

Prenatal Cell-Free DNA Screening Helps Uncover Maternal Colorectal Cancer: A Case Study



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Introduction

- Prenatal cell-free DNA (pcfDNA) screening is primarily used to detect fetal aneuploidies, but emerging evidence highlights its potential to uncover significant maternal health conditions, including malignancies. Although cancer during pregnancy is rare, affecting approximately 1 in 1,000 pregnant individuals, the implications for maternal and fetal outcomes are profound. The most commonly reported malignancies in pregnancy include melanoma, breast cancer, cervical cancer, lymphomas, and leukemias.¹
- Recent studies have demonstrated that atypical or unreportable pcfDNA results may serve as early indicators of maternal cancer. In one study, nearly half (48.6%) of patients with complex or non-reportable pcfDNA results were subsequently diagnosed with cancer. Particularly, results showing copy-number gains and losses across three or more chromosomes are highly predictive of malignancy.²
- This poster presents a compelling case in which pcfDNA screening led to the diagnosis of maternal colorectal cancer with liver metastases, significantly impacting pregnancy management and maternal care.
- The patient provided informed consent for the use of this case study.

Case History

- A 30-year-old patient with a singleton pregnancy conceived via in vitro fertilization (IVF) underwent routine prenatal cell-free DNA (pcfDNA) screening (**Figure 1**).
- Initial testing was performed through her obstetrician with Laboratory A, which utilized a targeted next-generation sequencing (NGS) platform and resulted in two failed screens. Following these inconclusive results, the patient was referred to a maternal-fetal medicine (MFM) specialist (**Figure 1**).
- At 18 weeks and 4 days gestation, a detailed ultrasound showed normal fetal growth and no notable ultrasound abnormalities (**Figure 1**).
- The MFM provider submitted a new pcfDNA sample to Laboratory B, which utilized whole-genome sequencing (WGS). The report flagged additional findings and the option to add expanded aneuploidy analysis (EAA). Results with EAA revealed a highly complex pattern with 17 autosomal aneuploidies (**Figure 2**), including:
 - Monosomies of chromosomes 4, 5, 9, 10, 11, 14, 18, 21, and 22
 - Trisomies of chromosomes 1, 7, 8, 12, 13, 16, 17, and 20
- The patient was referred to the IDENTIFY study for further evaluation. A comprehensive workup was initiated, including physical examination, whole-body magnetic resonance imaging (MRI), and blood, urine, and fecal testing.
- At 21 weeks and 5 days gestation, whole-body MRI identified a sigmoid colon mass with hepatic lesions suspicious for metastatic colorectal cancer. The patient reported mild constipation and intermittent rectal bleeding, which she had previously attributed to pregnancy-related changes.

Figure 1. Diagnosis and Treatment Timeline

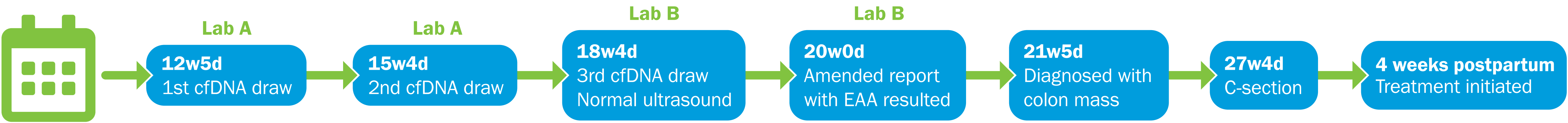
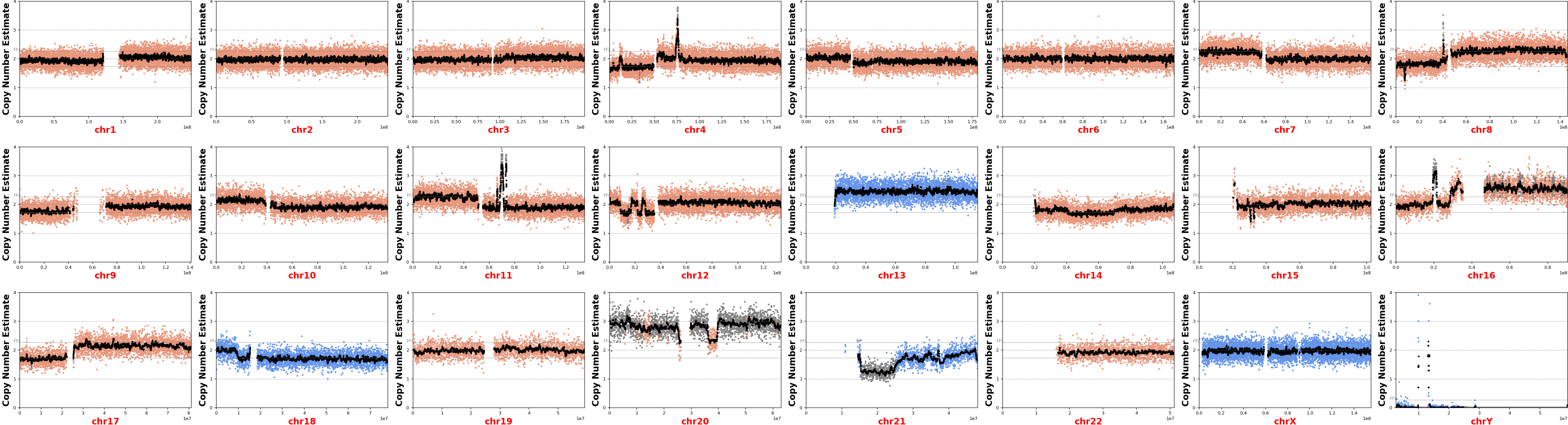


Figure 2. Patient WGS Profile



Management and Outcome

- The patient was referred to a local cancer center for confirmation of her diagnosis. She was subsequently referred to a leading oncology center for comprehensive oncologic management.
- To initiate timely oncologic treatment while minimizing fetal risk, the patient underwent an elective cesarean section at 27 weeks and 4 days gestation, resulting in the delivery of a female neonate. The infant required neonatal intensive care and was discharged after a 78-day NICU stay. She is currently healthy and thriving.
- Following delivery, the patient underwent placement of an ostomy bag and surgical resection of hepatic metastases. She is currently undergoing 11 cycles of chemotherapy prior to colorectal surgery. Additional treatment is planned to address newly identified pulmonary metastases.
- The patient's family history of cancer was limited to a paternal grandfather with skin cancer. Genetic testing for hereditary colorectal cancer syndromes was negative.
- The patient has exceeded her initial 3-month prognosis and remains under active oncologic management.

Discussion

Clinical Impact

- This case highlights the significant clinical implications of prenatal cell-free DNA (pcfDNA) screening beyond fetal aneuploidy detection. The incidental detection of maternal malignancy led to timely diagnosis and personalized treatment, helping to improve maternal outcomes. As shown in prior studies^{2,4}, pcfDNA screening can act as an early alert for maternal conditions, supporting its role in comprehensive prenatal care.

Counseling Challenges

- Counseling in these cases presents unique challenges. Not all pcfDNA platforms detect maternal abnormalities, and lab reporting practices vary widely. In this case, repeated test failures delayed diagnosis, highlighting the need to understand test limitations and the significance of “no-call” results.
- Additional barriers include⁵:
 - Lack of standardized disclosure guidelines
 - Limited insurance coverage for asymptomatic maternal evaluation
 - Incomplete workups that may falsely reassure
 - Low awareness among obstetricians and oncologists about cancer detection via prenatal screening
- Consistent with responses from Turiff et al. (2023), the patient was shocked by the diagnosis but relieved the fetus was unaffected

- and grateful for the early detection. These reactions reinforce the importance of transparency and disclosure during pregnancy care.
- Targeted education for obstetricians and oncologists is essential to ensure timely, empathetic counseling, urgent referrals, and coordinated follow-up. Without this, critical opportunities for early intervention may be missed.

Lack of Standardized Workflows

- No consensus exists for follow-up when maternal malignancy is suspected via pcfDNA. Recommendations range from full evaluations (history, labs, imaging) to stepwise approaches^{4,6,7}. Whole-body MRI shows high sensitivity (98%) and specificity (88.5%)², making it a valuable tool.
- The absence of standardized workflows can lead to delays and inconsistent care. Consensus guidelines would support genetic counselors and clinicians in managing these time-sensitive and complex cases.

Future Directions

- Further research should:
 - Explore whether whole-genome sequencing (WGS) from pcfDNA can help identify tumor origin.
 - Understand genetic counselors' experiences and develop effective strategies for counseling these rare but impactful cases.

References: 1. Hegner A, Negri D, Hase EA, et al. Cancer During Pregnancy: The Oncologist Overview. *World J Oncol*. 2019;10(12):28-34. doi:10.14740/wjon1177. 2. Turiff AE, Annunziata CM, Matiyeri AA, Redd B, Pavelova M, Goldlust IS, Rajagopal PS, Lin J, Bianchi DW. Prenatal cfDNA sequencing and incidental detection of maternal cancer. *N Engl J Med*. 2024;391(23):2101-2112. doi:10.1056/NEJMoa2401029. 3. Van der Meij, K. R., Sijm, E. A., Macville, M. V., Stevens, S. J., Bax, C. J., Bekker, M. N., et al. (2019). TRIDENT2: national implementation of genome-wide non-invasive prenatal testing as a first-tier in the Netherlands. *The American Journal of Human Genetics*. 105(5), 1091-1101. 4. Rink BD, Stevens BK, Norton ME. Incidental Detection of Maternal Malignancy by Fetal Cell-Free DNA Screening. *Obstet Gynecol*. 2022;140(1):121-131. doi:10.1097/AOG.0000000000004833. 5. Turiff A, Miner SA, Annunziata CM, Bianchi DW. Patients' Perspectives on Prenatal Screening Results That Suggest Maternal Cancer: A Qualitative Analysis. *Prenat Diagn*. 2023;43(9):1101-1109. doi:10.1002/pd.6273. 6. Heesterbeek TJ, van den Heuvel LM, Polak MG, et al. Noninvasive Prenatal Test Results Indicative of Maternal Malignancies: A Nationwide Genetic and Clinical Follow-Up Study. *JAMA Oncol*. 2022;8(6):857-865. doi:10.1001/jamaoncol.2022.1234. 7. Dow E, Freimund A, Smith K, et al. Cancer Diagnoses Following Abnormal Noninvasive Prenatal Testing: A Case Series, Literature Review, and Proposed Management Model. *JCO Precis Oncol*. 2021;5:1001-1012. doi:10.1200/Po.20.00452.

Disclosures: MK was an employee of Myriad Genetics, Inc. at the time of this study and received salary and stock as compensation.

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