**CASE REPORT**

**Monochorionic twins discordant for trisomy 13: A case report, systematic literature search and synthesis of available evidence**

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**Abstract**
This article presents the tenth reported case of monochorionic twins discordant for trisomy 13. Discordant aneuploidies in monochorionic twins are rare. Aetiologies include mitotic error in early cell division and “rescue” chromosome loss in an initially trisomic zygote. Clinicians should offer early amniocentesis of both sacs and consider selective termination.

**KEYWORDS**
amniocentesis, discordant anomalies, monochorionic twins, selective termination, trisomy 13

**1 | INTRODUCTION**

The frequency of multiple pregnancy has risen rapidly in the era of advancing maternal age and increasing availability of assisted reproductive technologies. While all twin pregnancies carry higher risks of congenital abnormalities and perinatal mortality, monochorionic twins present unique challenges derived from their dependence on a shared placental circulation. The associated risks of twin-to-twin transfusion syndrome, selective intrauterine growth restriction, and twin-anemia polycythemia sequence result in the majority of perinatal deaths in these pregnancies. Even with modern invasive fetal therapies, only 85% of monochorionic twin pregnancies result in two surviving twins.

Although monochorionic twins have traditionally been assumed to be genetically identical, rare cases of heterokaryotypic monochorionic twins have been documented over the last three decades. Most articles describe discordance for either fetal sex or sex chromosome aneuploidy, particularly Turner’s syndrome, but reports of autosomal aneuploidy (including trisomy 13, 18, and 21) are also starting to emerge. However, despite accumulating reports, there are no consensus statements on how to manage monochorionic twins with discordant fetal abnormalities: patients and doctors are therefore faced with challenging uncertainty when they arise.

Although heterokaryotypic abnormalities are rare, when discordant anomalies and markers of aneuploidy are identified in the first or early second trimester, the merits and risks of chorionic villus sampling vs. double amniocentesis at 15-16 weeks should be discussed; when both sacs are sampled, the individual karyotypes can be determined with certainty.

In this article, we present a case of spontaneously conceived monochorionic diamniotic twins discordant for trisomy 13 and use a systematic literature search to collate management and outcome data from previously published similar reports. We highlight the important role of double amniocentesis in confirming the suspicion of discordant aneuploidy in monochorionic twins, demonstrate the utility of selective termination, and propose potential underlying genetic aetiologies. Written informed consent for publication was obtained from the patient.

**2 | CASE REPORT**

This 26-year-old with previous medical termination of pregnancy at 22 weeks’ gestation for hypoplastic left heart syndrome was referred to our Fetal Medicine Unit in her second pregnancy. Dating ultrasound scan at 12 + 6 revealed monochorionic diamniotic twins with normal...
nuchal translucency (1.3 mm) and anatomy in Twin A but raised nuchal translucency (6.0 mm), generalized cutaneous edema and suspected encephalocele in Twin B. The patient was counseled on management options including expectant management, invasive testing, termination of the pregnancy, or selective termination of the affected twin. Findings for Twin B were confirmed on repeat ultrasound scans at 13 + 6 and 14 + 6, with multiple additional abnormalities identified that were suspicious for trisomy 13: semilobar holoprosencephaly, spina bifida, pulmonary atresia, ventricular septal defect, echogenic kidneys, and midline facial cleft. Management options were rediscussed at each scan and the patient eventually opted for selective termination of Twin B without prior invasive testing. This was performed uneventfully with radiofrequency cord ablation at 15 + 5 weeks. Microarray and karyotyping on amniotic fluid from Twin B revealed nondisjunctional trisomy 13.

Following additional counseling, the couple decided against genetic referral or further invasive testing. Close ultrasound surveillance of surviving Twin A confirmed normal anatomy, biometry and fetal echocardiogram, and fetal brain MRI was normal at 28 weeks. A 3470 g male infant was delivered in good condition by category 2 Cesarean section for failure to progress following induction of labor at 39 weeks and placental histopathology confirmed monochorionicity. Peripheral blood karyotyping of the surviving twin showed a normal male karyotype. Zygosity studies using a comparison of 16 short tandem repeats on chromosomes 13, 18, and 21 between the peripheral blood of Twin A and the amniocentesis sample from Twin B demonstrated that the samples were identical for all markers analyzed except for an increased chromosome 13 dosage in the amniocentesis sample, confirming discordance for trisomy 13. The surviving twin had an uncomplicated neonatal course and normal growth and neurodevelopmental follow-up at the age of 2 years.

3 | SEARCH STRATEGY

The search strategy (current to 08 August 2020) used textword variations and thesaurus terms for “monochorionic twins,” “trisomy 13,” and “discordance.” The databases searched were EMBASE and MEDLINE, with no language restrictions. Bibliographies of identified articles and conference abstracts from the Fetal Medicine Foundation and the International Society of Ultrasound in Obstetrics and Gynaecology were hand-searched for eligibility. The search identified fourteen eligible articles. Five were excluded, due to: duplicates (1); articles describing monochorionic twins with discordant structural anomalies but identical karyotypes (2); and articles describing discordant aneuploidies other than trisomy 13 (2). Nine remaining articles3-11 were selected for full-text review, all of which were included in the final analysis. These are summarized in Table 1.

4 | DISCUSSION

This unusual case is the tenth reported incidence of monochorionic twins discordant for trisomy 13. Of note, the case reported by Taylor et al.10 features a dichorionic triamniotic triplet pregnancy conceived through in vitro fertilization with two-embryo transfer: this article was eligible for inclusion in our analysis because the monochorionic twin pair was found to be discordant for trisomy 13. Details of the case reported by Vojtěch et al11 are incomplete because we were unable to access the full-text article despite contacting the authors.

In the first case, published by Heydanus et al. in,4 discordant structural anomalies were identified on ultrasound at 25 weeks. The affected Twin A subsequently died in utero and after delivery at 27 weeks, Twin B died in the early neonatal period. Although no invasive antenatal testing was done, postnatal karyotyping confirmed trisomy 13 in the affected twin but normal chromosome complement in Twin B. In at least seven of the subsequent nine cases3,9 (details unavailable from Vojtěch et al.,11 amniocentesis of both sacs was performed (at gestational ages ranging from 13 + 6 to 23 weeks) and confirmed discordant karyotypes, with one twin affected by trisomy 13 and the other with normal karyotype. Uniquely in this series, our patient decided against amniocentesis prior to selective reduction: given the obvious severity of the affected twin’s abnormalities, the result would not have altered her decision for selective termination but would have risked miscarriage of the unaffected twin. In addition, the normal sonographic appearances of Twin A provided relative reassurance both before and after the diagnosis of trisomy 13 in Twin B.

Selective termination was performed in seven of the ten cases, at gestational ages ranging from 15 + 5 to 23 + 0 weeks: three with radiofrequency ablation, three with bipolar cord occlusion, and one with laser cord coagulation. In the case of laser cord coagulation, the unaffected cotwin subsequently died at 18 + 4.10 In the other six cases, the unaffected cotwin survived, gestational age at delivery ranged from 32 + 2 to 40 weeks, with only one unaffected cotwin delivered before 36 weeks.6

Three cases were managed expectantly (one only diagnosed at 25 weeks so termination not offered,4 one case from Chile where termination is illegal under all circumstances,8 and one in which termination was offered but declined.7 One of these resulted in loss of both twins as discussed above,4 the other two both resulted in delivery at 32 weeks with neonatal death of the affected twin and survival of the unaffected cotwin.7,8
| Author and year | Maternal age | Fetuses | Timing and method | Selective termination of affected twin | Zygosity studies | Karyotype result | Outcome |
|----------------|--------------|---------|------------------|--------------------------------------|-----------------|-----------------|---------|
| Heydanus et al., 1993 | 40 | 1 MCDA pair | No | Not reported | IUFD of twin A (530 g), postnatal karyotype showed T13 and spontaneous preterm delivery at 27 40/7. NND of twin B (1060 g), postnatal karyotype normal | Not reported | No—abnormalities only detected at 25 weeks |
| Lewi et al., 2006 | 40 | 1 MCDA pair | Yes, both sexes | Bipolar cord coagulation at 17 + 0 | IUFD of surviving twin A at 25 40 (2590 g) with normal karyotype | T13 in twin B only | IUFD of twin A (850 g), postnatal karyotype showed T13 and spontaneous preterm delivery at 27 40/7. NND of twin B (1060 g), postnatal karyotype normal |
| Taylor et al., 2008 | 40 | 1 MCDA pair + 1 singleton | Yes | Laser cord coagulation at 16 + 4 | Live birth of surviving twin B at 36 40 (3220 g) with normal neuro-developmental follow-up | T13 in twin A only | Live birth of surviving twin A at 39 40 (3280 g) with normal neuro-developmental follow-up |
| Sepulveda et al., 2010 | 39 | 1 MCDA pair | Yes | Radiofrequency cord ablation at 22 + 0 | IUFD of surviving twin A at 33 40 due to FGR and nonreassuring CTG in the unaffected twin B. NND of affected twin A (1050 g); unaffected twin B survived (1520 g) with normal neuro-developmental follow-up | Monozygosity confirmed | IUFD of twin A (850 g), postnatal karyotype showed T13 and spontaneous preterm delivery at 27 40/7. NND of twin B (1060 g), postnatal karyotype normal |
| Ramsey et al., 2012 | 23 | 1 MCDA pair | No—illegal in Chile | No—offered but declined | Radiofrequency cord ablation at 18 + 0 | T13 in twin A only | Live birth of surviving twin A at 39 40 (3540 g) with normal neuro-developmental follow-up |
| Dritic et al., 2012 | 39 | 1 MCDA pair | Yes | Bipolar cord occlusion at 21 + 0 | Live birth of surviving twin B by emergency Cesarean section at 36 40/4. NND of affected twin A (530 g) at 36 40/4. NND of affected twin A (530 g) | T13 in twin A only | Live birth of surviving twin A at 39 40 (3540 g) with normal neuro-developmental follow-up |
| Spaccapietra et al., 2015 | 39 | 1 MCDA pair | Yes | Radiofrequency cord ablation at 23 + 0 | Monozygosity confirmed | T13 in twin B only | Live birth of surviving twin B by emergency Cesarean section at 36 40/4. NND of affected twin A (530 g) at 36 40/4. NND of affected twin A (530 g) |
| McFadden et al., 2017 | 29 | 1 MCDA pair | Yes | Monozygosity confirmed | T13 in twin B only | T13 in twin A only | Live birth of surviving twin B by emergency Cesarean section at 36 40/4. NND of affected twin A (530 g) at 36 40/4. NND of affected twin A (530 g) | Postnatal peripheral blood karyotype showed mosaic trisomy 13 (1 of 50 cells examined) |

(Continues)
As discussed by the cited authors, there are several potential mechanisms for discordant karyotypes in monochorionic twins. These include:

1. Dizygosity, in which monochorionic twins are assumed to be monozygotic but in fact result from dizygotic conception with early fusion of the outer cell mass.5,7
2. Mitotic error during an early postzygotic cell division, leading to aneuploidy in that cell lineage.3,5-7,9
3. Spontaneous “rescue” chromosome loss in an initially trisomic zygote.3,5-8

Both mitotic error and trisomic rescue can give rise to uniparental disomy and mosaicism.3,5-8,10 Uniparental disomy may lead to phenotypic abnormalities if the chromosome involved has a high proportion of imprinted genes, but as noted by Ramsey et al, four cases of paternal and one case of maternal uniparental disomy for chromosome 13 have been reported, all with normal phenotypes.7 Similarly, mosaicism in the surviving twin may arise due to transplacental transfer of trisomic cells from the affected twin, as seen in the cases reported by Ramsey et al and McFadden et al6,7. The possibility of mosaicism warrants postnatal karyotyping and close follow-up of the structurally normal twin in a discordant pair.

5 | CONCLUSION

This article reports the tenth case of monochorionic twins discordant for trisomy 13 and the first systematic synthesis of all previously published reports. Despite the obvious limitations of this analysis (including the small numbers, the variety of techniques used for selective termination and the fact that monozygosity was not always confirmed), it is likely that future similar cases will arise as rates of monochorionic twin conceptions and early detection of structural abnormalities increase, making this scenario increasingly relevant. Taken together, these ten cases support the use of selective termination and demonstrate good survival rates in the unaffected cotwin: 80% overall (8/10); 85.7% with selective termination (6/7). While all previous reports have advocated early amniocentesis of both sacs (which remains the standard management in these cases), they have not explicitly acknowledged the complexities of this decision for the parents, including the inherent risk of miscarriage, the psychological burden of additional waits for amniocentesis results and the likely increased risk to the cotwin from later termination.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.
AUTHOR CONTRIBUTIONS
EFC: conceived the article and wrote the first draft of the manuscript. RW and GA: provided critical revisions of the manuscript and edited the text. All authors contributed to manuscript revision and read and approved the submitted version.

EDITORIAL POLICIES AND ETHICAL CONSIDERATIONS
Written informed consent for publication obtained.

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REFERENCES
1. Lewi L, Jani J, Blickstein I, et al. The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study. *Am J Obstet Gynecol*. 2008;199(5):514.e1-514.e8.
2. Kilby M DBL, on behalf of the Royal College of Obstetricians and Gynaecologists. Management of monochorionic twin pregnancy. *BJOG*. 2016;124:e1-e45.
3. Dixit A, Tanteles G, Ocraft K, McEwan A, Sarkar A. Monozygotic twins discordant for trisomy 13: counselling and management issues. *J Perinatol*. 2012;32(8):639-641.
4. Heydanus R, Santema JG, Stewart PA, Mulder PG, Wladimiroff JW. Preterm delivery rate and fetal outcome in structurally affected twin pregnancies: a retrospective matched control study. *Prenat Diagn*. 1993;13(3):155-162.
5. Lewi L, Blickstein I, Van Schoubroek D, et al. Diagnosis and management of heterokaryotypic monochorionic twins. *Am J Med Genet A*. 2006;140(3):272-275.
6. McFadden P, Smithson S, Massaro R, Huang J, Prado GT, Shertz W. Monozygotic twins discordant for trisomy 13: a case of trisomic rescue supporting the continued need for first-trimester ultrasound. *Pediatr Dev Pathol*. 2017;20(4):340-347.
7. Ramsey KW, Slavin TP, Graham G, Hirata GI, Balaraman V, Seaver LH. Monozygotic twins discordant for trisomy 13. *J Perinatol*. 2012;32(4):306-308.
8. Sepulveda W, Wong AE, Ocaranza M. Heterokaryotypic pregnancy: monozygotic monochorionic twins discordant for trisomy 13. *Fetal Diagn Ther*. 2010;28(2):109-113.
9. Spacek RPJ, Matura D, Simekta O. Heterokaryotypic pregnancy: monozygotic monochorionic twins discordant for trisomy 13. Paper presented at the 14th World Congress in Fetal Medicine (2015), Greece. 2015. https://fetalmedicine.org/abstracts/2015/var/pdf/abstracts/1041.pdf
10. 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(5):2017.e5-2017.e9.
11. Vojtěch JHL., Pock R, Běhávková K, et al. Selective feticide in monochorionic twin pregnancies with discordant fetal anomalies: management and outcome. *Ceska Gynekol*. 2017;82(5):345-350.

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