

PERSISTENT MÜLLERIAN DUCT SYNDROME ASSOCIATED WITH ANORCHIA CAUSED BY A COMPOUND HETEROZYGOUS MUTATION IN THE AMHR-II GENE

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Background

The persistent Müllerian duct syndrome (PMDS; OMIM #261550) is a rare 46-XY disorder of sex development, characterized by the persistence of Müllerian derivatives (uterus, Fallopian tubes) in otherwise normally virilized males. The condition is transmitted as a recessive autosomal trait and is caused in most cases by a defect in either the anti-Müllerian hormone (AMH) or the AMH type-II receptor (AMHR-II) genes.

Case presentation

A 9 years old male was born with bilateral cryptorchidism, scrotum hypoplasia and normal penis. There were no relevant conditions in his familiar (no consanguinity), or personal history. Blood karyotype showed normal result (46 XY; SRY+). Two **beta-hCG stimulation tests** (1000 Ux3 doses) were performed. First at 2.3 years of age (Testosterone post-hCG peak=150 ng/dl) and then at 8.9 years (Testosterone post-hCG peak = 15.8 ng/dl; normal values >200 ng/dl). Basal AMH at 9 years was also low (3.1 ng/ml (44–173 ng/ml)). Postnatal ultrasonography detected a tubular-shaped structure close to the urinary-bladder. Laparoscopy was performed at the age of 9. Structures resembling rudimental uterus and Fallopian ducts were found behind the urinary-bladder and were resected (Figures A & B). The histological-immunohistochemistry examination (Figures C & D) confirmed the Müllerian origin of both structures. No gonad tissue was found with the exception of epididymis tissue. Karyotype was performed in both structures with a normal 46-XY result. Sequencing of the AMHR-II confirmed compound heterozygosity. One of the mutations was the recurrent 27 bp deletion in exon 10. The other was a c.6101 C>T (p.Arg423Cys), in the intracellular serine/threonine kinase domain of the receptor (Figure E & F). This **mutation is described for the first time.**

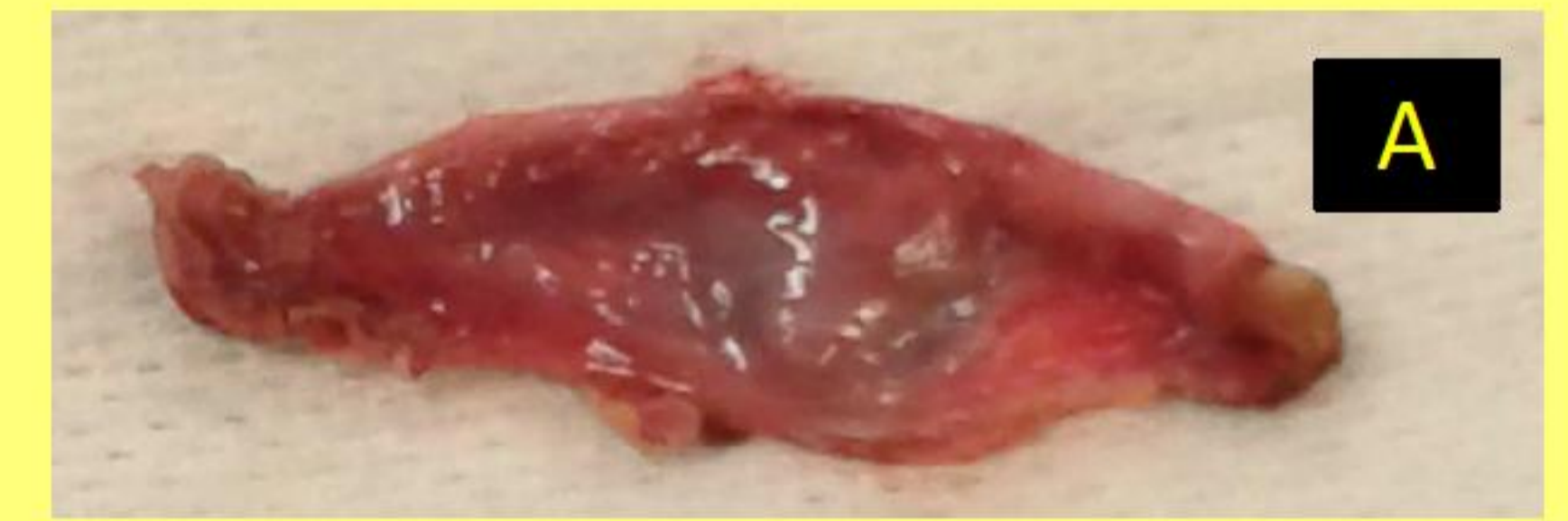


Figure A: Uterine remnant ; Figure B: left vas deferens

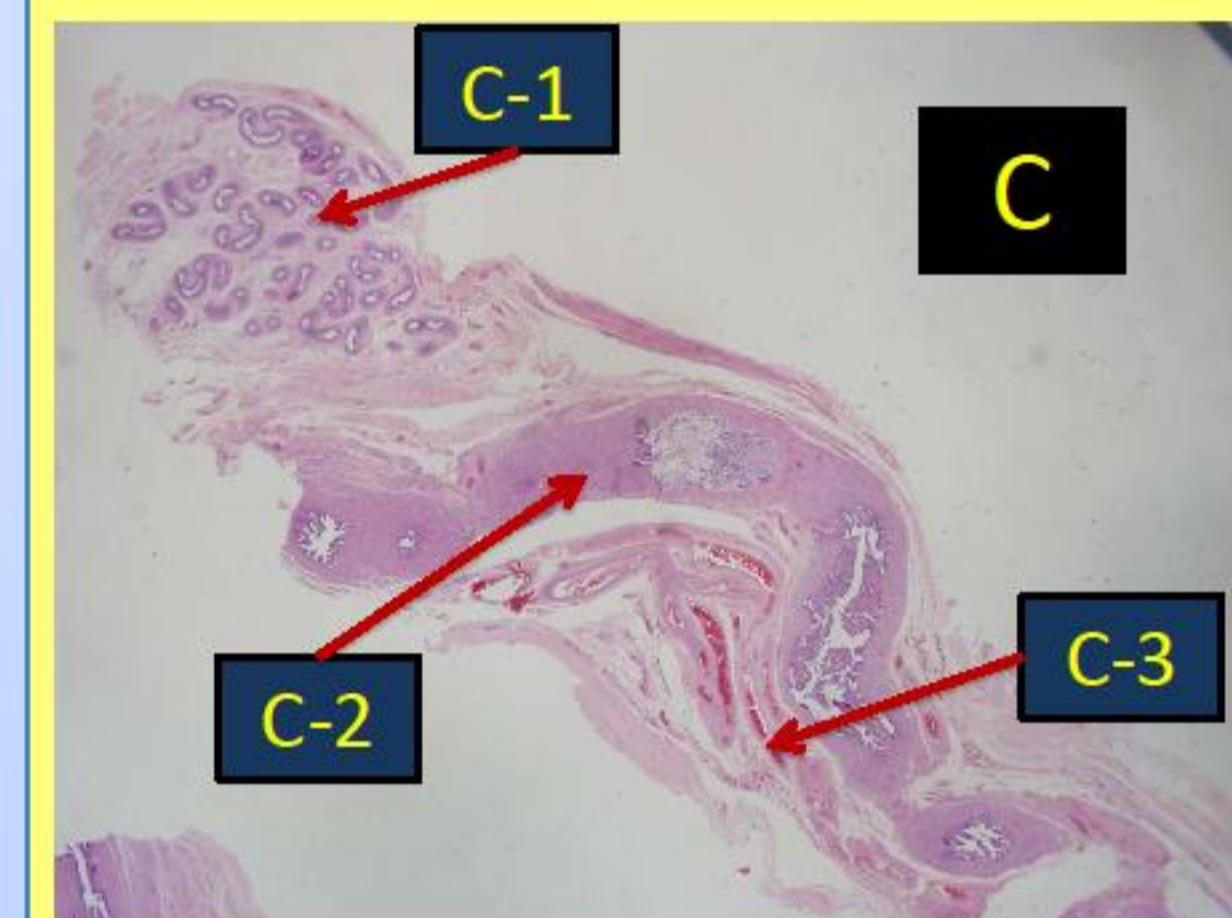


Figure C:
 C-1: epididymis
 C-2: Fallopian Tube
 C-3: Uterine tissue

Figure D:
 immunohistochemical staining for estrogen & progesterone receptors

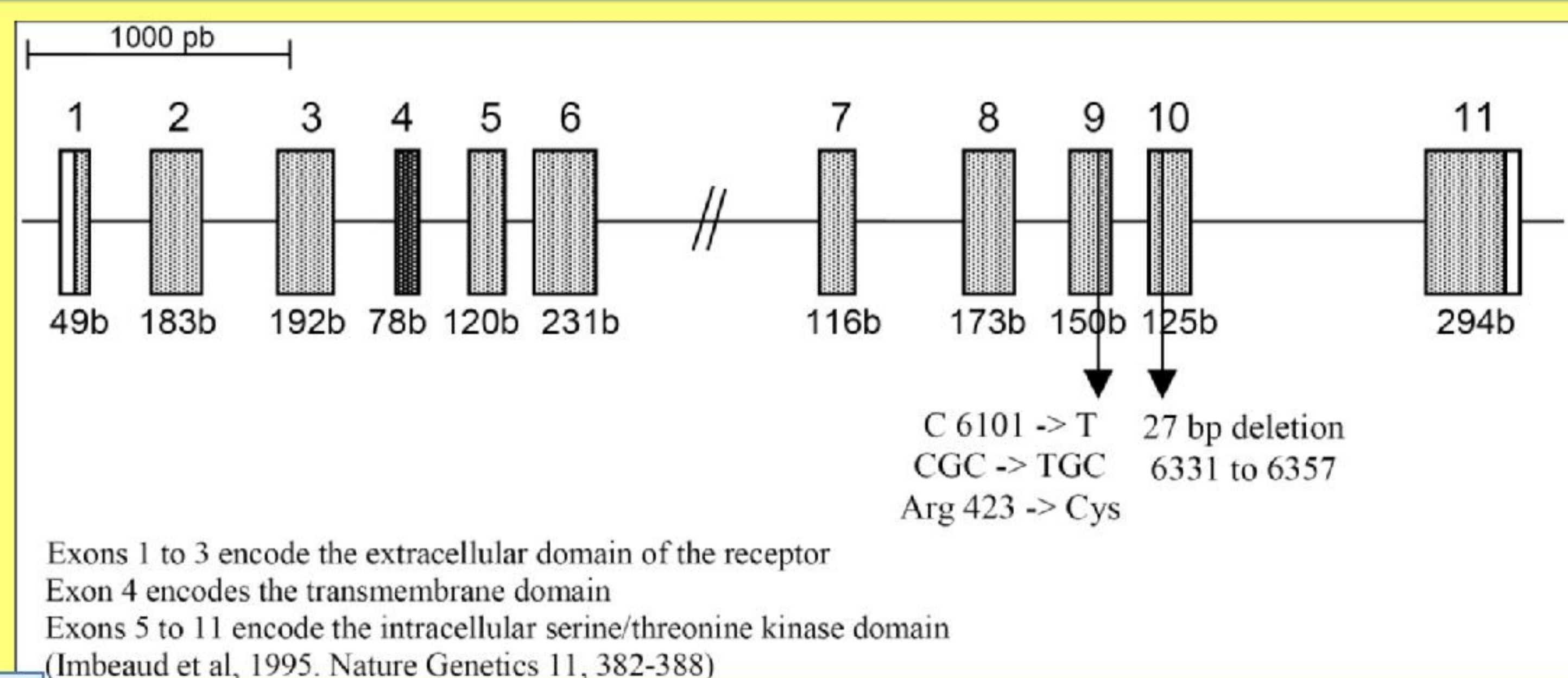
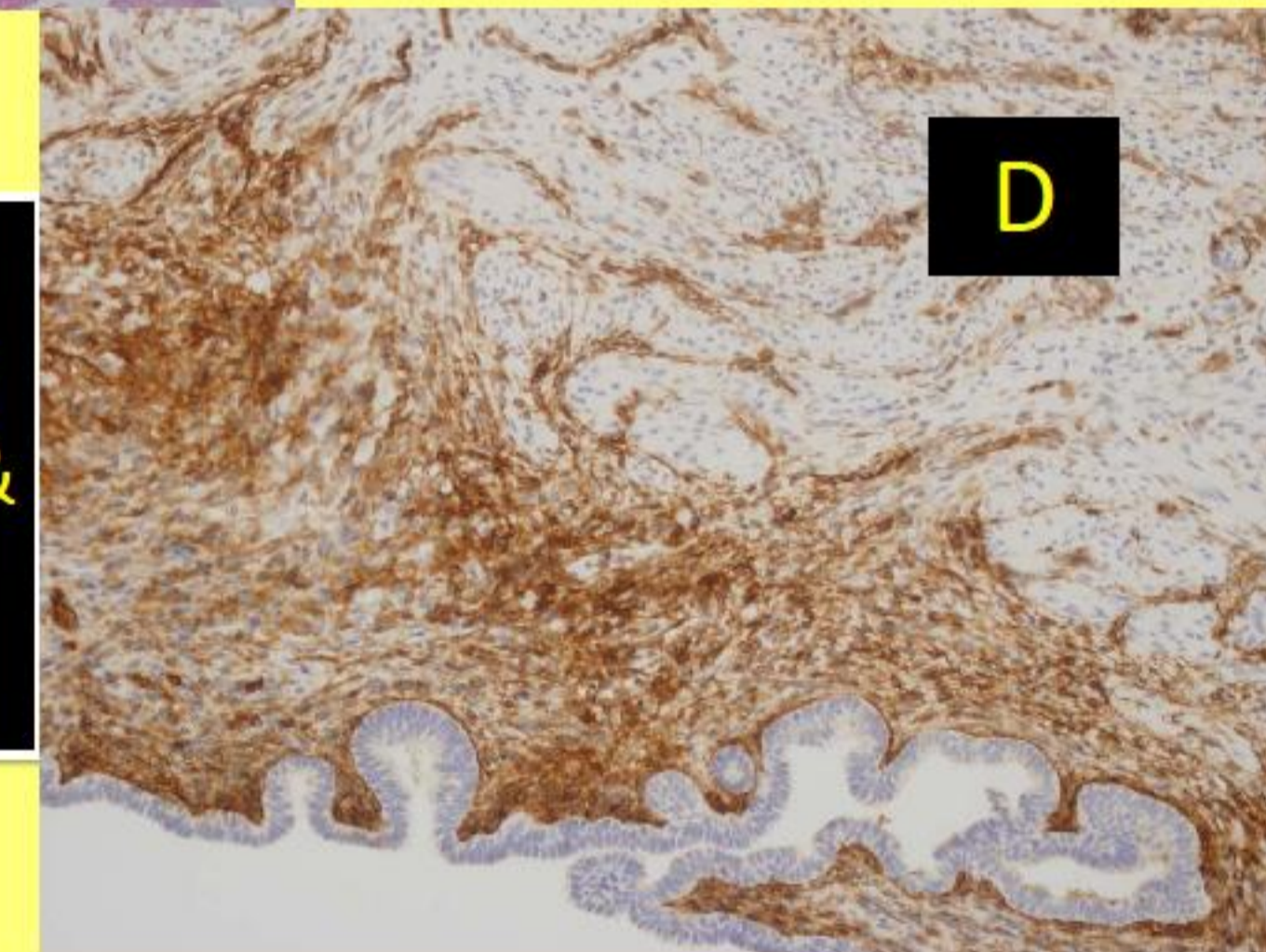
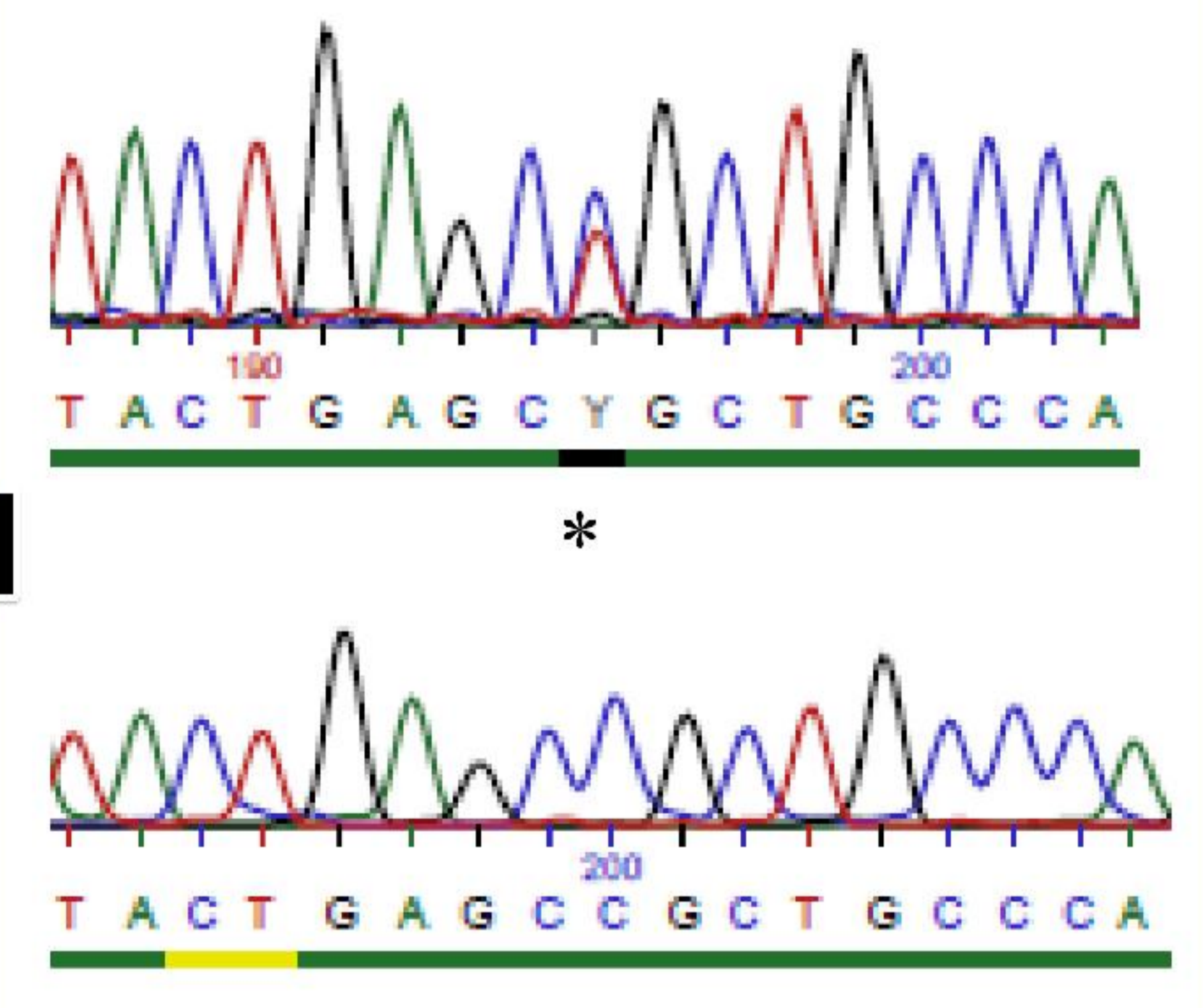


Figure E

Figure F



Conclusion

We describe a case of PMDS caused by a compound heterozygous mutation in AMHR-II; one of this mutations (c.6101 C>T; p.Arg423Cys) is described for the first time. The association with anorchia is occasionally seen, and is thought to be caused by the **increased risk of torsion and subsequent degeneration of the testes.** As the beta-hCG stimulation test, was normal at 2.3 years of age, and abnormal at 8.9 years, we hypothesize that the testicular degeneration occurred in the first years of life.

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