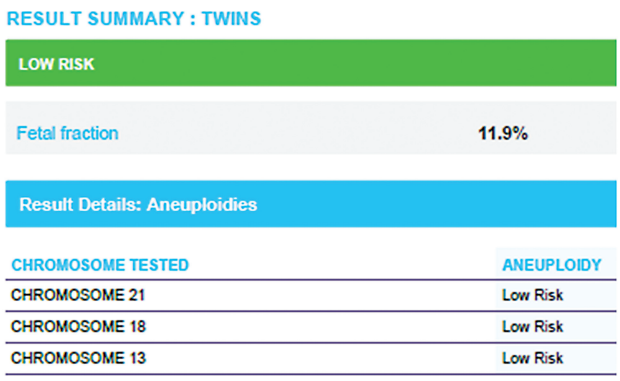
Increased and discordant NT in a monochorionic twin could be an early sign of TTTS, which was also indicated by differential growth of the fetuses (►**Table 1**). We advised

**Table 1** Depicting the surveillance chart and anomalies detected in monochorionic twins

| Date | POG LMP/ 06/01/ 2020 (wk) | Twin I (wk)/ weight (g) | Twin II (wk)/ weight (g) | Weight (g)/% of bigger difference | Amniotic fluid index in twin I/II | No. of vessels in cord | Other fetal abnormality |
|---|---|---|---|---|---|---|---|
| | | **NT: 1.40 mm; double marker: trisomy 21: < 1/10,000** | **NT: 3.9 mm; double marker: trisomy 21: < 1/213** | | | | **NIPT: fetal fraction 11.9%; twins; low risk of trisomy 21/18/13** |
| April 27, 2020 | 16 + 2 | 16 + 2 | 14 + 5 | | | | |
| May 21, 2020 | 19 + 3 | 19 + 0/270 | 17 + 3/186 | | | 3/3 | Bilateral kidneys in both fetuses within normal range |
| June 29, 2020 | 25 + 0 | 25 + 2/791 | 23 + 0/526 | 265/33.5% | | 3/3 | Bilateral kidneys in both fetuses within normal range |
| July 18, 2020 | 27 + 5 | 28 + 6/1,253 | 25 + 1/733 | 520/41.5% | 18.0/25.7 | 3/2 (single umbilical artery [SUA]) | Hypoplastic right kidney (TII) |
| August 17, 2020 | 32 + 0 | 33 + 4/2,101 | 30 + 0/1,351 | 750/35.6% | 16.6/28.0 | 3/2 (SUA) | Hypoplastic right kidney (TII) |
| August 31, 2020 | 34 + 0 | 34 + 2/2,178 | 31 + 0/1,460 | 718/32.9% | 16.5/22.2 | 3/2 (SUA) | Dilated small bowels (TII); suspected gut malrotation |

Abbreviations: LMP, last menstrual period; NT, nuchal translucency; POG, period of gestation; TII, twin II.


RESULT SUMMARY : TWINS

LOW RISK

Fetal fraction 11.9%

Result Details: Aneuploidies

| CHROMOSOME TESTED | ANEUPLOIDY |
|---|---|
| CHROMOSOME 21 | Low Risk |
| CHROMOSOME 18 | Low Risk |
| CHROMOSOME 13 | Low Risk |

**Fig. 1** Noninvasive prenatal screening testing (NIPT). Fetal fraction: 11.9%; result: low risk.

monitoring of the monochorionic twin pregnancy at 2-week intervals to exclude the development of TTTS.

Twin A had normal amniotic fluid, growth, and normal structural anatomy. However, the biometry of twin B was at the 5th percentile with discordant twin growth. Congenital abnormalities like choroid plexus cyst, congenital cardiac defect, omphalocele, clenched hands, and rocker bottom feet were absent. Both the fetuses had two umbilical arteries and three vessel cords at 16 weeks of pregnancy; kidney volumes in both the fetuses were also within normal range.

This pregnancy was kept under close surveillance and was observed to have occlusion of one of the umbilical arteries in twin B leading to a single umbilical artery (SUA; ►**Fig. 2**); right kidney hypoplasia was also noted at 28 weeks (►**Fig. 3**) of pregnancy with discordant twin growth and amniotic fluid levels in twin B (►**Table 1**). Twin B showed dilatation of the small intestine, predominantly on the right side of the fetal abdomen with suspected malposition (►**Fig. 4**). At 34 weeks of pregnancy, twin B was noted to have a malpositioned dilated small bowel with a two-vessel cord with growth less than the 5th percentile for gestational age (►**Table 1**).

Twin B faced a rough course after delivery: difficult resuscitation to start, ventilator dependency, and failure to thrive in the immediate postnatal period.

Postnatal examination of the fetus demonstrated trisomy 18 stigmata (►**Fig. 5**), which led to ordering of routine interphase peripheral blood fluorescence in situ hybridization (FISH) analysis with karyotype in both fetuses.

The monozygosity of both fetuses was confirmed by short tandem repeat (STR) molecular analysis by using the molecular markers D16S539, D7S820, D13S317, D5S818, CFS1PO, TPOX, THO1, vWA, and AMEL, and uniparental disomy was excluded.

FISH and karyotype examination showed mosaic trisomy 18 in twin B: three signals for chromosomes 18 in 160 cells and two signals for 40 cells of 200 cells studied. Twin A had a normal female chromosome complement. High-grade mosaicism with a trisomic cell line (nuc ish wcp 18 × 3[80]/wcp 18 × 2[20]) was confirmed in twin B.

## Discussion

The incidence of SUA varies from 0.2 to 0.87%.[12] It has been reported to be associated with a 6.77 times higher risk of congenital abnormalities, and growth delays. The most common anomalies associated with SUA are renal (6.48%), cardio-

**Table 2** NIPT test depicting the sensitivity and specificity

| | Trisomy 21 | Trisomy 18 | Trisomy 13 |
|---|---|---|---|
| Sensitivity | 96.4% | 95.7% | 93.6% |
| 2-sided 95% CI | 99.9% | > 99.9% | (64.1%, 98.9%) |
| Specificity | 99.9% | > 99.9% | > 99.9% |
| 2-sided 95% CI | (99.8%, > 99.9%) | (99.9%, > 99.9%) | (99.9%, > 99.9%) |

Abbreviations: CI, confidence interval; NIPT, noninvasive prenatal screening testing.

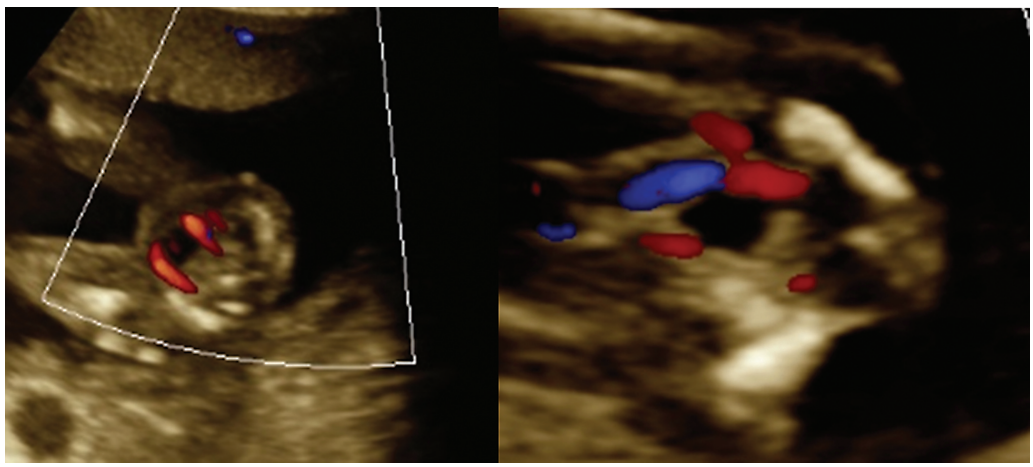


**Fig. 2** Three- and two-vessel (single umbilical artery [SUA]) cord of monochorionic fetuses.

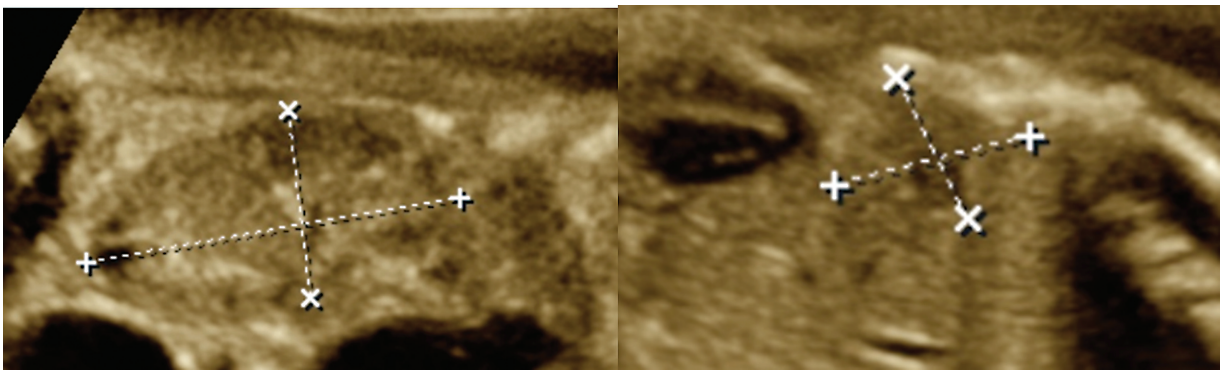


**Fig. 3** Antenatal ultrasound depicting normal left and hypoplastic right kidney of twin II.

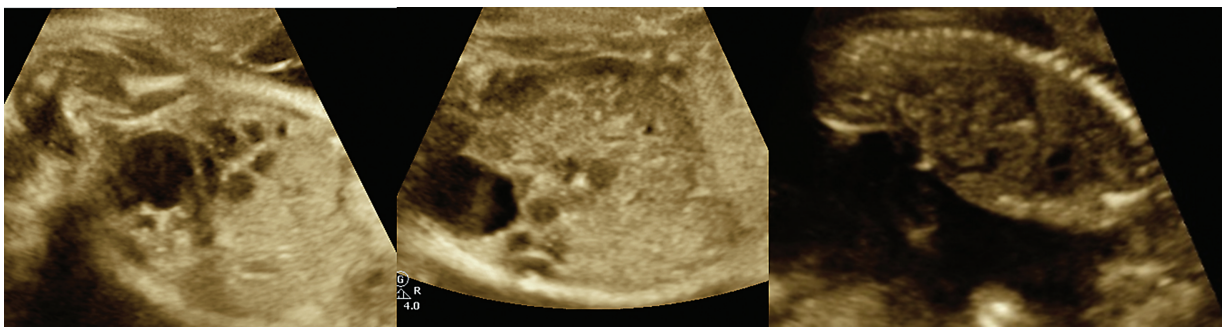


**Fig. 4** Dilated small bowel? Malpositioned in twin II.

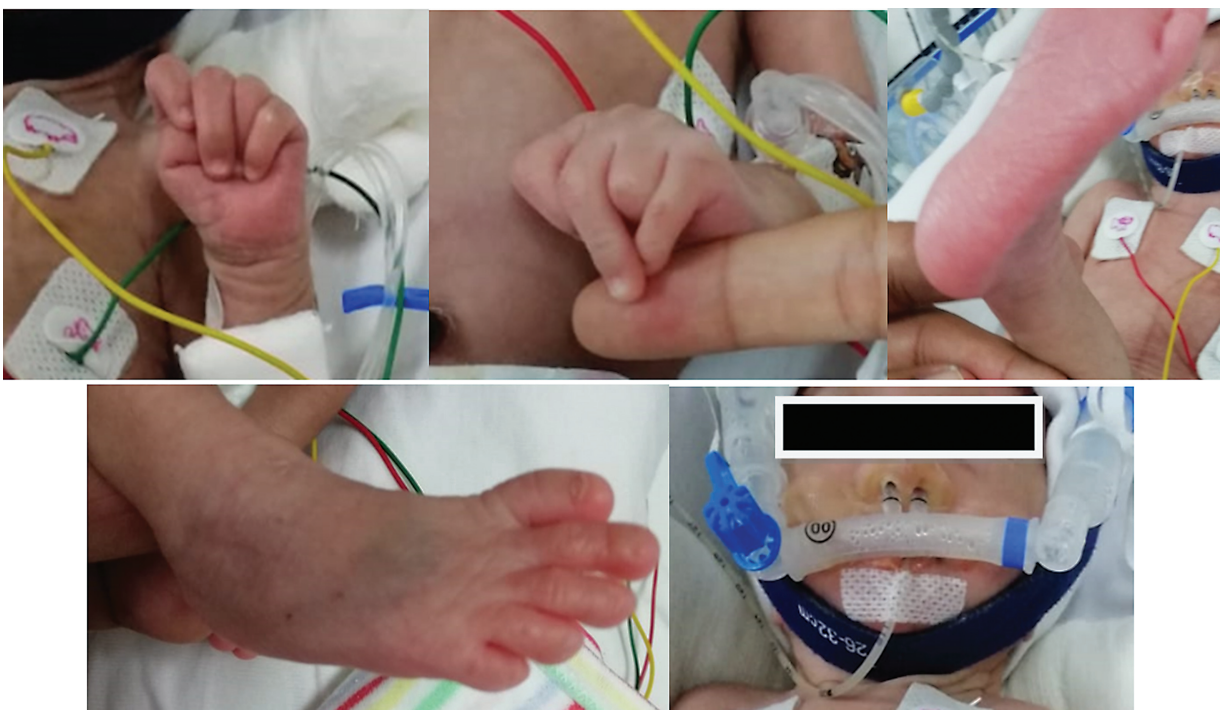


**Fig. 5** Postnatal examination of twin II with trisomy 18 stigmata: overlapping fingers, rocker bottom feet, macrodactyly, and typical facies.

vascular (6.25%), and musculoskeletal (5.44%).[13] SUA has been reported to be more common in multiple pregnancies. In our case, the second-trimester ultrasound done at 27 weeks showed SUA with no other associated anomalies. Isolated SUA is a risk factor for adverse pregnancy outcomes and increased risk of intrauterine growth restriction. Premature, intrauterine, and intrapartum deaths are more common among neonates with SUA when compared with those with a three-vessel cord.[13,14]

Monozygotic twins are formed from one fertilized oocyte; if twinning happens between 4 and 8 days postfertilization, it results in monochorionic-diamniotic twins. Most

monozygotic twins are not identical; they may be discrepant in birth weight, genetic abnormality, and congenital anomalies. As monochorionic twins share a single placenta with almost ubiquitous intertwin vascular anastomoses, it is not surprising to find persistent cord blood lymphocytic mosaicism.

Monozygotic twins having discordant genetic makeup are rare but a known phenomenon with multiple potential explanations.[5] Possible genetic mechanisms responsible include postzygotic mitotic errors leading to mosaicism, skewed X chromosome inactivation, and postzygotic dominant or recessive genetic mutations.[7] With the ever-increasing use of assisted reproductive technology (ART) and pregnancies, discordant epigenetic aberrations are also on the rise and being reported in monozygotic twins.[15]

The incidence of discordant monochorionic twins is difficult to estimate; it is a rare phenomenon and monozygotic twins with an abnormal karyotype suffer early fetal demise. Traditionally, monozygotic twins are presumed to be genetically identical. As the evidence of discordant genotype and phenotype in monozygotic twins is increasingly reported, the use of the term "identical" to describe these twins should be used cautiously.[7] Both fetuses should be examined with amniocentesis if chromosomal anomalies are suspected in only one fetus.

In our case, parent-of-origin (STR markers) studies suggested maternal origin of the trisomic chromosomal complement. The normal twin show a 1:1 ratio of maternal and paternal microsatellite markers, but the trisomic twins show a 2:1 inheritance pattern. In our case, either a trisomic zygote underwent a very early postzygotic nondisjunction, resulting in one normal and one aneuploid twin (trisomic rescue), or a euploid zygote with a very early nondisjunction of chromosome 18, resulting in a normal cell line and a trisomic cell line. As demonstrated by our case, it is pertinent to perform twin sac amniocentesis for the determination of genetic complement and zygosity in monochorionic-diamniotic twins, which has been advocated by other authors as well[9] (►**Table 3**).

CVS in monochorionic twins may provide a false-negative (normal karyotype) report in an aneuploid fetus [9,17] and single sac amniocentesis may not exclude aneuploidy in the second fetus. Single sac amniocentesis has been advocated in monochorionic twin pregnancy on the presumption that both fetuses have the same chromosomal complement and due to fear of higher procedure-related miscarriages in twin pregnancies as compared with singletons. Twin sac amniocentesis is warranted for timely diagnosis of zygosity and chromosomal complement, genetic counseling, and timely referral for selective fetal reduction.

The risk of spontaneous fetal death is very high; it is estimated to be around 36.5% (11–69.7%) in aneuploid fetuses,[32] which further increases for a trisomic fetus in monochorionic twins. The risk of fetal demise and neurological injury to the surviving co-twin after the demise of one in monochorionic twins is 12 and 18%, respectively.[33] The best method for selective fetal termination would be the use of either bipolar diathermy cord occlusion or interstitial laser; radiofrequency ablation has also been shown to be safe and effective.[4]

Women with twin pregnancies are more hesitant for invasive testing, whether CVS or amniocentesis, because of the perceived increased procedure-related risks of pregnancy loss.[34,35] NIPT has now been endorsed by the International Society for Prenatal Diagnosis.[36] The American College of Obstetricians and Gynecologists (ACOG) also recommends NIPT.[37]

Prenatal screening is important in ART pregnancies, as ART-conceived fetuses have a higher rate of chromosome abnormalities compared with the general population.[38]

The fetal fraction of cfDNA in maternal plasma for twin pregnancies is higher, but less than twofold compared to women with singleton pregnancies.[39,40] In monozygotic pregnancies (MCDA twins), this higher concentration of cfDNA and the fact that both fetuses almost always have the same genotype theoretically mean that NIPT in MCDA twins will be equivalent to or better than that for singletons.[41] Conversely, for dizygotic twins (dichorionic-diamniotic [DCDA] twins), the individual cfDNA contributed by each fetus is generally lower than that for a singleton and usually only one of the fetuses will be affected with an aneuploidy.

However, in twin pregnancies, cfDNA testing is more complex than earlier thought because if trisomy occurs in a

**Table 3** Reported different genetic discordance in monozygous twins

| | |
|---|---|
| Trisomy 21 | Rogers et al,[15] Dahoun et al,[16] and Nieuwint et al[17] |
| Trisomy 13 | Taylor et al[18] |
| Trisomy 18 | Reuss et al[19] |
| 7q34 del; [46,XX,del(7)(q34)] | Rock et al[20] |
| 46,XX with 45,X | Gilbert et al[21] and Jang et al[22] |
| 46,XY with 45,X | Costa et al,[23] Dallapiccola et al,[24] Gonsoulin et al,[25] Perlman et al,[26] Schmid et al,[10] and Fernández-Martínez et al[27] |
| 47,XYY with 45,X | Kurosawa et al[28] |
| 47,XYY with 46,XY | Wuttikonsammakit et al[29] |
| 47,XXY zygote resulting in 46,XX and 46,XY offspring | Zech et al[30] |

dizygous twin pregnancy, usually only one of the fetuses will be affected and the cfDNA contribution of the two fetuses can vary by nearly twofold, the normal twin contributing more cfDNA into maternal circulation and masking the cfDNA from the aneuploid fetus.[42,43] If the cfDNA contribution from any or affected fetus is below the threshold of 4% necessary for a successful analysis, a higher contribution from the normal cotwin can lead to false-negative results. Consequently, the complexity in the assessment of fetal fraction in twin pregnancies has raised concerns about potentially increased false-negative results of NIPT in twin gestations.

It is absolutely imperative that each twin contributes a sufficient amount of cfDNA into maternal circulation in order for NIPT testing to accurately distinguish between aneuploid and euploid pregnancies.

Some authors, including Bevilacqua et al, have demonstrated that NIPT testing is feasible in twin pregnancies, but with high failure rates and lower detection rate than in singleton pregnancies.[44] Currently, due to the lack of data on twin pregnancy, professional societies have called for more research on NIPT performance in twin gestations.[45]

More and more cases of monochorionic twins discordant for trisomy 18 are being reported, highlighting counseling and management difficulties. Our case report further supports the recommendation of dual amniocentesis in monochorionic-diamniotic twin pregnancies. The increase in the diagnostic yield has necessitated a reevaluation of the pathomechanisms responsible for discordant anomalies in monochorionic-diamniotic twins. A greater understanding of the genetics of both fetuses in a twin pregnancy is likely to influence how the patients are counseled on their management options.

## Conclusion

Our publication emphasises that rather than assuming that elevated or discordant NT is an early symptom of TTTS, amniocentesis should be performed on both monochorionic fetal sacs to diagnose heterokaryotypic abnormalities or chromosomal mosaicism. This will contribute to the best possible outcome for heterokaryotypic monochorionic pregnancies by facilitating prompt counseling and referral for selective fetal reduction.

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Conflict of Interest
None declared.

## References

1 Keith L, Machin G. Zygosity testing. Current status and evolving issues. J Reprod Med 1997;42(11):699–707
2 Asztalos E, Barrett JF, Lacy M, Luther M. Evaluating 2 year outcome in twins < or = 30 weeks gestation at birth: a regional perinatal unit's experience. Twin Res 2001;4(06):431–438
3 Mastroiacovo P, Castilla EE, Arpino C, et al. Congenital malformations in twins: an international study. Am J Med Genet 1999;83 (02):117–124
4 Paramasivam G, Wimalasundera R, Wiechec M, Zhang E, Saeed F, Kumar S. Radiofrequency ablation for selective reduction in complex monochorionic pregnancies. BJOG 2010;117(10): 1294–1298
5 Hall JG. Twinning. Lancet 2003;362(9385):735–743
6 Machin G. Non-identical monozygotic twins, intermediate twin types, zygosity testing, and the non-random nature of monozygotic twinning: a review. Am J Med Genet C Semin Med Genet 2009;151C(02):110–127
7 Machin GA. Some causes of genotypic and phenotypic discordance in monozygotic twin pairs. Am J Med Genet 1996;61(03): 216–228
8 Bohec C, Douet-Guilbert N, Basinko A, et al. Difficult diagnosis and management of an heterokaryotypic monochorionic twin pregnancy with discordant fetal sex and 45,X/47,XYY karyotypes. Fetal Pediatr Pathol 2010;29(06):424–430
9 Lewi L, Blickstein I, Van Schoubroeck D, et al. Diagnosis and management of heterokaryotypic monochorionic twins. Am J Med Genet A 2006;140(03):272–275
10 Schmid O, Trautmann U, Ashour H, Ulmer R, Pfeiffer RA, Beinder E. Prenatal diagnosis of heterokaryotypic mosaic twins discordant for fetal sex. Prenat Diagn 2000;20(12):999–1003
11 Hillman SC, Morris RK, Kilby MD. Co-twin prognosis after single fetal death: a systematic review and meta-analysis. Obstet Gynecol 2011;118(04):928–940
12 Vasanthalakshmi GN, Pushpalatha T, Mehta P, Devi SA. Single umbilical artery and pregnancy outcomes: cause for concern. J South Asian Fed Obstet Gynecol 2012;4:103–105
13 Murphy-Kaulbeck L, Dodds L, Joseph KS, Van den Hof M. Single umbilical artery risk factors and pregnancy outcomes. Obstet Gynecol 2010;116(04):843–850
14 Leung AK, Robson WL. Single umbilical artery. A report of 159 cases. Am J Dis Child 1989;143(01):108–111
15 Rogers JG, Voullaire L, Gold H. Monozygotic twins discordant for trisomy 21. Am J Med Genet 1982;11(02):143–146
16 Dahoun S, Gagos S, Gagnebin M, et al. Monozygotic twins discordant for trisomy 21 and maternal 21q inheritance: a complex series of events. Am J Med Genet A 2008;146A(16):2086–2093
17 Nieuwint A, Van Zalen-Sprock R, Hummel P, et al. "Identical" twins with discordant karyotypes. Prenat Diagn 1999;19(01): 72–76
18 Taylor DM, Thum MY, Abdalla H. Dichorionic triamniotic triplet pregnancy with monozygotic twins discordant for trisomy 13 after preimplantation genetic screening: case report. Fertil Steril 2008;90(05):2017.e5–2017.e9
19 Reuss A, Gerlach H, Bedow W, et al. Monozygotic twins discordant for trisomy 18. Ultrasound Obstet Gynecol 2011;38(06):727–728
20 Rock KR, Millard S, Seravalli V, et al. Discordant anomalies and karyotype in a monochorionic twin pregnancy: a call for comprehensive genetic evaluation. Ultrasound Obstet Gynecol 2017;49 (04):544–545
21 Gilbert B, Yardin C, Briault S, et al. Prenatal diagnosis of female monozygotic twins discordant for Turner syndrome: implications for prenatal genetic counselling. Prenat Diagn 2002;22(08):697–702
22 Jang JH, Kyeong KS, Hong DH, Hong SH. A case report of heterokaryotypic monochorionic twin pregnancy with discordant for Turner syndrome. Korean J Perinatol 2014;25(04):292
23 Costa T, Lambert M, Teshima I, Ray PN, Richer CL, Dallaire L. Monozygotic twins with 45,X/46,XY mosaicism discordant for phenotypic sex. Am J Med Genet 1998;75(01):40–44
24 Dallapiccola B, Stomeo C, Ferranti G, Di Lecce A, Purpura M. Discordant sex in one of three monozygotic triplets. J Med Genet 1985;22(01):6–11
25 Gonsoulin W, Copeland KL, Carpenter RJ Jr, Hughes MR, Elder FF. Fetal blood sampling demonstrating chimerism in monozygotic twins discordant for sex and tissue karyotype (46,XY and 45,X). Prenat Diagn 1990;10(01):25–28

 

26 Perlman EJ, Stetten G, Tuck-Müller CM, et al. Sexual discordance in monozygotic twins. Am J Med Genet 1990;37(04):551–557
27 Fernández-Martínez FJ, Galindo A, Moreno-Izquierdo A, et al. Application of QF-PCR for the prenatal assessment of discordant monozygotic twins for fetal sex. Prenat Diagn 2007;27:648–652
28 Kurosawa K, Kuromaru R, Imaizumi K, et al. Monozygotic twins with discordant sex. Acta Genet Med Gemellol (Roma) 1992;41 (04):301–310
29 Wuttikonsammakit P, Tanawattanacharoen S, Uerpairojkit B. Monochorionic twins with the same blood karyotype of 46,XY/ 47,XYY but different phenotypes. J Obstet Gynaecol Res 2010;36 (01):178–182
30 Zech NH, Wisser J, Natalucci G, Riegel M, Baumer A, Schinzel A. Monochorionic-diamniotic twins discordant in gender from a naturally conceived pregnancy through postzygotic sex chromosome loss in a 47,XXY zygote. Prenat Diagn 2008;28(08):759–763
31 Shur N. The genetics of twinning: from splitting eggs to breaking paradigms. Am J Med Genet C Semin Med Genet 2009;151C(02): 105–109
32 Hook EB, Topol BB, Cross PK. The natural history of cytogenetically abnormal fetuses detected at midtrimester amniocentesis which are not terminated electively: new data and estimates of the excess and relative risk of late fetal death associated with 47,+21 and some other abnormal karyotypes. Am J Hum Genet 1989;45(06):855–861
33 Ong SS, Zamora J, Khan KS, Kilby MD. Prognosis for the co-twin following single-twin death: a systematic review. BJOG 2006;113 (09):992–998
34 Di Mascio D, Khalil A, Rizzo G, et al. Risk of fetal loss following amniocentesis or chorionic villus sampling in twin pregnancy: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2020;56(05):647–655
35 Vink J, Fuchs K, D'Alton ME. Amniocentesis in twin pregnancies: a systematic review of the literature. Prenat Diagn 2012;32(05): 409–416
36 Palomaki GE, Chiu RWK, Pertile MD, et al. International Society for Prenatal Diagnosis Position Statement: cell free (cf)DNA screening for Down syndrome in multiple pregnancies. Prenat Diagn 2021;41(10):1222–1232
37 Screening for fetal chromosomal abnormalities: ACOG practice bulletin summary, number 226. Obstet Gynecol 2020;136(04): 859–867
38 Gjerris AC, Loft A, Pinborg A, Christiansen M, Tabor A. First-trimester screening markers are altered in pregnancies conceived after IVF/ICSI. Ultrasound Obstet Gynecol 2009;33(01):8–17
39 Struble CA, Syngelaki A, Oliphant A, Song K, Nicolaides KH. Fetal fraction estimate in twin pregnancies using directed cell-free DNA analysis. Fetal Diagn Ther 2014;35(03):199–203
40 Hedriana H, Martin K, Saltzman D, Billings P, Demko Z, Benn P. Cell-free DNA fetal fraction in twin gestations in single-nucleotide polymorphism-based noninvasive prenatal screening. Prenat Diagn 2020;40(02):179–184
41 Norwitz ER, McNeill G, Kalyan A, et al. Validation of a single-nucleotide polymorphism-based non-invasive prenatal test in twin gestations: determination of zygosity, individual fetal sex, and fetal aneuploidy. J Clin Med 2019;8(07):937
42 Qu JZ, Leung TY, Jiang P, et al. Noninvasive prenatal determination of twin zygosity by maternal plasma DNA analysis. Clin Chem 2013;59(02):427–435
43 Leung TY, Qu JZ, Liao GJ, et al. Noninvasive twin zygosity assessment and aneuploidy detection by maternal plasma DNA sequencing. Prenat Diagn 2013;33(07):675–681
44 Bevilacqua E, Gil MM, Nicolaides KH, et al. Performance of screening for aneuploidies by cell-free DNA analysis of maternal blood in twin pregnancies. Ultrasound Obstet Gynecol 2015;45 (01):61–66
45 Committee on Practice Bulletins—Obstetrics CoG. Practice bulletin no. 163: screening for fetal aneuploidy. Obstet Gynecol 2016; 127(05):e123–e137


 