



Clinical Vignette: SMALL MARKER CHROMOSOME IDENTIFIED BY CHROMOSOMAL MICROARRAY ANALYSIS

This case illustrates the clinical utility of prenatal array CGH

A 36-year-old woman at 17.3 weeks' of gestation was referred for prenatal chromosome analysis due to advanced maternal age and club foot seen on ultrasound. No evidence of numerical abnormalities for chromosomes 13, 21, 18, X and Y were detected by interphase fluorescence in situ hybridization (FISH). Chromosome analysis on cultured amniocytes showed male chromosomes with mosaicism for an additional small marker chromosome: 47,XY,+mar[9]/46,XY[6] (Figure 1). Parental karyotypes were normal. Microarray analysis was performed and results detected a gain of ~6.1 of the the short arm of chromosome 17 (Figure 2). Confirmatory FISH on interphase cells consistently demonstrate three distinct signals. While metaphase FISH show two normal 17 chromosomes in addition to the marker chromosome 17p, signifying a duplication of 17p (Figure 3). The marker was determined to be a gain of 17p consistent with mosaicism for partial trisomy 17p.

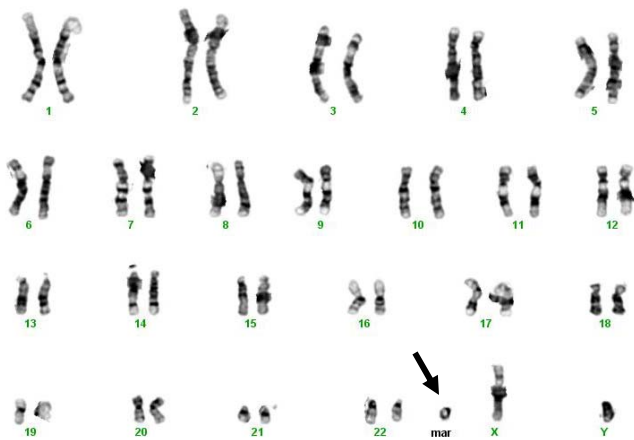


Figure 1. Chromosome karyotype of cultured amniotic fluid cells showing male chromosomes with mosaicism for an additional small unidentified marker chromosome: 47,XY,+mar[9]/46,XY[6]

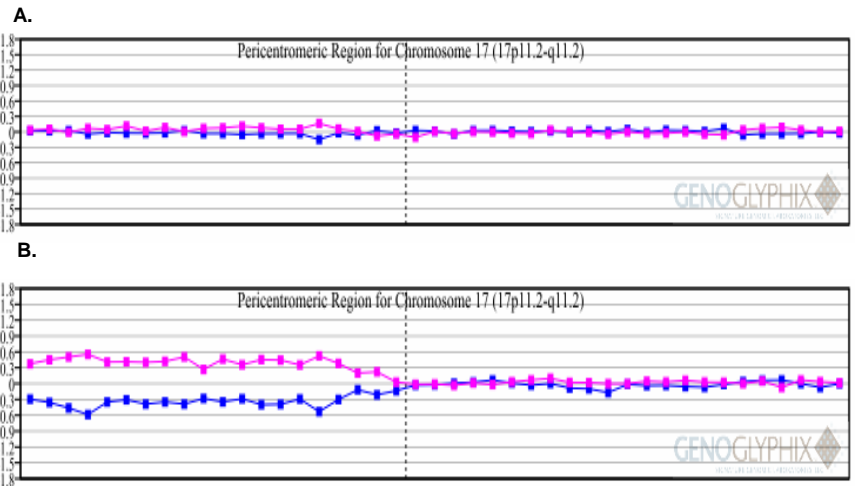


Figure 2. Microarray plots for a single-copy gain of 17p11.2-p11.1. Each clone represented on the array is arranged along the x-axis according to its location on chromosome 17 with the most distal/telomeric p-arm clones on the left and the most distal/telomeric q-arm clones on the right. The blue line represents the ratios for each clone from the first slide for the patient (control Cy5/patient Cy3), and the pink line represents the ratios for each clone obtained from the second slide for the patient in which the dyes have been reversed (patient Cy5/control Cy3). (A) Plot for a normal chromosome 17 showing a log₂ ratio of 0 for all clones. (B) Plot showing a single-copy gain of 20 BAC clones at 17p11.2p11.1, approximately 6.1 Mb in size.

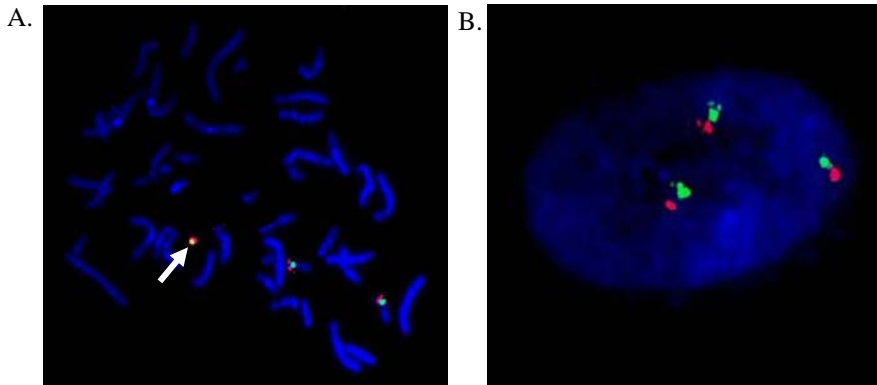


Figure 3. Cells derived from amniotic fluid for confirmatory FISH analysis. FISH images showing the marker chromosome derived from 17p. (A) Metaphase FISH with probe RP11-1149K20 from the RAI1 locus on 17p labeled in red and chromosome 17 centromere probe D17Z1 labeled in green as a control. The normal chromosomes 17 show one green and one red signal each. The arrow indicates the marker chromosome showing both signals. (B) Interphase FISH with chromosome 17 probes RP11-1149K20 labeled in green and RP11-849N15 labeled in red shows three signals for each probe, consistent with partial trisomy of 17p.