Incidental detection of colon cancer via non-invasive prenatal screening and comparative re-screen after treatment

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Introduction

Identification of maternal malignancy is well-described as an incidental finding of non-invasive prenatal screening (NIPS)[1]. As NIPS continues to be incorporated into clinical practice, these findings are likely to increase. Little is known about the value of repeat testing in such pregnancies. We present the case of a 34-year-old woman diagnosed with colon cancer as a direct result of follow-up prompted by NIPS findings, who later requested repeat analysis post-treatment for the purpose of fetal aneuploidy screening.

Background

Maternal cancer occurs with a frequency of 1 in 1000 pregnancies[2]. While incidental detection of maternal cancer has a long history in prenatal care, as seen with elevated maternal serum alpha-fetoprotein (MS-AFP) levels as well as ultrasound, detection of maternal malignancy initiated by abnormal NIPS is a new and evolving arena. The highest correlation between cancer risk and abnormal NIPS is observed in those who screen positive for multiple aneuploidies[3]. A paucity of literature exists regarding the psychosocial impact and needs of women diagnosed with cancer during pregnancy, but available data suggest that these needs are unique. The combination of pregnancy and cancer diagnosis may create higher levels of distress than either category alone[4].

Results

Figure 1. Pre- and post- treatment NIPS results

NIPS performed at 14 weeks gestation via whole genome sequencing (WGS) cfDNA analysis revealed multiple aneuploidies of both target and non-target chromosomes (blue). Repeat cfDNA analysis after treatment returned a negative NIPS result at 31 weeks gestation with no aneuploidy detected (red). Gray region indicates normal z-score range, while peaks outside this range are observed aneuploidies.

Case Report

Prior to cancer diagnosis

- A gravida 3, para 2, 34 year-old woman underwent routine NIPS for common aneuploidy screening (13,18, 21, X and Y) via WGS cell-free DNA (cfDNA) analysis
- 16 weeks gestational age (GA): NIPS- Positive for Trisomy 13 and Klinefelter (XXY) see fig 1
- 17 weeks GA: Patient receives genetic counseling regarding findings and potential explanations. Normal Level II ultrasound. Amniocentesis declined. Maternal health review "completely normal" with the exception of rectal bleeding attributed to common complication of pregnancy (constipation and hemorrhoids). No family history of colon or other heritable cancers. Colonoscopy offered in view of unusual NIPS results and rectal bleeding

Diagnosis and treatment

- 19 weeks GA: Abnormal colonoscopy (7.6x5x3.2cm tumor). Patient diagnosed with stage IV adenocarcinoma of the colon
- 20 weeks GA: Chose to pursue treatment and to continue pregnancy. Patient declined amnio and requested repeat NIPS post-treatment for additional insight into health of her baby. Partial colectomy performed
- 24 weeks to 31 weeks GA: Chemotherapy

Re-screen and follow up

- 31 weeks GA: Repeat NIPS NORMAL with no evidence of prior aneuploidies detected in target or non-target chromosomes. (fig 1)
- 34 weeks GA: Planned delivery -Healthy baby boy. 46,XY on peripheral blood chromosomes, congruent with NIPS re-screen
- 4 weeks post-partum: Chemotherapy resumed
- 6 months post-partum: Chemo and surgery complete. Stable and under clinical surveillance for recurrence

Discussion

In addition to contributing to the growing body of literature that maternal cancer should be considered in the differential for unusual NIPS results, this case also illustrates that collaboration between the clinical genetic counselor and NIPS laboratory allows for customized care, potentially leading to earlier diagnosis and treatment, as well as reassurance for patients managing multiple psychosocial stressors.

The laboratory GC and clinical GC jointly considered possible etiologies of the unusual NIPS results. WGS provided additional useful information beyond that typically available with targeted approaches[1], as the number and type of aneuploidies among non-target chromosomes indicated a possible maternal condition, including cancer. Rectal bleeding that had been regarded as a common, relatively benign complication of pregnancy was further investigated as a direct result of the unusual NIPS findings.

The clinical GC and laboratory worked together to create a customized plan for re-screen that addressed the patient's express desire for additional screening information regarding the chromosomal health of her baby. Post-treatment NIPS was explicitly performed for the sole purpose of fetal aneuploidy screening (not tumor monitoring), recognizing that remaining maternal tumor DNA could potentially obscure results. The result of the re-screen was reassuring and ultimately reflected the true karyotype of the fetus.

Conclusions

- The dramatic change in cfDNA results before and after treatment illustrates that re-screen may be a reasonable consideration for those cases in which prenatal diagnosis is not pursued
- NIPS via WGS provides additional useful information versus targeted methods as the number and type of aneuploidies detected may influence follow-up strategy
- Collaboration between the laboratory GC and clinical GC can lead to customized care that may improve detection and better meet the unique needs of patients identified with occult malignancy post-NIPS
- Additional research is needed regarding the psychosocial needs of women diagnosed with cancer during pregnancy and the role that cfDNA screening may play

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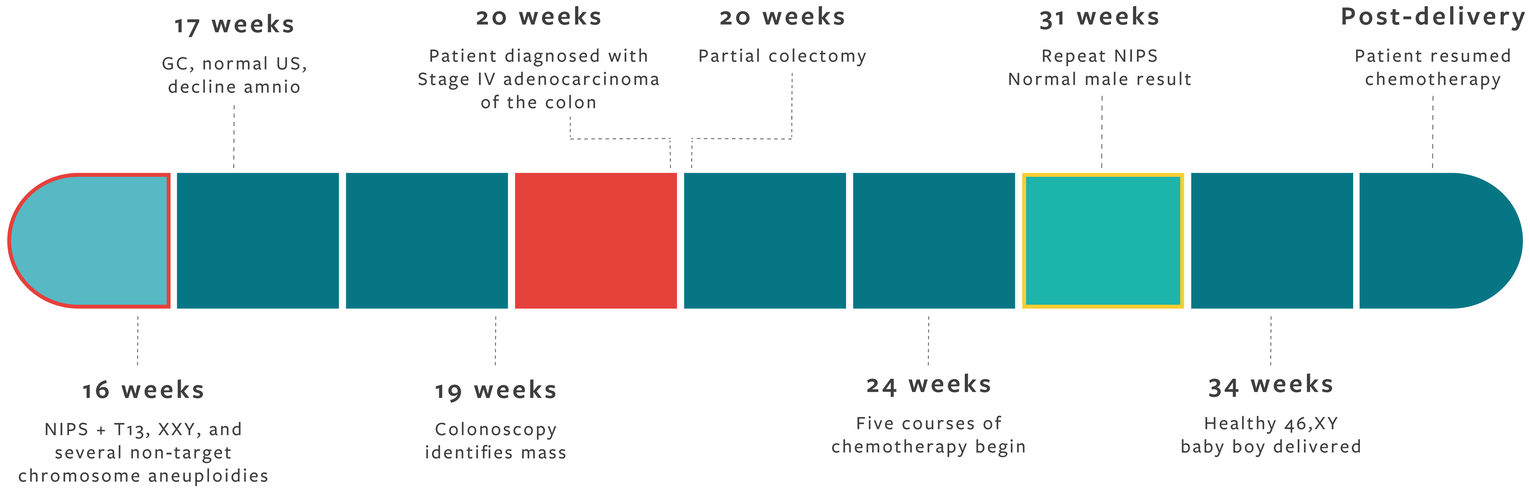
Timeline

Key events by gestational age



REFERENCES: **1.** Bianchi, DW, et al. Noninvasive Prenatal Testing and Incidental Detection of Occult Maternal Malignancies. JAMA 2015 Jul 14;314(2):162-9. **2.** Pavlidis, NA. Coexistence of pregnancy and malignancy. The Oncologist 2002;7:279-287. **3.** Snyder, HL et al. Follow-up of multiple aneuploidies and single monosomies detected by noninvasive prenatal testing: implications for management and counseling. Prenat Diagn. 2016 Mar;36(3):203-9. **4.** Vandenbroucke, et al Psychological distress and cognitive coping in pregnant women diagnosed with cancer and their partners. Psycho-Oncology 2017 Aug 26:8: 162-9