

# Is Pericentromeric Inversion of the Heterochromatic Region of Chromosome 9 Involved in Couple Infertility?

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## Abstract

Pericentromeric inversion of the heterochromatic region of chromosome 9 has been reported in almost 4% of the cases of male infertility.

**Objective:** Determining the karyotype from an infertile couple scheduled to perform *in vitro* fertilization (IVF).

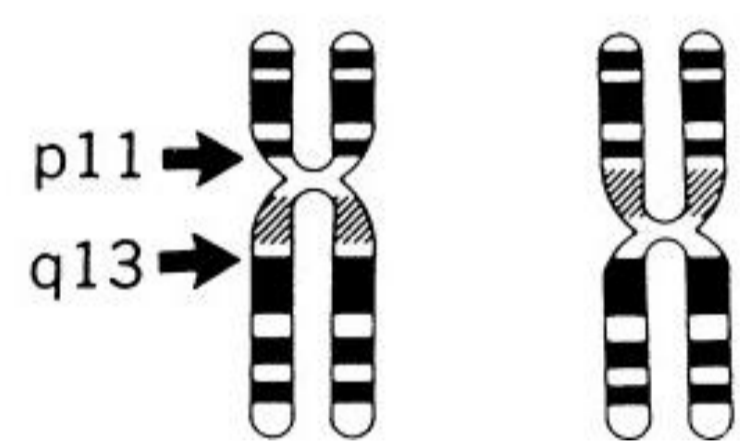
**Materials and methods:** Slides with metaphasic chromosomes were GTG-banded according to standard protocol for cytogenetic analysis (karyotype). FISH analysis – inverted DAPI (4'-6-diamidino-2-phenylindole) staining was used to confirm the anomaly in chromosome structure.

**Results:** The karyotype revealed modification of the heterochromatic region of both chromosome 9 in the male partner. The karyotype for female partner was normal. In case of male partner we suspected the pericentromeric inversion of the heterochromatic region of the long arm (q) of chromosome 9. Using Inverted-DAPI staining we confirmed the inversion on both chromosomes.

**Conclusion:** Karyotyping followed by FISH is useful to select appropriate couples to improve the success rate of IVF. Further investigation of the hormonal profile and seminal liquid analyses for male partner will show the involvement of the chromosomal abnormality in the hypothalamic-pituitary-testicular axis.

## Introduction

Chromosomal abnormalities, numerical - Klinefelter syndrome (Karyotype: 47, XXY) or Gonadal dysgenesis (Karyotype: 46, XX) and structural - Y chromosome microdeletions in (AZF region) or paracentromeric and pericentromeric inversions - are described as the main cause in male infertility.



Pericentromeric inversion of the heterochromatic region in long arm (q) of chromosome 9 is relatively common. According to studies, the incidence in normal population is between 1 and 3%.

Although this structural alteration is considered by some researchers as a normal family heteromorphism with Mendelian transmission without phenotypic consequences, there are researchers who argue that the incidence is increased in subjects studied for male infertility (approximately 5% of total inversion occurred) and the inversion may be associated with recurrent miscarriages and subfertility.

## Objectives

The case presented is the male partner of an infertile couple who addressed to our laboratory for karyotype evaluation before performing the procedure of *in vitro* fertilization (IVF).

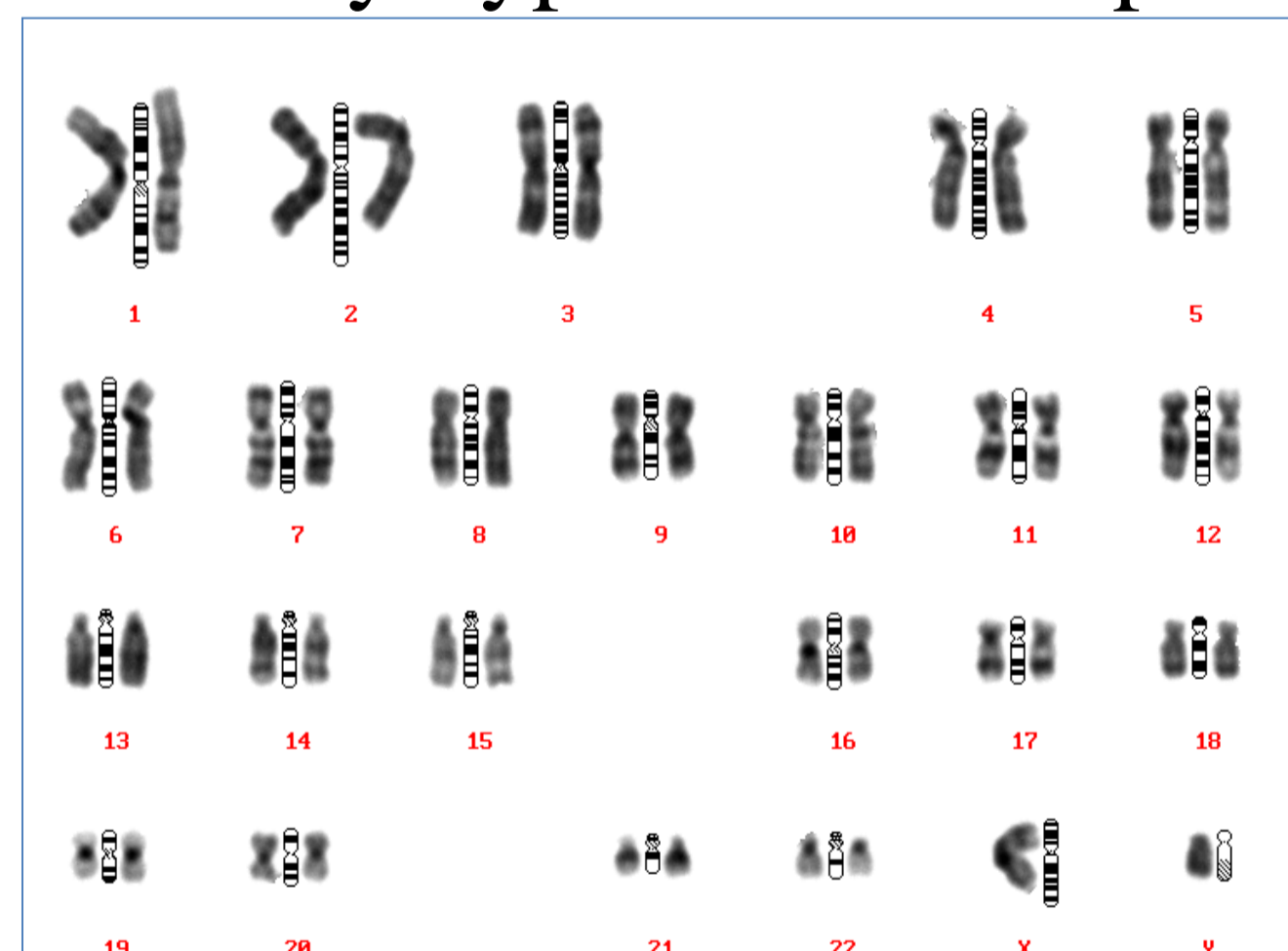
## Materials and methods

Peripheral blood was collected from both partners by venipuncture in the cubital vein to achieve lymphocyte cultures. Blood was seeded in culture medium RPMI 1640 with phytohemagglutinin (Euroclone-Antisel Selidis Romania) according to the protocol, and incubated for 72 hours at 37°C

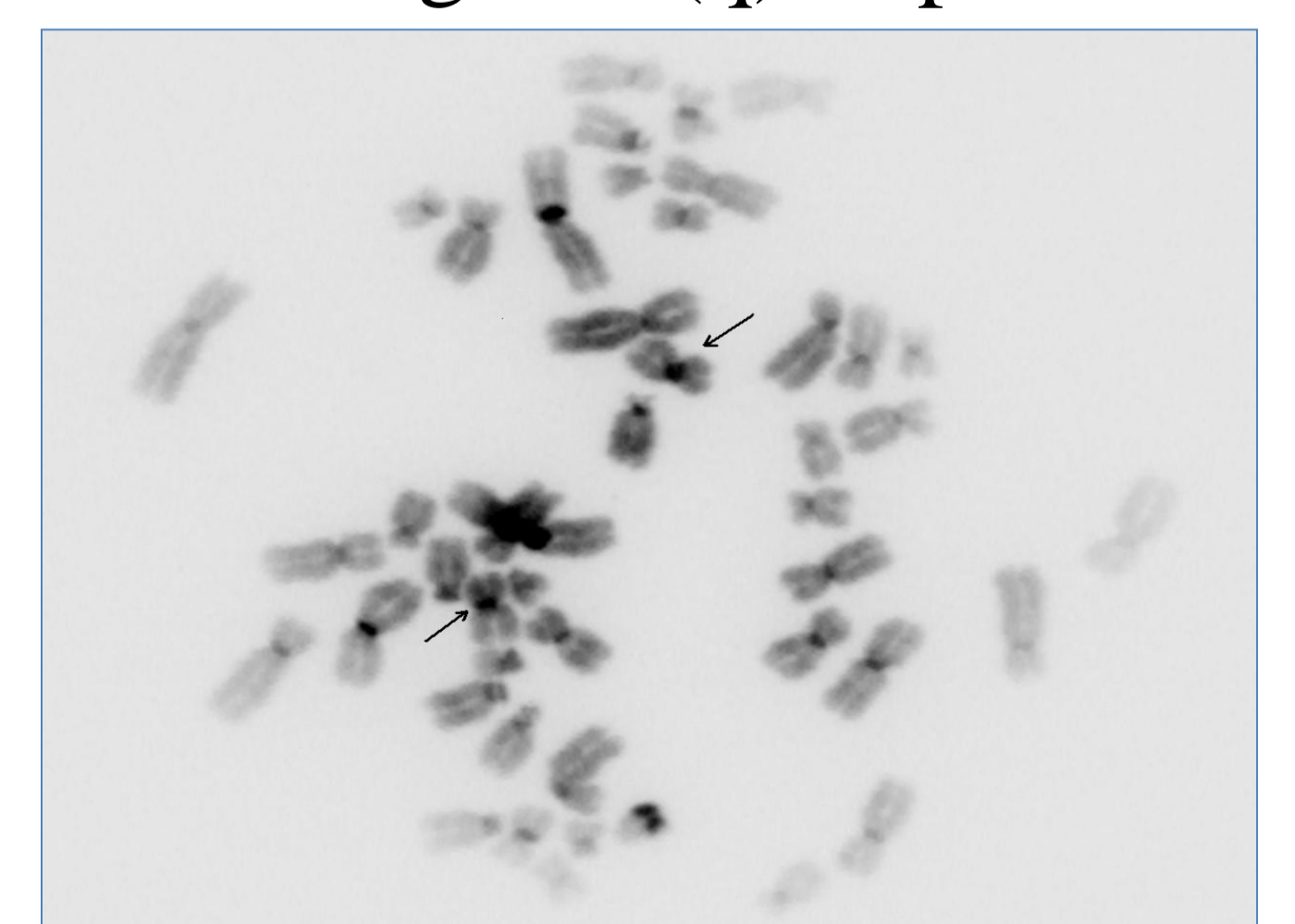
After incubation period, slides with metaphasic chromosomes were made and were stained using conventional G banding with 500 bands resolution, according to standard protocol for cytogenetic analysis (karyotype) and we used FISH staining – inverted DAPI for confirmation (Cytocell-Biogenetix Romania).

## Results

The karyotype for female partner was normal.



In case of male partner determination of karyotype highlighted changes in the heterochromatic area of the long arm (q) of both 9 homologues chromosome. 30 metaphases GTG banded were analyzed using Leica CW4000 Karyo program. In all metaphases studied were revealed changes in the pair 9 of homologous chromosome. We suspected pericentromeric inversion of heterochromatic area in the long arm (q) of pair 9 of homologous chromosome.



For confirmation we performed FISH staining - Inverted DAPI for heterochromatic region. FISH staining - Inverted DAPI confirmed that the proband is homozygous for this chromosomal abnormality and the karyotype is: 46,XY,inv(9)(p11q13).

Analyt	Rezult	Reference range
FSH	3.04 mIU/mL	1.5-12.4 mIU/mL
LH	4.09 mIU/mL	1.7-8.6 mIU/mL
Prolactin	14.90 ng/mL	1.04-15.2 ng/mL
Testosteron	3.79 ng/mL	2.49-8.36 ng/mL

The hormonal profile was normal and the spermogram shown normospermia with good mobility, without any changes in the sperm.

## Conclusions

To an infertile couple is important to assess karyotype for both partners, especially if recurrent miscarriages occur; Karyotyping followed by FISH is useful to select appropriate couples to improve the success rate of IVF.