

# Prenatal Diagnosis Of Catch22 Syndrome

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Deletions involving the long arm of chromosome 22 (22q11) are involved in various congenital heart diseases and congenital anomalies. In most cases, patients also have the features of DiGeorge Syndrome (DGS), Velocardiofacial Syndrome (VCFS), Shprintzen Syndrome, Conotruncal Anomaly Face Syndrome (CTAF), Caylor Cardiofacial Syndrome or Autosomal Dominant Opitz G/BBB Syndrome. CATCH22 is the summarizing name of all the syndromes caused by 22q11 deletion. We present a prenatally diagnosed case at 19<sup>th</sup> week of gestation with tetralogy of Fallot. Amniocyte tissue cultures resulted in normal karyotype at 550 band level. 22q11.2 deletion was detected by using DiGeorge/VCFS TUPLE1 (Cytocell) FISH probe. 22q11 testing is necessary in case of detection of conotruncal heart anomalies in pregnancies. Chromosome analysis is not enough in many cases and FISH testing combined with chromosome analysis is an effective way of diagnosing affected cases.

**Key Words:** Catch 22 syndrome, Prenatal diagnosis

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## Introduction

Deletions involving the long arm of chromosome 22 (22q11) are involved in various congenital heart diseases and congenital anomalies. The most frequent associating heart malformations are conotruncal anomalies (tetralogy of Fallot, interrupted aortic arch, ventricular septal defect, and truncus arteriosus).<sup>1</sup> In most cases, patients also have the features of DiGeorge Syndrome (DGS), Velocardiofacial Syndrome (VCFS), Shprintzen Syndrome, Conotruncal Anomaly Face Syndrome (CTAF), Caylor Cardiofacial Syndrome or Autosomal Dominant Opitz G/BBB Syndrome. CATCH22 is the summarizing name of all the syndromes caused by 22q11 deletion. Palatal abnormalities, particularly velopharyngeal incompetence, submucosal cleft palate and cleft palate, characteristic facial features, learning difficulties, immune deficiency, hypocalcemia, significant feeding problems, renal

anomalies, hearing loss (both conductive and sensorineural), laryngotracheoesophageal anomalies, growth hormone deficiency, autoimmune disorders, seizures (without hypocalcemia), and skeletal abnormalities are the most frequent features.

Prenatal diagnosis of this condition is available by cytogenetic or FISH, or molecular studies in most fetuses with the malformations listed above. We are here presenting a prenatally diagnosed case with cardiac malformations.

## Case Report

A 30-year-old pregnant woman was admitted for routine antenatal follow up at 19<sup>th</sup> weeks of gestation. She and her 31 year old husband were both healthy. They were not relatives and there was no positive family history. The current pregnancy was the woman's fourth pregnancy. Her previous pregnancies have resulted in first trimester spontaneous abortions. Cytogenetic analyses of the couple and thrombophilia mutation screening of the woman (Factor V Leiden, Protrombin 20210 and MTHFR 677- MTHFR 1298) revealed normal results. Obstetric ultrasound at the 19<sup>th</sup> week of pregnancy revealed tetralogy of Fallot which was confirmed by fetal echocardiography. The family was informed and amniocentesis was performed. Amniocyte tissue cultures resulted in normal karyotype at 550 band level. FISH was planned to investigate 22q11 deletion as the fetus has a conotruncal anomaly and 22q11.2 deletion was detected by using DiGeorge/VCFS

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TUPLE1 (Cytocell) FISH probe revealing the result [ish del(22)(q11.2q11.2)(HIRA-)] (Figure 1). Parental FISH studies were normal. Genetic counseling and termination of pregnancy was performed after informed consent was obtained from the parents.

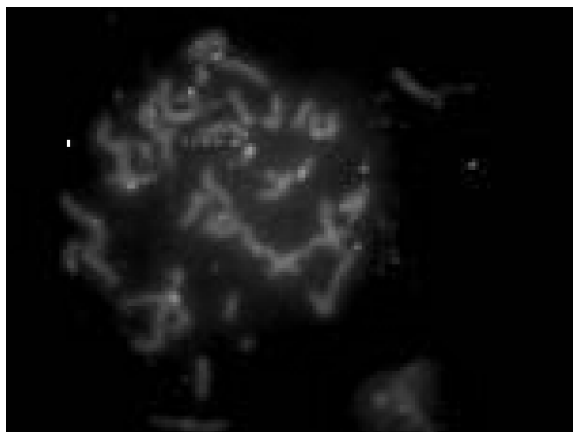


Figure 1: FISH testing by which 22q11.2 deletion was detected

## Discussion

22q11 microdeletion syndromes are frequent disorders. Estimates of prevalence vary from one in 4000<sup>2</sup> to one in 6395.<sup>3</sup> Given the variable expression of the deletion 22q11.2, the incidence is probably much higher than previously estimated. In a population-based study in Sweden, the mean annual incidence was 14.1 per 100,000 live births.<sup>4,5,6</sup> A U.S. population-based study conducted by the Centers for Disease Control (CDC) found an overall prevalence of about one in 6000 in whites, blacks, and Asians, and one in 3800 in Hispanics.<sup>7</sup> Therefore, prenatal diagnosis of this syndrome has an importance and the obstetricians must be alert in case of detection of cardiac and palatal anomalies. However, clinical spectrum of cases is very wide and very few cases have all characteristic features. Congenital heart defects are present in 74% of affected individuals and are the major cause of mortality (>90% of all deaths).<sup>8</sup> The major indications of investigations 22q11 deletion and frequency of 22q11 deletion were; interrupted aortic arc (50-80%), truncus arteriosus (35%), tetralogy of Fallot (15%), double outlet right ventricle (rare) and transposition of the great vessels.<sup>1</sup> The other most frequent indications were affected parents and previous affected child. The rate of 22q11 deletion in total of cardiac anomalies is 3%.<sup>9</sup>

The 22q11.2 deletion syndrome is diagnosed in individuals with a submicroscopic deletion of chromosome 22 detected by fluorescence in situ hybridization (FISH). Fewer than 5% of individuals with clinical symptoms of the 22q11.2 deletion syndrome have normal routine cytogenetic studies

and negative FISH testing. When a deletion 22q11.2 is suspected, it is recommended that routine cytogenetic analysis be performed at the time of FISH testing because a small percentage (<1%) of individuals with clinical findings of the 22q11.2 deletion syndrome have chromosomal rearrangements involving 22q11.2, such as a translocation between chromosome 22 and another chromosome. Parents may be affected in 8 % of cases.<sup>10</sup> Molecular methods like array CGH or MLPA can also detect the deletion but FISH is the most frequent method in use worldwide.

In summary, 22q11 testing is necessary in case of detection of conotruncal heart anomalies in pregnancies. Chromosome analysis is not enough in many cases and FISH testing combined with chromosome analysis is an effective way of diagnosing affected cases.

## Catch Sendromunun Prenatal Tanısı

Fromozom 22 (22q11) uzun kkolunda delesyonlar birçok konjenital kalp hastalıklarında ve konjenital anomalilerde görülür. Birçok vakada hastalarda DiGeorge Sendromunda, Velocardiofacial Sendromda (VCFS), Shprintzen Sendromda, Conotruncal Anomali Yüz Sendromunda (CTAF), Caylor Cardiofacial Sendromda veya Autosomal Dominant Opitz G/BBB Sendromunda. Görülen belirtiler olur. CATCH 22 22q11 delesyonuna bağlı tüm sendrom isimlerini özetlemektedir. Biz 19. haftada Fallot tetralojisi olan bir vakada prenatal tanı konan olguyu rapor ettik. 55 Band seviyesinde amniyotik sıvı doku kültürlerinde normal karyotip olarak sonuçlandı. DiGeorge/VCFS TUPLE1 (Cytocell) FISH probu kullanıldığında 22q11.2 delesyonu tesbit edildi. Kolotrunkal kalp anomalilerinde 22q11 testi yapmak gereklidir. Bir çok vakada kromozom analizi yeterli değildir ve buna ek olarak etkilenmiş vakaları yakalamak için FISH testi gereklidir.

**Anahtar Kelimeler:** Catch 22 sendromu, Prenatal tanı

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