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Case Report Open Access

A female with 46, X,i(Y)(q10)(Case Report)

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Abstract

Introduction: Differences in sex development (DSD) is a group ofrare conditions involving genes, hormones and reproductive organs, including genitals. The presence of an isochromosome Y, specifically 46, X,i(Y) (q10), is a rare chromosomal abnormality. This case report aims to detail the clinical presentation, genetic analysis, and management of a female patient with the 46, X,i(Y)(q10) karyotype.

Case Report: A 16-years-old girl with developmental disorders in childhood and suspected Turner syndrome was referred to Imam Khomeini Hospital in Tehran.

Results: The results of the karyotype was as follows: 46,X,i(Y)(q10). The results of FISH test is XY but this test unable to show isochromosomes.

Discussion: The karyotype 46,X,i(Y)(q10) indicates the presence of a structurally abnormal Y chromosome in a female, which is a rare occurrence. Females with 46,X,i(Y)(q10) may present with a range of phenotypes, from typical female characteristics to those resembling Turner syndrome, depending on the extent of Y chromosome material.

Keywords: Isochromosome- Sex development - Turner syndrome- Differences in sex development (DSD)

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Introduction

The presence of an isochromosome Y, specifically 46, X,i(Y)(q10), is a rare chromosomal abnormality that typically leads to atypical phenotypic manifestations in individuals assigned female at birth [1]. Isochromosomes result from a failure in the normal segregation of chromosomes during cell division, leading to the duplication of one arm while the other is lost. In this case, the isochromosome involves the long arm of the Y chromosome, which is significant given that the Y chromosome is traditionally associated with male sex determination and development [2].

Females with this chromosomal configuration may present with a range of clinical features, including variations in secondary sexual characteristics, reproductive anomalies, potential developmental delays and amenorrhea [3]. The phenotypic expression can vary widely, influenced by factors such as the degree of mosaicism and the presence of other genetic or environmental factors [4].

Disorders of sex development (DSD) are a congenital condition in which processes of chromosomes, gonads, and phenotypic sex is atypical [1, 2]. There are several types of DSDs and their effect varies on the internal and external reproductive organs and in some cases, it is not probably to make a definite diagnosis of the underlying condition [5]. The overall incidence of 46, XY DSD is estimated to be 1in 20,000 births [3]. The inability of the bipotential gonads to differentiate can

result in 46, XY DSD [4]. The 46, XY DSD female refers to phenotypic females with a male genotype. Subjects with 46, XY DSD have been diagnosed mainly through clinical and usually identified during an examination for delayed puberty or primary amenorrhea.46,XY agonadism characterized as lack of secondary sexual development, normal female external genitalia and have not gonadal structures and internal genitalia that represents an exceptional clinical finding [6].

Some findings suggest Swyer syndrome. Swyer syndrome is a rare disorder characterized by the failure of the sex glands (i.e., testicles or ovaries) to develop [7]. Swyer syndrome is classified as a disorder of sex development (DSD), which encompasses any disorder in which chromosomal, gonadal or anatomic sex development is abnormal. Girls with Swyer syndrome have an XY chromosomal makeup (as boys normally do) instead of an XX chromosomal makeup (as girls normally do). Despite having the XY chromosomal makeup, girls with Swyer syndrome look female and have functional female genitalia and structures including a vagina, uterus and fallopian tubes [8]. Girls with Swyer syndrome lack sex glands (ovaries). Instead of sex glands, women with Swyer syndrome have “gonadal streaks”, in which the ovaries do not develop properly (aplasia) and are replaced by functionless scar (fibrous) tissue. Because they lack ovaries, girls with Swyer syndrome do not produce sex hormones and will not undergo puberty (unless treated with hormone replacement therapy) [8]. Mutations in several different genes are known to cause Swyer syndrome. This condition can occur as the result of a new gene mutation or can be inherited in an autosomal dominant, autosomal recessive, X-linked or Y-linked manner [7].

Although SRY, the mammalian sex-determining gene on the Y chromosome (MIM 480000), is considered to be a master switch for testicular differentiation, its presence is insufficient to induce testicular development.2 Several other components of the male pathway have been identified, including Sox9,3 Dmrt1,4 Fgf9,5 Dhh,6 Sox8,7 and Dax1.8 WNT4 appears to be essential for sexual differentiation in women[8,9].An additional player was identified when in mice targeted ablation of M33, an ortholog of Drosophila Polycomb[9].

An isochromosome is an unbalanced structural abnormality in which the arms of the chromosome are mirror images of each other.[1] The chromosome consists of two copies of either the long (q) arm or the short (p) arm because isochromosome formation is equivalent to a simultaneous duplication and deletion of genetic material. Isochromosomes can be created during mitosis and meiosis through a mis division of the centromere or U-type strand exchange. The most common isochromosome is the X sex chromosome [10]. Acrocentric autosomal chromosomes 13, 14, 15, 21, and 22 are also common candidates for isochromosome formation [1]. Chromosomes containing smaller arms are more likely to become isochromosomes because the loss of genetic material in those arms can be tolerated [10].

This case report aims to detail the clinical presentation, genetic analysis, and management of a female patient with the 46, X,i(Y)(q10) karyotype. By examining this unique case, we hope to contribute to the understanding of the implications of Y chromosome abnormalities in females and provide insights into the potential clinical outcomes associated with this condition.

Case Report

A 16-years-old girl with developmental disorders in childhood and suspected Turner syndrome was referred to Imam Khomeini Hospital in Tehran. The patient experienced frequent abdominal pain during puberty, and after performing an ultrasound, a common cyst was reported. As the pain continued, the doctor ordered an abdominal MRI and after testing, the patient was diagnosed with uterine and ovarian cancer. Pathology results include; left ovary mass, malignant tumor, highly suspicious for germ cell tumor. It reported Yolk sac tumor and tumor size is 30 cm in greatest dimension. Pulmonary angiography is as follows: The patient has developed tachycardia following surgery. Multiple hypodense lesions are seen in the liver. Moderate ascites fluid is seen in the abdominal space. The patient underwent immediate surgery and is currently undergoing chemotherapy. Initially, the patient had a peripheral blood karyotype performed at another center. After the patient referred to our center, a peripheral blood FISH test was performed. The FISH test was repeated twice for her. The FISH test results did not match to the karyotype, so the patient had the peripheral blood karyotype test repeated at our center.

Results

The study patient was initially admitted to our clinic with suspicion of Turner syndrome. The initial diagnosis for the patient was isochromosome short arm of Chromosome X, i(Xp) with karyotype technique(G-Banding). To confirming this genotype, molecular cytogenetic FISH testing was performed. The result of the test was two green and red signals, with the green signal indicating the female gender and the red signal indicating the male gender. Since the result was not consistent with the patient's initial diagnosis, the FISH test was repeated and the test result showed male gender for the second time.

For further investigation and more accurate diagnosis, the peripheral blood karyotype test was repeated. The results of the karyotype was as follows: 46,X,i(Y)(q10). The FISH test was not able to detect isochromosome, but the karyotype clearly showed this abnormality. However, the initial diagnosis which was isochromosome X(P), was rejected. An isochromosome Y (q10) is a chromosome that has two identical arms, resulting from the abnormal division of a chromosome during mitosis or meiosis. In the case of the isochromosome Y (q10), the long arm of the Y chromosome is duplicated, while the short arm is lost. In this case, the risk of other congenital abnormalities or developmental problems may be increased due to the chromosomal abnormality. Isochromosome Y (q10) represents a rare chromosomal abnormality with significant clinical implications. Understanding its effects on development and fertility is essential for managing affected individuals. Ongoing research is needed to explore the long-term outcomes and best practices for care.

Discussion

The karyotype 46,X,i(Y)(q10) indicates the presence of a structurally abnormal Y chromosome in a female, which is a rare occurrence. The notation "i(Y)" refers to an isochromosome of the Y chromosome, where the long arm (q) is duplicated, and the short arm (p) is lost. This condition is significant as it can have implications for sexual development and fertility. Females with 46,X,i(Y)(q10) may present with a range of phenotypes, from typical female characteristics to those resembling Turner syndrome, depending on the extent of Y chromosome material. Common features may include short stature, gonadal dysgenesis, and primary amenorrhea. The presence of an abnormal Y chromosome can lead to ambiguous genitalia or the development of male characteristics, despite the individual being genetically female. Evaluation of gonadal function through imaging and hormonal assays is crucial for understanding the individual's reproductive potential. Women with this chromosomal anomaly may have reduced fertility due to ovarian dysgenesis. Options for assisted reproductive technologies should be discussed, including the potential for oocyte donation if ovarian function is compromised. Genetic counseling is essential for the patient and her family to understand the implications of the isochromosome. Risk of recurrence in future pregnancies should be addressed, particularly if there are family histories of chromosomal abnormalities. The psychological impact of living with a chromosomal anomaly can be significant. Support groups and counseling services may be beneficial. Review of existing literature reveals a limited number of reported cases of females with 46,X,i(Y)(q10). Most cases highlight a spectrum of clinical presentations, emphasizing the need for individualized assessment and management. Comparing this case with others in the literature can provide insights into the variability of clinical outcomes and the importance of early diagnosis.

Table 1. Results of the hormonal and serum evaluation.

Test	Patients value	Female reference range
Calcium	7.7	8.5-10.3
Phosphorus	3.1	2.6-4.5
FBS	96	70-100
Urea	16	15-50
Cr	0.5	0.5-10
Uric Acid	1.9	2.3-7.7
Albumin	1.8	3.5-5.2
CRP Quantitative	26	Adult < 6.0
Mg	1.7	1.8-2.6
K	3.7	3.5-5.0
Na	135	135-145
Beta-HCG Titer	<2.39	Negative : <5
AMH	0.41	0.4-7.8
Anti TPO	<10.0	Up to 35.0
T3	163.0	80-200
T4	9.1	5.0-12.5
TSH	3.6	0.4-5.0
Luteinizing hormone (LH)	21.2	Follicular Phase :1.1-11.6 Ovulatory Phase: 17.0-77.0 Luteal Phase: 0.4-14.7
Follicl Stimulation (FSH) Hormone	46.7	Follicular Phase: 2.8-11.4 Mid-Cycle Peak: 5.8-21.0 Luteal Phase: 1.2-9.0 Postmenopausal : 21.7-153.0

Conclusion

The case of a female with 46,X,i(Y)(q10) underscores the complexity of chromosomal abnormalities and their diverse clinical manifestations. A multidisciplinary approach involving endocrinologists, geneticists, and psychologists is essential for optimal management. Further studies are needed to elucidate the long-term outcomes and best practices for individuals with this rare chromosomal condition.

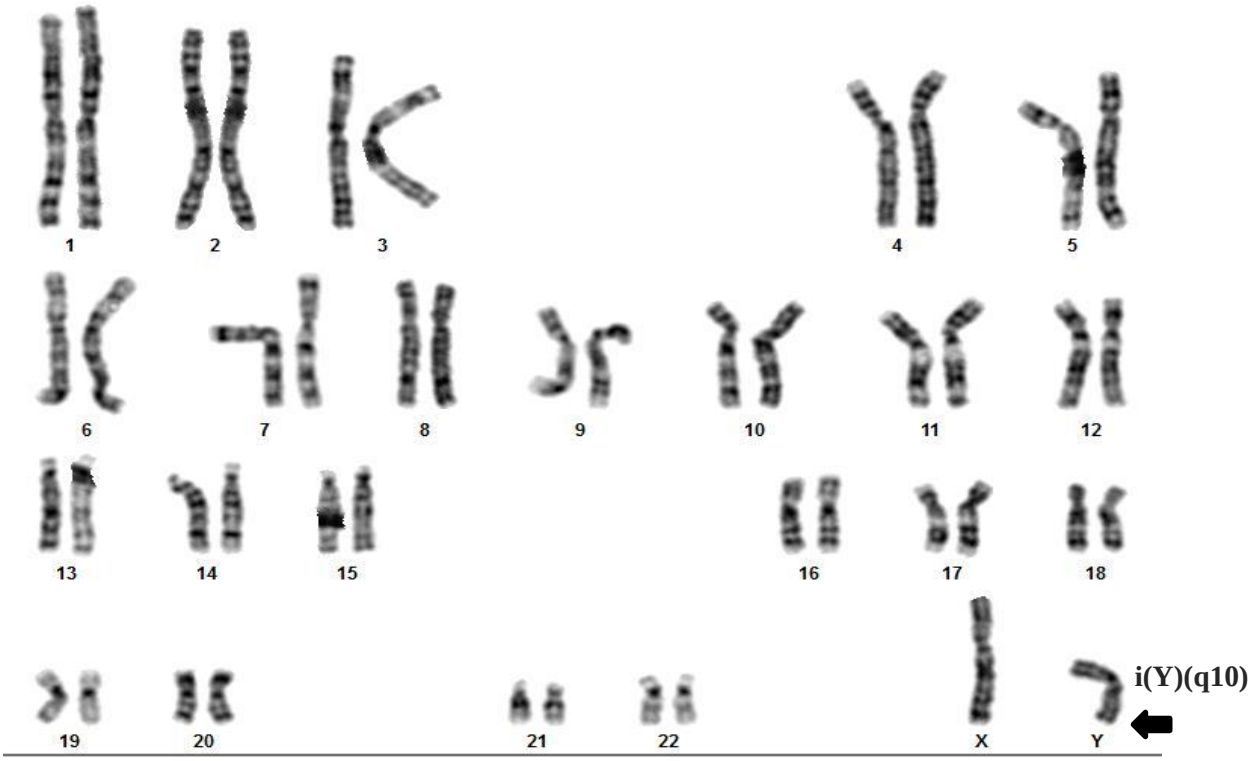

Figure 1. G-banding
Conclusion: 46, X,i(Y)(q10)

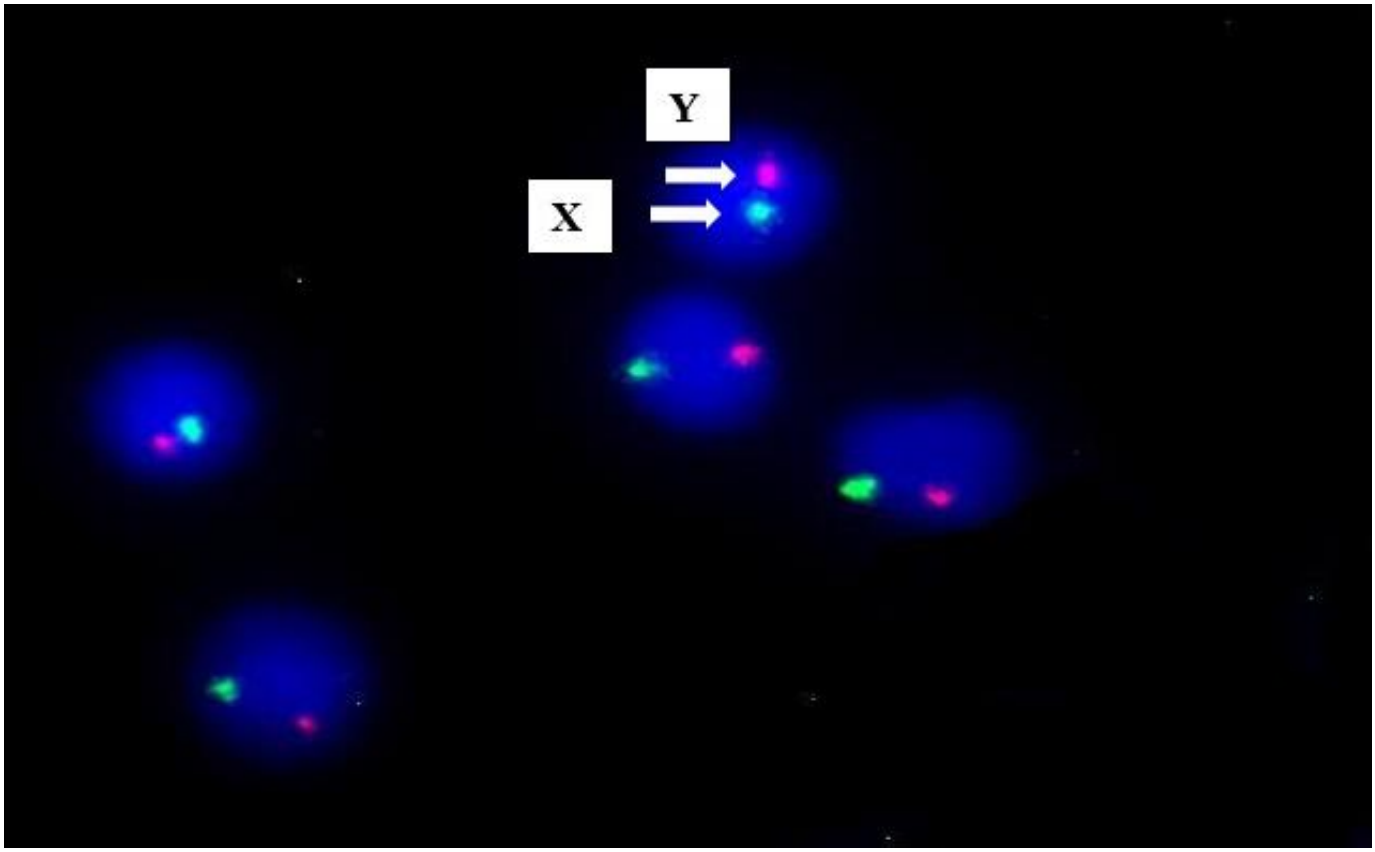

Figure 2. FISH Technique (**Red signals:** Y chromosome/ **Green Signals:** X chromosome)

Highlights

What Is Already Known?
46,X (Turner syndrome) and 46,XY (normal male) are the most common sex karyotypes. Yq isochromosomes i(Y)(q10) result in the deletion of the Y short arm (which contains the sex-determining gene SRY) and are frequently associated with a female or ambiguous external genitalia phenotype and gonadal dysgenesis.

What Does This Study Add?
Description of a rare/specific case of 46,X,i(Y)(q10) karyotype (or mosaicism involving this cell line) with a special focus on complementary molecular findings (such as methylation status or key gene expression analysis) that have been less addressed in previous reports. Providing a comprehensive diagnostic protocol (including FISH, SRY gene analysis, etc.) useful for differentiating this anomaly from other sex chromosome mosaicisms.

Authors' Contributions
Dr. Naseri : first author
others : revision

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Conflicts of Interest Disclosures
The authors report no financial or non-financial conflicts of interest relevant to this article.

Consent For Publication
Written informed consent for the publication of this case report was obtained from the patient.

Ethics approval
This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board/Ethics Committee of IKHC.

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The extent of AI use
AI tools were not used for data analysis or information gathering in this study.

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