OLGU SUNUMU / *CASE REPORT*

Clinical and Cytogenetic Evaluation of a Case with Mosaic 45,X/46,X,i(Y) Karyotype

Mozaik 45,X/46,X,i(Y) Karyotipli bir Olgunun Klinik ve Sitogenetik Değerlendirmesi

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ABSTRACT

Turner syndrome (TS) is a chromosomal disorder that affects only females and is typically characterized by a 45, X karyotype. In addition to the classic form, TS may present with various karyotypes. In this study, we report a rare mosaic karyotype, 45, X/46, X, i(Y)(p), identified in an 8-year-old girl who was referred for evaluation due to a preliminary diagnosis of TS. Conventional cytogenetic and FISH analyses revealed that 80% of the cells harbored an isochromosome Yp structure containing the SRY gene but lacking the Yq12 region. The clinical phenotype was completely female, and no follicles were observed in the ovaries on pelvic ultrasound. Due to the presence of Y chromosomal material, the patient was evaluated for the risk of gonadoblastoma and underwent prophylactic gonadectomy. This rare case highlights the importance of utilizing both karyotyping and FISH analysis in the diagnostic evaluation of Turner syndrome.Moreover, the case may also be considered within the spectrum of mixed gonadal dysgenesis (MGD), emphasizing the need for careful clinical and cytogenetic assessment.

Key words: *Turner syndrome, isochromosome, karyotype, FISH (Fluorescence ın situ hybridization)*

ÖZET

Turner sendromu (TS), yalnızca kadınları etkileyen ve tipik olarak 45 X karyotipi ile karakterize bir kromozomal hastalıktır. Klasik forma ek olarak, TS çeşitli karyotiplerle ortaya çıkabilir. Bu çalışmada, TS ön tanısı nedeniyle değerlendirme için sevk edilen 8 yaşında bir kız çocuğunda tanımlanan nadir bir mozaik karyotip olan 45,X/46,X,i(Y)(p)'yi bildiriyoruz. Konvansiyonel sitogenetik ve FISH analizleri, hücrelerin %80'inin SRY genini içeren ancak Yq12 bölgesinden yoksun bir izokromozom Yp yapısına sahip olduğunu ortaya koydu. Klinik fenotip tamamen dişi idi ve pelvik ultrasonda overlerde folikül gözlenmedi. Y kromozomal materyalinin varlığı nedeniyle hasta gonadoblastom riski açısından değerlendirildi ve profilaktik gonadektomiye alındı. Bu nadir vaka, Turner sendromunun tanısal değerlendirmesinde hem karyotiplemenin hem de FISH analizinin kullanılmasının önemini vurgulamaktadır. Ayrıca, olgunun mikst gonadal disgenezi (MGD) spektrumu içinde de değerlendirilebileceği, bu nedenle dikkatli klinik ve sitogenetik değerlendirme yapılmasının gerektiği vurgulanmaktadır.

Anahtar kelimeler: *Turner sendromu, izokromozom, karyotip, FISH (Floresan ın situ hibridizasyon)*

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Introduction

Turner syndrome (TS) is a chromosomal disorder affecting approximately 1 in 2.500 live-born females. Although the classic karyotype is 45, X, approximately half of patients present with mosaic or structural chromosomal abnormalities (1,2). Although uncommon, Y-chromosome material in Turner syndrome has important clinical implications due to its association with an increased risk of gonadoblastoma (3,4). We report a rare case of mosaic 45,X/46,X,i(Y)(p) diagnosed by conventional cytogenetic analysis and fluorescence in situ hybridization (FISH).

Case Presentation

An 8-year-old girl was referred to the Department of Medical Biology and Genetics with a preliminary diagnosis of Turner syndrome because of short stature and dysmorphic features. Physical examination revealed a webbed neck, cubitus valgus, attention deficit, and hyperactivity. There was no parental consanguinity, and both parents had normal karyotypes.

Pelvic ultrasonography revealed a hypoplastic uterus, absence of ovarian follicles, and a 30-mm right gonadal mass. Conventional GTG-banded karyotyping of 12 metaphases identified mosaicism: 45, X in six cells and 46, X, i(Y)(p) in six cells (Fig. 1). Fluorescence in situ hybridization analysis with SRY, DYZ1, and DXZ1 probes confirmed the presence of i(Y)(p). Eighty percent of nuclei showed one DXZ1 signal, two SRY signals, and no DYZ1 signal, while the remaining nuclei exhibited a 45, X pattern (Fig. 2).

Given the presence of Y-chromosomal material and the associated risk of gonadoblastoma, the patient underwent prophylactic bilateral laparoscopic gonadectomy in accordance with current clinical guidelines (3,5). Histopathological evaluation of the excised gonads revealed fibrotic streak tissue with occasional primordial follicle remnants. No gonadoblastoma or other malignant lesions were identified. The patient recovered well after surgery and was scheduled for regular endocrinological follow-up. The study was approved by the institutional ethics committee (Approval No. 2024/223), and written informed consent for publication was obtained from the patient's legal guardian.

Discussion

Mosaic Turner syndrome with an isochromosome of the short arm of the Y chromosome is an exceptionally rare cytogenetic finding. The identification of Y chromosomal material is clinically significant because it is associated with an increased risk of gonadal tumors, particularly gonadoblastoma (3–5). In the present case, conventional cytogenetic analysis suggested a structural Y chromosome abnormality, whereas FISH accurately demonstrated the presence of duplicated SRY signals and the absence of the Yq12 region, confirming an i(Y)(p) chromosome (6,7).

Despite the presence of SRY, the patient exhibited a completely female phenotype. This finding may be explained by tissue-specific mosaicism and the absence of Yq sequences, including the TSPY locus, which has been implicated in the development of gonadoblastoma (4,8). Although no malignant changes were

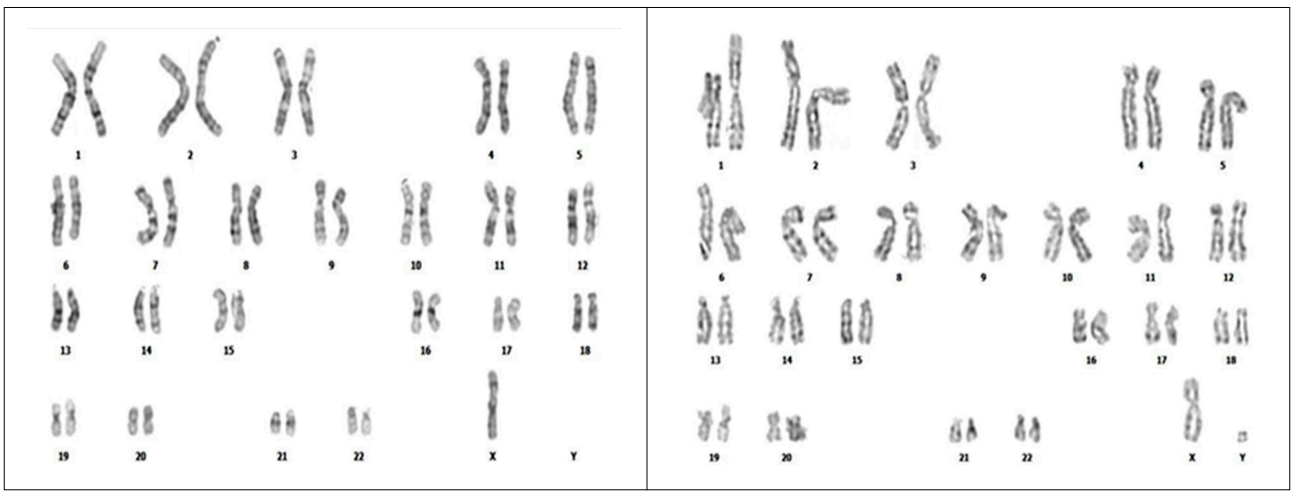

Figure 1. *Representative GTG-banded metaphase cells illustrating the mosaic karyotype. (A) Metaphase cell with a 45,X karyotype. (B) Metaphase cell with a 46,X,i(Y)(p) karyotype. Twelve metaphases were analyzed, including six cells with a 45,X karyotype and six cells with a 46,X,i(Y)(p) karyotype.*

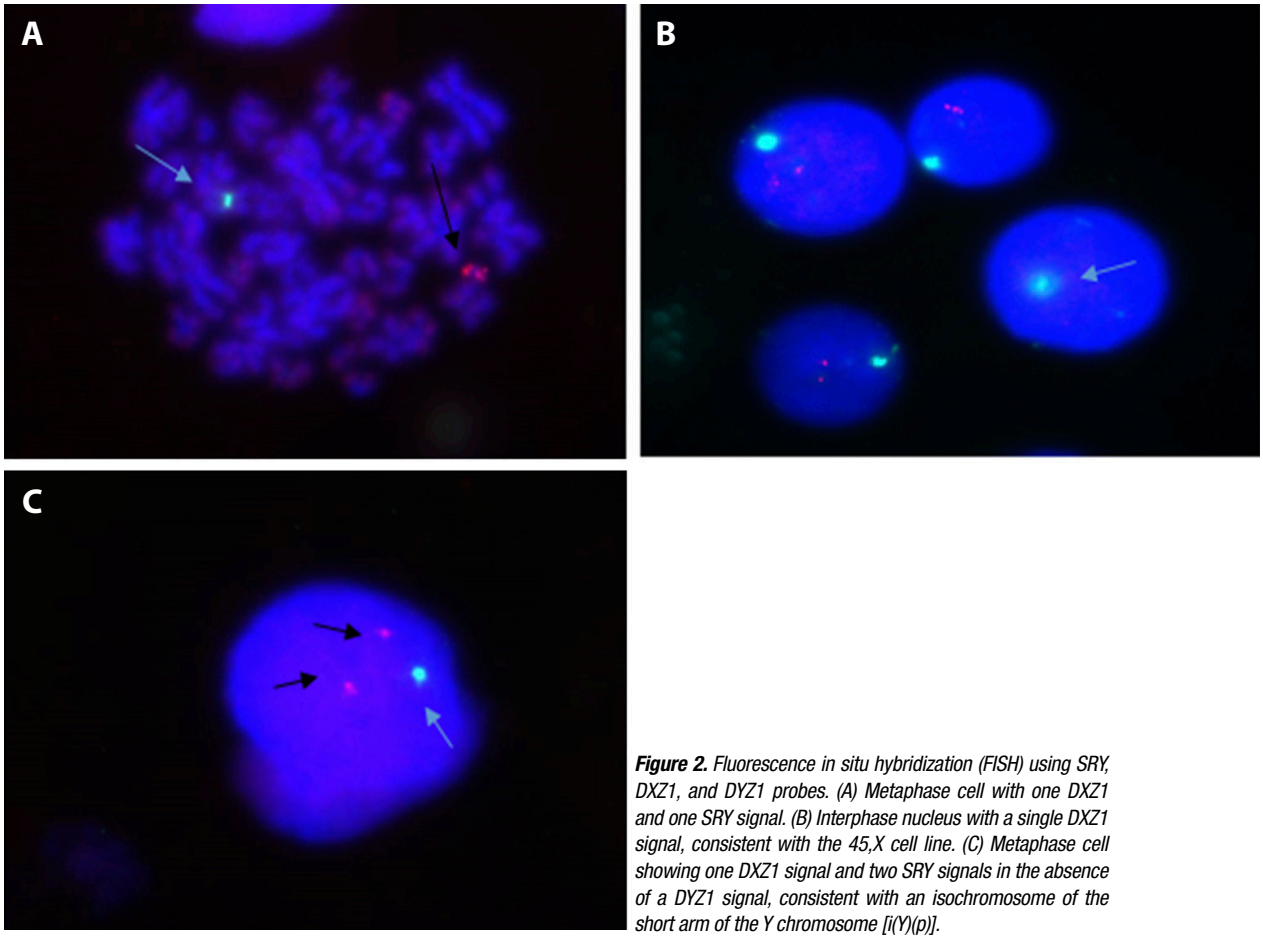

Figure 2. *Fluorescence in situ hybridization (FISH) using SRY, DXZ1, and DYZ1 probes. (A) Metaphase cell with one DXZ1 and one SRY signal. (B) Interphase nucleus with a single DXZ1 signal, consistent with the 45,X cell line. (C) Metaphase cell showing one DXZ1 signal and two SRY signals in the absence of a DYZ1 signal, consistent with an isochromosome of the short arm of the Y chromosome [i(Y)(p)].*

identified on histopathological examination, prophylactic gonadectomy was undertaken because the presence of Y-chromosomal material is associated with an increased risk of gonadoblastoma, and current international guidelines recommend surgical intervention in such patients with Turner syndrome (3,9). The present case demonstrates that the combined use of conventional cytogenetic analysis and FISH is valuable for accurately characterizing rare Y-chromosome abnormalities, thereby facilitating appropriate clinical management (2,10).

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