

# PRENATAL DETECTION OF A FAMILIAL $der(18)t(9;18)$ AND A *DE NOVO* BALANCED $t(7;11)$ : A COMPLICATED PREGNANCY AND OUTCOME



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## Abstract

A phenotypically normal woman with a  $46,XX,t(9;18)(p13.1;p11.21)$  had two consecutive pregnancies with unbalanced chromosome complements. Ultrasound investigation during her second pregnancy at 27 weeks gestation identified a small for gestational age fetus with short bones as well as some concerns about the renal structure. Chromosome analysis of amniotic fluid cells revealed  $46,XY,der(18)t(9;18)(p13;p11.2)$ . Peripheral blood chromosome analysis performed on both parents identified the mother to have a  $t(9;18)(p13.1;p11.21)$ . Interphase FISH studies on her third pregnancy at 14 weeks gestation revealed the presence of three copies of P16 (9p21 region) with two copies of 9 and 18 centromeres each. Chromosome studies confirmed that this pregnancy was complicated by an unbalanced translocation resulting in partial duplication of chromosome 9p and partial deletion of 18p. In addition to the  $der(18)t(9;18)(p13;p11.21)mat$  a *de novo* apparently balanced translocation involving the short arms of chromosomes 7 and 11 was detected. The presence of a second translocation was an unexpected finding. However, individuals with one chromosome abnormality have a slightly increased risk for other rearrangements. The karyotype of the fetus was described as  $46,XX,t(7;11)(p13;p13),der(18)t(9;18)(p13.1;p11.21)mat$ . At birth, the baby mostly had the features reported to be associated with duplication 9p including mild intrauterine growth retardation, deepset eyes, broad nasal bridge, downturned corners of the mouth, dysplastic ears with thick, upturned earlobes, short and broad neck, diastasis recti, brachydactyly with hypoplastic nails, 5th finger clinodactyly, hydronephrosis, and bicuspid aortic valve with thickening of the aortic and pulmonary valves. A duplication 9p is a well recognized chromosomal syndrome with consistent phenotype regardless of the size of 9p duplication, and predominates even in the presence of other deleted segments.

## Introduction

In 1970, Rethore et al. reported on four patients with duplication of 9p as "trisomy 9p syndrome." Since then, more than 100 patients were reported with duplication of various segments of 9p, usually derived from familial translocation. The phenotype of the duplication 9p syndrome was shown to be clinically recognizable and is characterized by growth and developmental retardation, microbrachycephaly, deep and wide-set eyes with down-slanting palpebral fissures, "globular" nose, down-turned corners of the mouth, prominent apparently low-set ears, and short fingers and toes with small nails [Centerwall and Beatty-DeSana, 1975]. In this report, we describe a family with an inherited translocation between chromosomes 9 and 18.

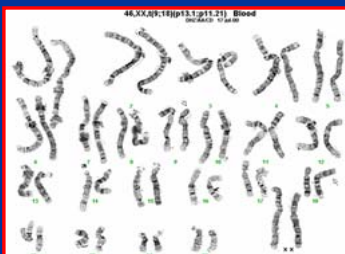
## Case Report

After ultrasound investigation during the patient's second pregnancy at 27 weeks gestational age identified a small for gestational age fetus with short bones and concerns about the fetal kidneys, an amniocentesis was performed. It should be noted that a triple screen was screened negative. Chromosome findings following culture of amniocytes revealed  $46,XY,der(18)t(9;18)(p13;p11.2)$  (Figure 1).

Figure 1

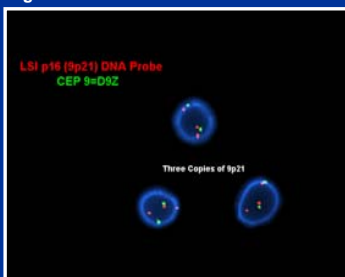


Figure 2



Peripheral blood chromosome analysis performed on both parents identified the mother to have a  $t(9;18)(p13;p11.21)$  (Figure 2).

Figure 3



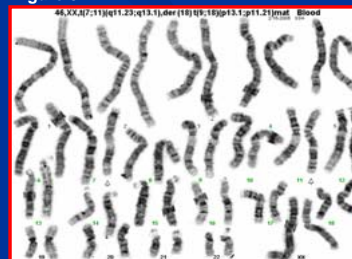
Interphase FISH studies on her third pregnancy at 14 weeks gestational age revealed the presence of three copies of P16 (9p21 region) with two copies of 9 and 18 centromeres each (Figure 3).

Figure 4



Subsequent chromosome studies confirmed that this pregnancy was complicated by an unbalanced translocation resulting in partial duplication of chromosome 9p and partial deletion of 18p. In addition to the  $der(18)t(9;18)(p13;p11.2)mat$  a *de novo* apparently balanced translocation involving the short arms of chromosomes 7 and 11 was detected. The presence of a second translocation was an unexpected finding. However, individuals with one chromosome abnormality have a slightly increased risk for other rearrangements. We would not expect the  $t(7;11)(p13;p13)$  to add any additional concerns. The karyotype of the fetus was described as  $46,XX,t(7;11)(p13;p13),der(18)t(9;18)(p13.1;p11.21)mat$  (Figure 4).

Figure 5



At birth, the baby mostly had the features reported to be associated with duplication 9p including mild intrauterine growth retardation, deep-set eyes, broad nasal bridge, down-turned corners of the mouth, dysplastic ears with thick, upturned earlobes, short and broad neck, diastasis recti, brachydactyly with hypoplastic nails, 5th finger clinodactyly, hydronephrosis, and bicuspid aortic valve with thickening of the aortic and pulmonary valves. Peripheral blood chromosome analysis was performed to further delineate the breakpoints of the  $t(7;11)$ . With the high resolution blood study, the karyotype of the baby was described as  $46,XX,t(7;11)(q11.2;q13.1),der(18)t(9;18)(p13.1;p11.21)mat$  (fig 5).

## Discussion

Trisomy 9p, monosomy 9p, and monosomy 18p are each well recognized syndromes. Case reports involving a translocation between chromosomes 9 and 18 resulting in an unbalanced chromosome complement are extremely rare. The spectrum of physical and developmental findings in duplication 9p syndrome is remarkably consistent despite the varying sizes of the duplicated segments and also involvement of a small deletion of another chromosome. A duplication 9p is a well recognized chromosomal syndrome with consistent phenotype regardless of the size of 9p duplication, and predominates even in the presence of other deleted segments.