Suspected maternal mosaic trisomy 8: insights into this uncommon finding on cell-free DNA screening

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1. Introduction

Trisomy 8 is a common cytogenetic finding in high-risk indications.

2. Methods

A retrospective review of cases with suspected maternal mT8 was conducted from clinical samples on both the traditional (karyotyping) and genome-wide cfDNA platforms performed at our laboratory. Data collection was focused on the ordering provider when available and/or cross-referenced and matched with diagnostic testing performed internally at the same laboratory. Referral indications were extracted from the test requisition and/or by calculating the patient’s age at the time of delivery to categorize them as advanced maternal age or over 35 years of age. The multiple indications category included cases with two or more high-risk indications.

3. Results

Supported maternal mT8 was identified in cfDNA sequencing data of 28 separate patients between December 2014 and November 2021. Five patients had two separate samples analyzed at our laboratory, both producing the same result regardless of whether the maternal finding was the same or a different pregnancy. Trisomy 8 was determined as easily as possible in all cases. Samples requested for genomic-wide analysis were typically positive trisomy 8 with a likely maternal mosaicism comment. Samples requested for traditional analysis were typically reported as non-reportable and accompanied by a proactive call to the provider to continue their maternal testing

4. Conclusions

The series of cases provides insight into one cfDNA laboratory’s experience with suspected maternal mT8. Given that the majority of patients in which this finding was identified were pursuing screening for advanced maternal age or had no high-risk indication provided, it is clear that maternal mT8 is often an incidental finding on cfDNA screening.

References


Figures

Figure 1. Breakdown of diagnostic outcomes for suspected maternal mT8 cases

Figure 2. Examples of 50 kb sequencing data

Figure 3. Indications for screening

The series of cases provides insight into one cfDNA laboratory’s experience with suspected maternal mT8. Given that the majority of patients in which this finding was identified were pursuing screening for advanced maternal age or had no high-risk indication provided, it is clear that maternal mT8 is often an incidental finding on cfDNA screening.

Although an unreviewed cfDNA screening result may prompt maternal genetic evaluation to assess potential implications for future pregnancies. Due to tissue specificity and/or baseline low mosaicism, standard cytogenetic analysis may yield normal results while an abnormal cell line for mT8 may be present but not identifiable.

Conclusion

In addition to its role in non-reportable results, standard cytogenetic analysis may yield normal results while an abnormal cell line for mT8 may be present but not identifiable. Unreviewed maternal findings can lead to a non-reportable screening result due to low Z-score expression of other aneuploid chromosomes. In addition to its role in non-reportable results, suspected maternal mT8 on cfDNA screening may prompt maternal genetic evaluation to assess potential implications for future pregnancies. Due to tissue specificity and/or baseline low mosaicism, standard cytogenetic analysis may yield normal results. An abnormal cell line for mT8 may be present but not identifiable.