THREE CEP18 FISH SIGNALS IN AMNIOCYTES AND A CLINICALLY NORMAL FETUS

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ABSTRACT

Rapid prenatal FISH for aneuploidy detection is increasingly utilized for the detection of trisomies 13, 18, 21, and sex chromosome aneuploidies, particularly in high-risk pregnancies. Our laboratory received amniotic fluid for a rapid aneuploid screen and chromosome analysis because of maternal age and a history of previous pregnancies with chromosome abnormalities. This prenatal screen revealed the presence of three CEP18 signals in the interphase cells. Typically this would indicate a fetus with trisomy 18. We had studied a previous pregnancy of this patient in which the fetus had an unbalanced chromosome complement 46,XY,der(18);t(9;18)(p11.2;p11.1). Maternal chromosomes were then investigated which revealed that the mother was a carrier of a balanced t(9;18)(p11.2;p11.1) translocation. However, we had not performed interphase FISH studies on the mother. We performed FISH on archived lymphocytes from the mother which revealed three copies of CEP18 indicating that one of the 18 centromere signals was splitting due to the balanced translocation involving the 18 centromeric region. This resulted in three interphase FISH signals. In retrospect, two of the chromosome 18 signals were somewhat smaller than the other one; however, without knowing about the presence of a translocation, this would have resulted in a diagnosis of a fetus with trisomy 18. Subsequent cytogenetic studies on cultured amniocytes from this pregnancy revealed the same balanced translocation inherited from the mother. Although prenatal aneuploid screening is quite specific and accurate, it is important for laboratories to be cognizant of unusual translocations or situations which could give rise to abnormal numbers of FISH signals in potentially clinically normal pregnancies. This study further supports the necessity to follow up all prenatal FISH studies with cytogenetics.

Case Report

An amniotic specimen from a 27 year old female with a known balanced t(9;18) was sent in for analysis. FISH studies on amniotic fluid specimen from two previous pregnancies result in two copies of the eighteen centromere and three copies of the p16 gene region at 9p21 resulted in unbalanced translocations exhibiting two normal chromosome 9’s and a der(18), resulting in extra chromosome 9 material. G-band analysis determined that both of these previous amniocentesis samples had unbalanced translocations exhibiting two normal chromosome 9’s and a der(18), resulting in extra chromosome 9 material. Studies on the current amniocentesis specimen were negative for aneuploidy of p16 suggesting that this pregnancy did not have an unbalanced translocation. However, studies did show three copies of the CEP18 signal in interphase FISH analysis. Due to the unexpected FISH result, the mother’s archived lymphocytes were analyzed to determine whether the mother exhibited a CEP18 signal pattern that was similar to the signal pattern observed in the current amniocentesis interphase FISH. Upon analysis of the metaphase cells from this lymphocyte specimen, it was determined that the chromosome 18 centromere signal was split suggesting that the current pregnancy had the same balanced translocation that was observed in the mother.

Conclusion

Based on the possible implications of a false trisomy report, it is imperative to follow-up all rapid prenatal FISH studies with cytogenetics. Maternal chromosomes should be screened in addition to rapid FISH to rule out the presence of balanced translocations.

Figure 1

Rapid interphase FISH aneuploid screen on amniotic fluid. All interphase cells show three 18 centromere signals, which is indicative of trisomy 18; however, two of the signals were less intense than the other 18 centromere signal. It was later determined that one of the CEP18 signals was split based on analysis of archived maternal lymphocytes.

Figure 2

Metaphase analysis of archived maternal lymphocytes indicates a split of the CEP18 signals as a result of a balanced translocation involving the 18 centromere region.

Figure 3

Metaphase G-band analysis of cultured amniocytes. The analysis revealed a balanced translocation involving a t(9;18), indicating the balanced translocation was inherited from the mother.

Figure 4

Metaphase G-band analysis of maternal peripheral blood specimen. The analysis revealed a balanced translocation involving a t(9;18).