

Multiple Aneuploidy Pattern Detected by Non-Invasive Prenatal Screening in Successive Pregnancies



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Introduction

In 2011, aneuploidy screening using cell-free DNA (cfDNA) present in maternal blood became clinically available. Non-invasive prenatal screening (NIPS) is now commonly used to screen for trisomies 13, 18, and 21, sex chromosome aneuploidies, and certain microdeletions during pregnancy. Though much research has been done regarding NIPS since its inception, occasionally unexpected results are returned, such as the detection of multiple aneuploidies, which can be difficult to interpret. We present a case where NIPS detected a similar pattern of multiple aneuploidies in sequential pregnancies and review the subsequent work-up that followed.

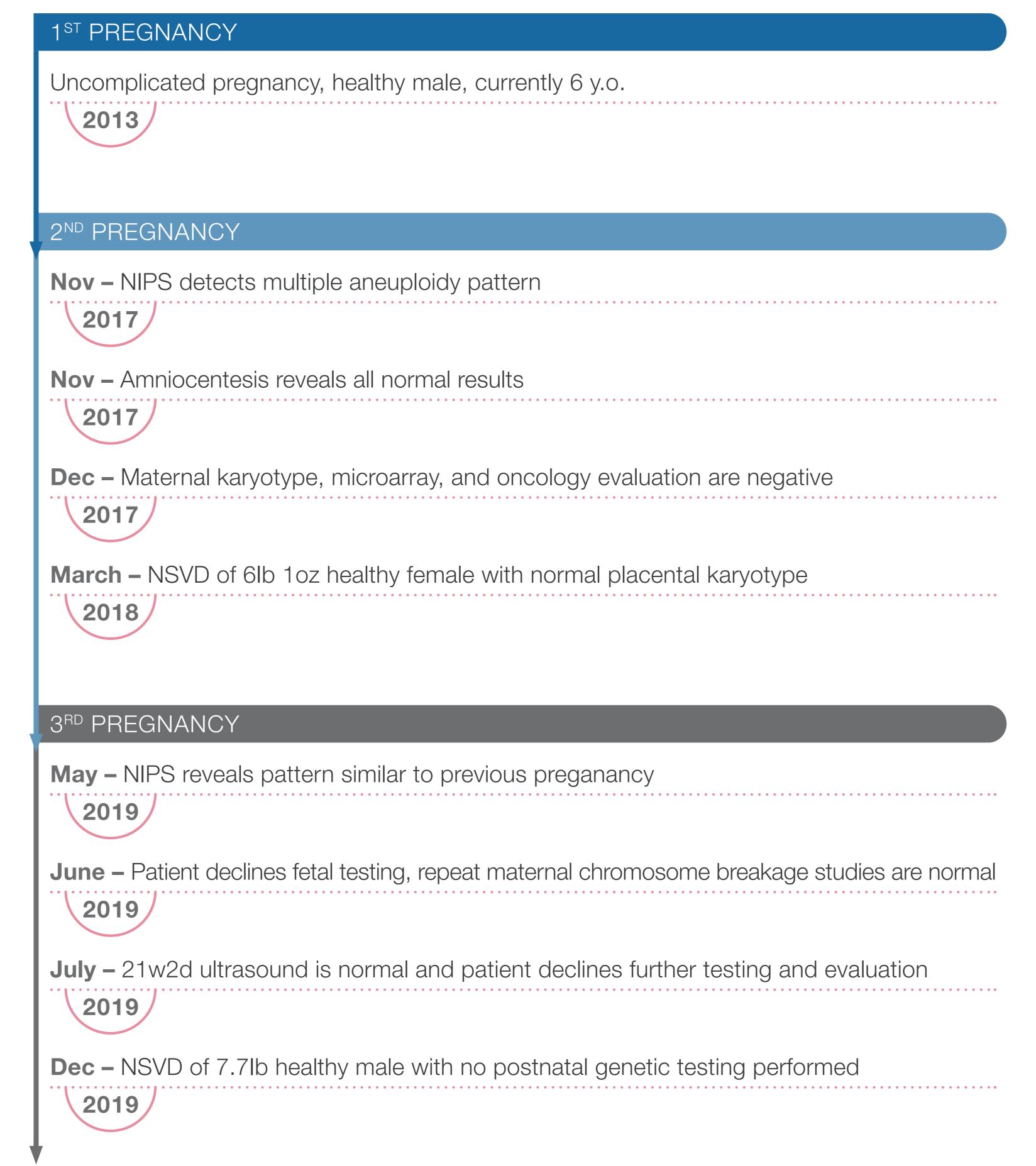
Case Presentation

A 25 year-old G3P2 patient had NIPS, by massively parallel sequencing (MPS), in her second and third pregnancies that revealed a pattern of multiple aneuploidies. During her second pregnancy, her NIPS result was positive for trisomies 18 and 21. Further bioinformatics review revealed possible partial trisomy 13 and complete trisomies 14 and 20, in addition to the previously reported trisomies. NIPS by MPS repeated at another lab was non-reportable. Verbal explanation from the other lab indicated they were seeing similar data, but there was a lot of noise in addition to soft elevations and depressions. Amniocentesis revealed normal karyotype, microarray, FISH for chromosomes 13, 14q, 18, 20p, 20q, and 21, and chromosome 14 uniparental disomy test results. Maternal karyotype and microarray were normal. The patient had a negative oncology evaluation which included chest, abdominal and pelvic MRIs, breast ultrasound, and maternal chromosomal breakage studies. The patient had an insignificant medical and medication history. The patient delivered a healthy 6 lbs 1 oz female baby by normal spontaneous vaginal delivery (NSVD). The placenta was small for gestational age, but the placental karyotype was normal, 46,XX.

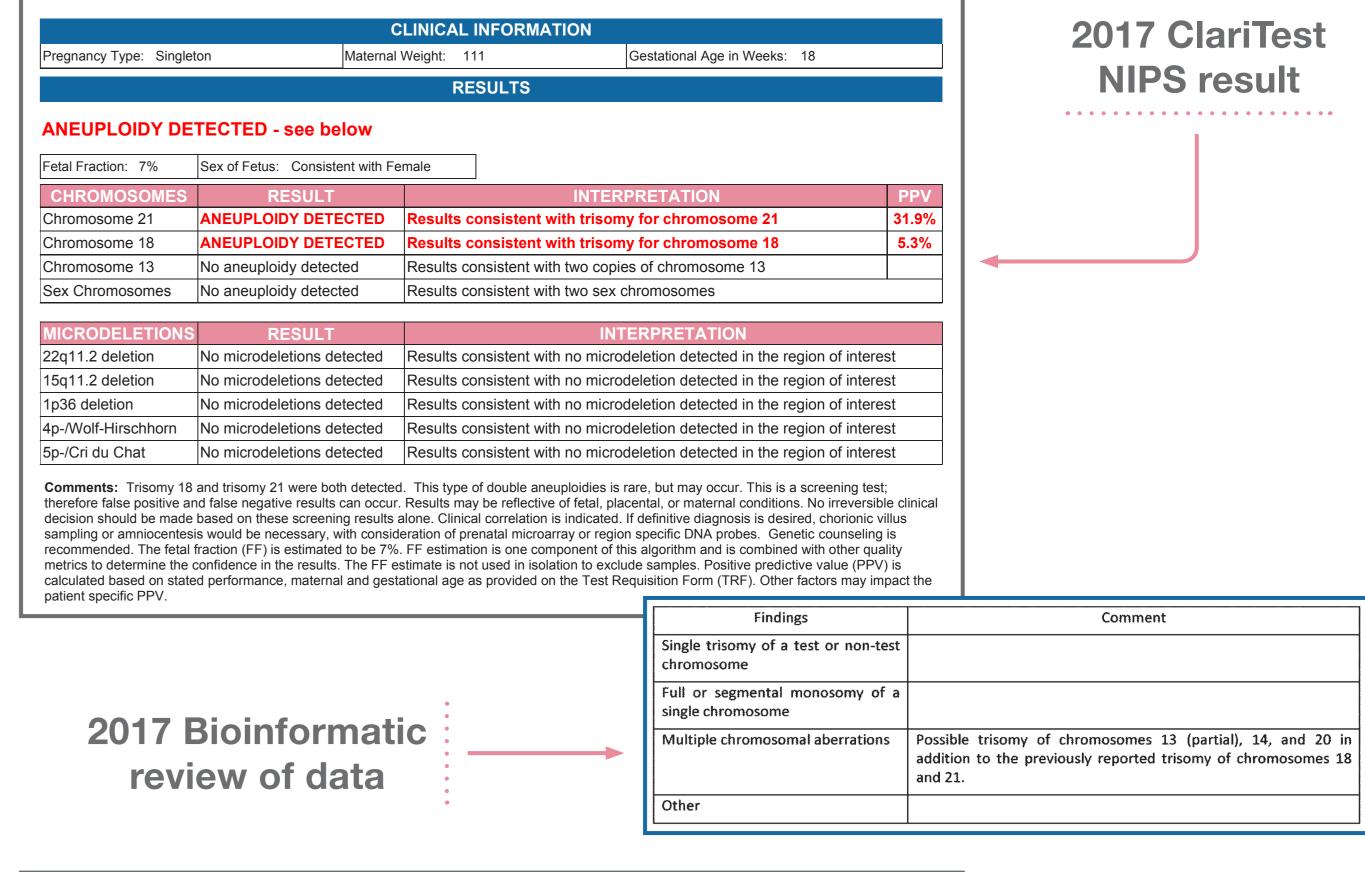
During the patient's third pregnancy (most recent pregnancy), she had blood drawn for NIPS, by MPS, at 12 weeks gestation. The laboratory reported that a similar NIPS pattern to her previous pregnancy was detected, therefore precluding evaluation of fetal aneuploidy screening using this platform. The patient declined the amniocentesis and further fetal aneuploidy screening. The second trimester ultrasound at 15w4d detected fetal hyperechoic bowel, and a subsequent detailed ultrasound at 21w2d gestation was within normal limits and the hyperechoic bowel had resolved. Maternal chromosomal breakage studies were repeated and were normal. The patient also declined additional follow-up with the oncologist.

Since the submission of our abstract, the patient reportedly had a NSVD of a healthy, 7.7 lbs male baby. No postnatal genetic testing was performed on the baby or the placenta.

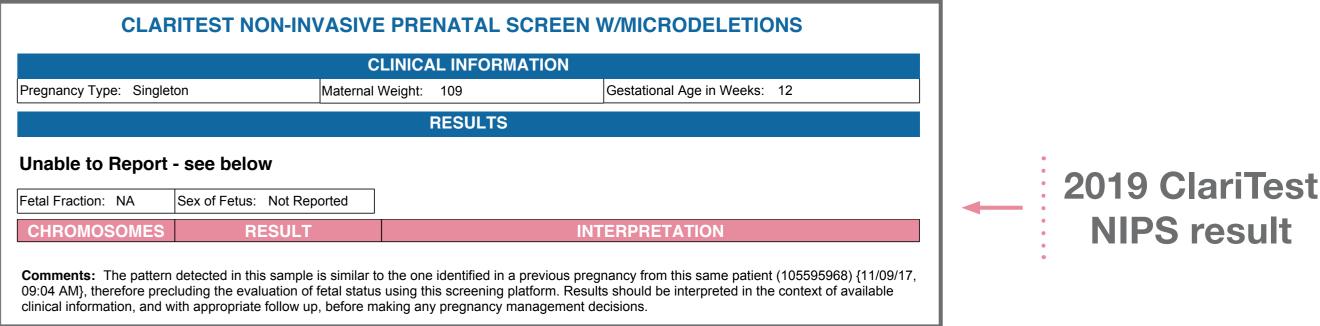
Pregnancy History



NIPS Results



CLARITEST NON-INVASIVE PRENATAL TEST W/MICRODELETIONS



Conclusion/Implications

NIPS analyzes cfDNA in maternal blood originating from maternal and cytotrophoblast cells. The similar NIPS pattern observed in both of this patient's pregnancies indicates a likely maternal etiology. When multiple aneuploidies are observed by NIPS, possible etiologies include maternal benign tumor or malignancy and fetal, placental or maternal chromosome abnormalities. However, for this patient, subsequent fetal and maternal evaluations were normal. This case highlights that NIPS may yield unexpected results that are not representative of the fetal or maternal karyotypes and an extensive multi-specialty work-up may be recommended in these scenarios.