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Exploring Positive Diagnostic Results after Receiving "Aneuploidy Suspected" Screen Results via Non-Invasive Prenatal Screening

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I. Introduction

Prenatal risk assessment by means of non-invasive prenatal screening (NIPS) has become a vastly utilized screening method in recent years. Different labs offering this testing utilize various reporting strategies. Integrated Genetics' informaSeq® screens for trisomy 13, 18, and 21, as well as sex chromosome aneuploidies, with three reporting categories for the autosomal chromosomes: aneuploidy detected, aneuploidy not detected, or aneuploidy suspected. To date, little information is available regarding the outcomes of "aneuploidy suspected" screen results. Here we discuss our experience concerning "aneuploidy suspected" screen results with available follow-up abnormal fetal karyotypes.

II. Methods

Screen positive informaSeq results were tracked and genetic counselors followed up on these results six weeks post-test or post-delivery, if needed, to gather clinical information including diagnostic testing results, ultrasound findings, and pregnancy outcomes.

III. Results

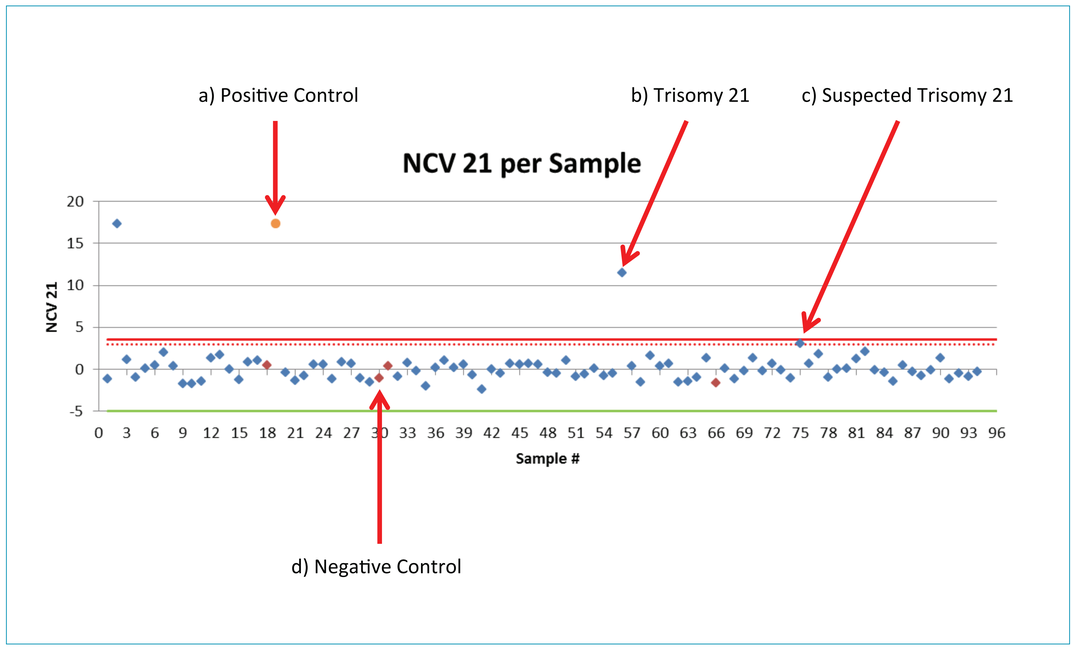
Less than 0.1% of all samples received for NIPS resulted "aneuploidy suspected." Of the 75 patients with diagnostic testing results, a total of 16 patients were reported to have abnormal fetal karyotype results after receiving an "aneuploidy suspected" informaSeq screen result. Four of the "aneuploidy suspected" results were confirmed to be due to mosaicism, three of which were confined placental mosaicism and one of which was tissue specific mosaicism. In eight of the cases (50%) the reported aneuploidy suspected result was the true result of the fetus.

Table 1. Diagnostic testing results and reported ultrasound findings compared to NIPS aneuploidy suspected results

Case	NIPS Result	Specimen Type	Diagnostic Results	U/S Findings	Notes
1	Aneuploidy Suspected T21	Amniocentesis	47,XY,+21	Increased NT	
2	Aneuploidy Suspected T21	Amniocentesis	47,XX,+21		
3	Aneuploidy Suspected T21	Amniocentesis	47,XY,+21		
4	Aneuploidy Suspected T21	Amniocentesis	47,XY,+21	Increased NT	
5	Aneuploidy Suspected T21	CVS	47,XY,+21		
6	Aneuploidy Suspected T21	CVS Amniocentesis	47,XY,+21[3]/46,XY[17] arr(1-22)x2,(XY)x1 (normal male)	CPC	Confined placental mosaicism
7	Aneuploidy Suspected T21	CVS Amniocentesis	47,XX,+21[2]/46,XX[44] arr(21)x2~3 (mosaic gain of whole chromosome 21) arr(1-22,X)x2 (normal female)		Confined placental mosaicism
8	Aneuploidy Suspected T21	Buccal swab Blood	arr[hg19](21)x2~3 (mosaic gain of chromosome 21) 46,XX		Tissue specific mosaicism
9	Aneuploidy Suspected T21	POC	arr[hg19](4)x3 (extra whole chromosome 4)	CPC, clenched hand, fetal heart in right chest, hydronephrosis, stomach bubble not visualized	
10	Aneuploidy Suspected T21 and Monosomy X	POC	arr[hg19](X)x1 (Turner syndrome)		
11	Aneuploidy Suspected T18	Amniocentesis	47,XY,+18	CPC	
12	Aneuploidy Suspected T18	Amniocentesis	47,XY,+i(18)(p10)	NT 3.6mm	
13	Aneuploidy Suspected T18	CVS Amniocentesis	47,XX,+18[18]/46,XX[2] 46,XX		Confined placental mosaicism
14	Aneuploidy Suspected T13	Amniocentesis	47,XY,+13	Cystic hygroma, CHD, 2 vessel cord	
15	Aneuploidy Suspected T13	Amniocentesis	45,XX,der(13;15)(q10;q10)		Trisomy rescue
16	Aneuploidy detected T18 and Aneuploidy Suspected T13	Amniocentesis	47,XY,+18	Clenched hands, possible tetralogy of fallot	

CVS=chorionic villus sampling, POC=products of conception, NT=nuchal translucency, CPC=choroid plexus cyst, CHD=congenital heart defect

Figure 1. NIPS data plots for a) positive control, b) aneuploidy detected, c) aneuploidy suspected, and d) negative control.



IV. Discussion

While NIPS has proven to be a highly accurate screening method, these outcomes underscore the importance of confirmatory diagnostic testing. Referral to a genetic counselor after receipt of an abnormal NIPS result may aid in patients understanding the nuances of non-invasive prenatal screening and the potential results, including, but not limited to, confined placental mosaicism.

V. References

Eversley C, Williams E, Burch M, et al. Clinical performance of informaSeq non-invasive prenatal screening. Poster presented at: *ACMG Annual Clinical Genetics Meeting*; 2016 March 8-12; Tampa, FL.

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