# A Novel Androgen Receptor Gene Mutation in a 46, XY Patient: Complete Androgen Insensitivity Syndrome

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## Background

Androgen insensitivity syndrome (AIS) is a disorder caused by a mutation of the gene encoding the androgen receptor (*AR*; Xq11-q12). According to the degree of androgen resistance, clinical manifestations range from phenotypically normal males with infertility to phenotypically normal women with primary amenorrhea. CAIS occurs due to inactivating mutations in the *AR* gene. So far, more than 800 mutations were detected in the *AR* gene. Among them, more than 500 mutations causing AIS have been reported.

## Aim

In this study, we report a novel *AR* gene mutation in an adolescent patient presenting with primary amenorrhea.

## Case Report

A 16-year-old patient complaining of primary amenorrhea was admitted to our department. According to past medical history, her breast development began when she was 12 years old. She was born at term with a birth weight of 3,500 grams and underwent a bilateral inguinal hernia operation at four months old. She is the first child of non-consanguineous parents.

**On physical examination;**

Weight: 96 kg (2.1 SDS)

Height: 174 cm (1.7 SDS)

Pubic hair: Tanner stage 1 with no axillary hair

Breast development: Tanner stage 5

External genitalia structure was totally consistent with a female phenotype.

## Clinical Progress

Laboratory tests revealed that basal luteinizing hormone (LH): 24.44 mIU/mL (N: 1.4–7.0 mIU/mL); follicle stimulating hormone (FSH): 1.36 mIU/mL (N: 1.3–7.0 mIU/mL); total testosterone: 5.29 ng/mL (N: 2.65-8.00 ng/mL); estradiol (E2): 37 pg/mL (N: <10 pg/mL); dehydroepiandrosterone sulfate: 712.2 µg/dL (N:10-248µg/dL); Δ-4 androstenedione (Δ-4 AS): 8.6 ng/mL (N: 0.3-3.3 ng/mL). Pelvic ultrasonography failed to identify bilateral gonads, an image in 30x7 mm, which could be related to a hypoechoic rudimentary uterus was obtained. Karyotype analysis was reported to be 46,XY, and SRY (+). Molecular genetic analysis of the patient revealed a hemizygous mutation c.1629_1630insA (p.R544KfsX8) in the *AR* gene, which had not previously been reported (Figure 1.). The patient was characterized as a female phenotype and bilateral gonadectomy was performed by the department of pediatric surgery and began oral estradiol treatment.

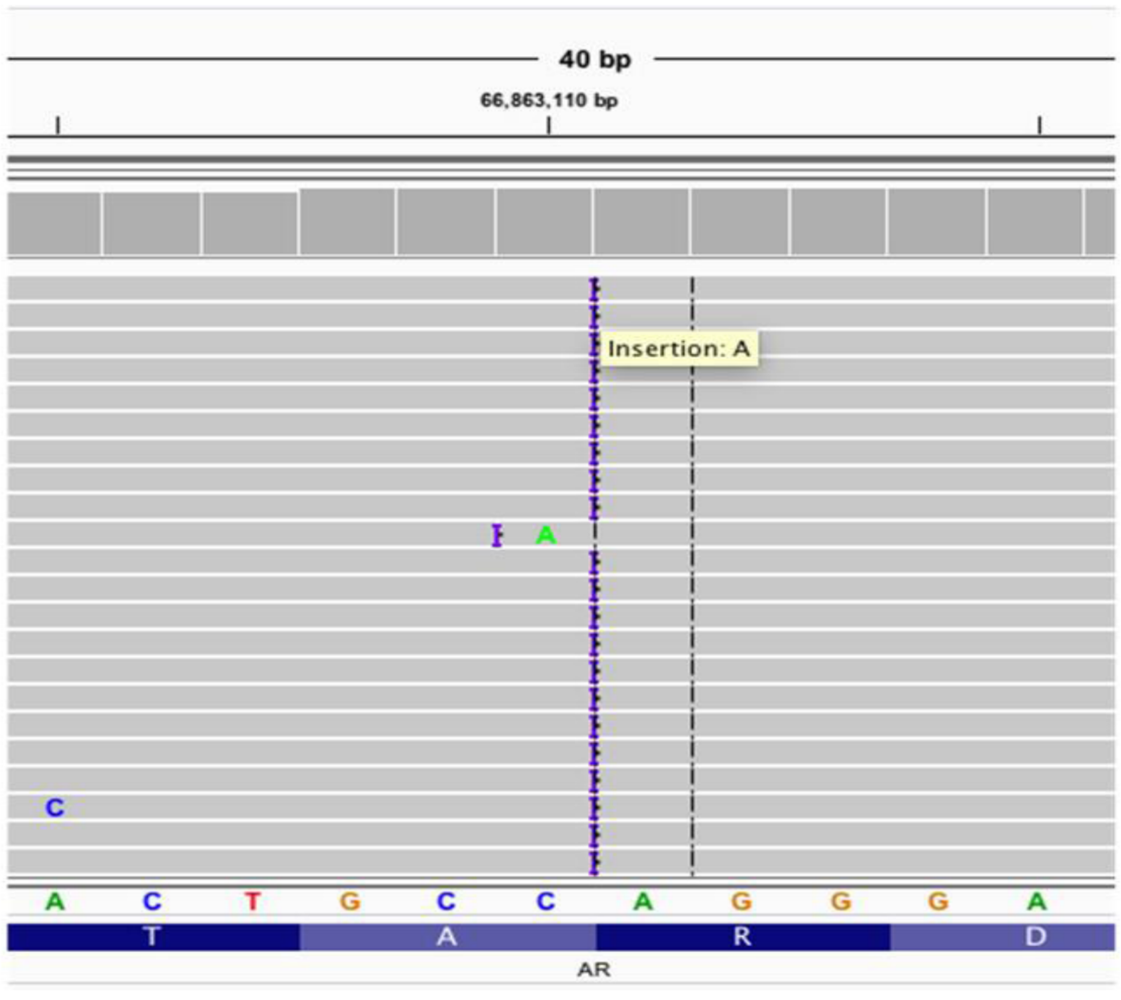


**Figure 1.** A novel hemizygous insertion mutation [c.1629-1630insA (p.R544KfsX8)] was detected in the *AR* gene with sequencing using the Illumina MiSeq system.

## Discussion

- AIS is the most common cause of 46,XY disorders of sex development (DSD) inherited in an X-linked recessive pattern.
- Complete androgen insensitivity syndrome should be considered in differential diagnosis of patients with female phenotype and breast development presenting with primary amenorrhea.
- 46,XY DSD should be considered in differential diagnosis of the patients with female phenotype presenting with bilateral inguinal hernia during the early infancy period
- Testicular tumor risk is reported to be between 5-10% in prepubertal cases with CAIS; however, the risk increases to 30% after puberty if a gonadectomy is not performed.

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