Novel AMH and AMHR2 Mutations in Two Egyptian Families with Persistent Mullerian Duct Syndrome

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OBJECTIVE

- Studying molecular pattern of 46,XY DSD with persistent mullerian ducts

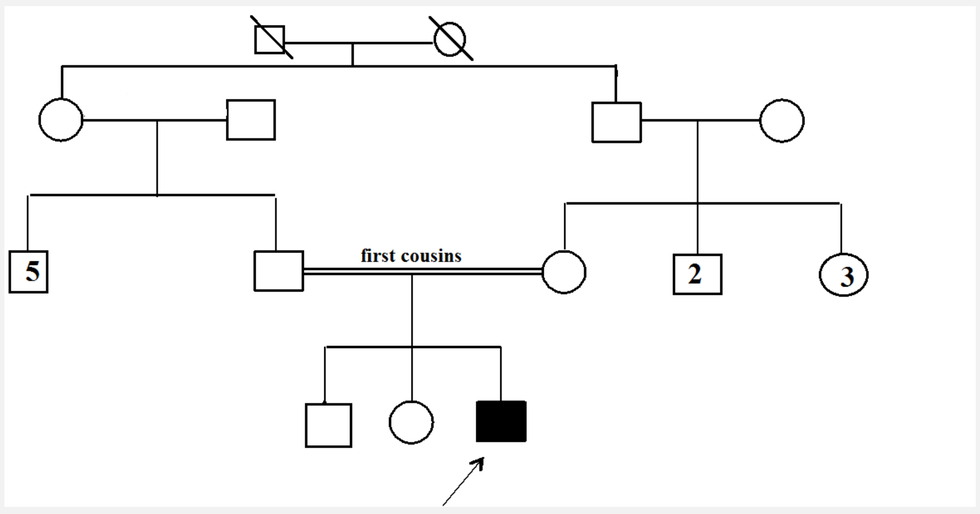
METHODS

- The entire coding regions of AMH and AMHR-II were amplified by PCR and directly sequenced in both directions
- The sequenced data were compared with the reference genomic and cDNA sequence of the two genes.

Graphs and tables

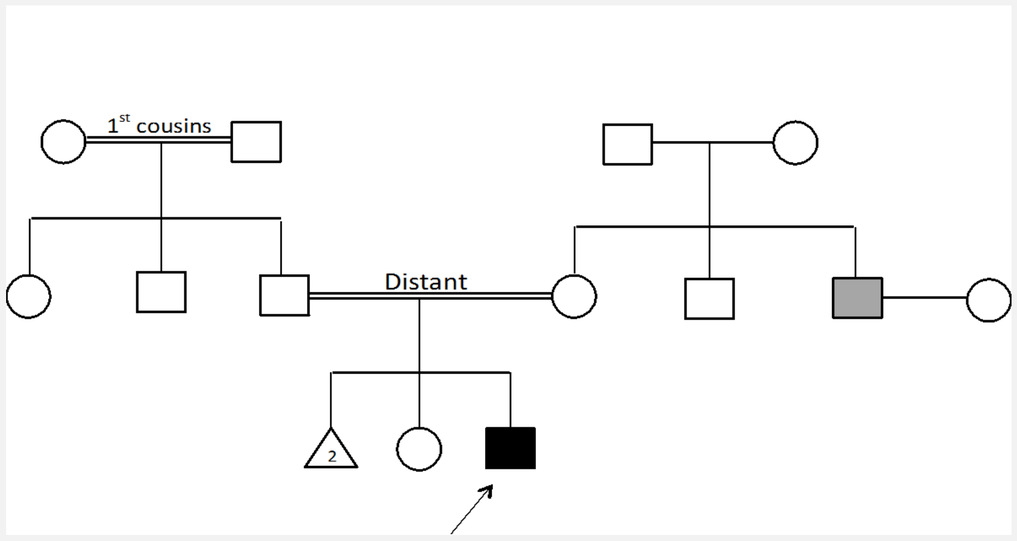
Patient (1)

Graph (1) Family Pedigree:



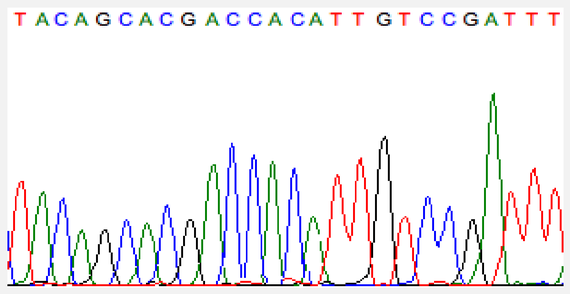
Patient (2)

Graph (3) Family Pedigree:



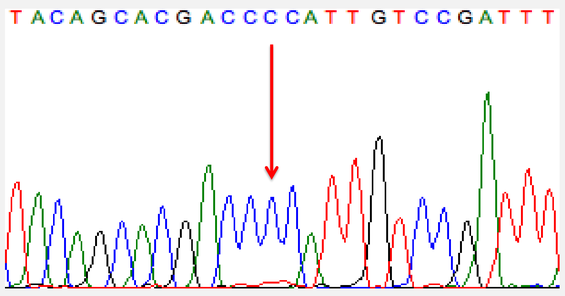
Graph (2): Portion of the sequencing electrophoregram showing The novel missense mutation identified in exon 6 of the *AMHR2*.

Normal:



Wild type

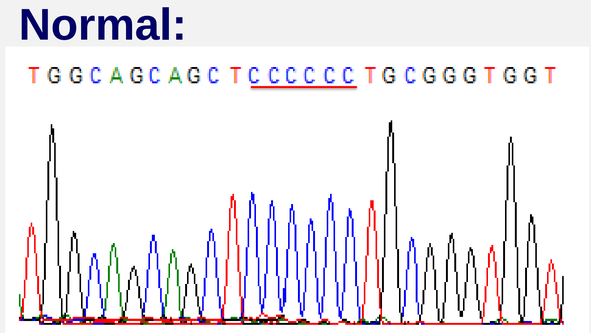
Patient:



c.767A>C (p.H256P)

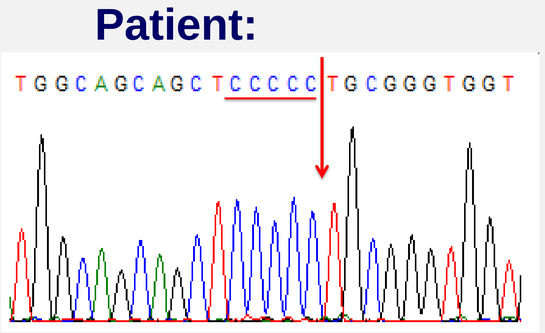
Graph (4): Portion of the sequencing electrophoregram showing the novel frameshift mutation identified in exon 1 of the *AMH* gene

Normal:



Wild type

Patient:



c.203_203delC (p.L70Cfs*7)

Table (1) Predicted effect of *AMH and AMHR2* mutations identified in the in this study.

Mutation		Gene	Exon	Mutation Taster	Polyphen2	SIFT
cDNA	Protein			(Score)	(Score)	
c.203_203delC	p.L70Cfs*7	AMH	1	Disease causing	NA	NA
c.767A>C	p.H256P	AMHR2	6	Disease causing (77)	Probably damaging (0.95)	Affect protein function

RESULTS

- Two Egyptian 46,XY DSD patients presented with **bilateral cryptorchidism,** and both had persistent mullerian ducts
- Mutational analysis of the AMH and AMHR2 genes identified **pathogenic mutations** in the two families confirming the diagnosis of PMDS
- **A new missense mutation in exon 6 of the AMHR2 gene was identified in patient 1(Graph 2).**
- **A novel single nucleotide deletion in exon 1 of the AMH gene was identified in patient 2(Graph 4).**
- The two mutations co-segregated perfectly with the phenotype in both families being homozygous in the probands and heterozygous in their respective parents
- The two mutations were **not present** in the 1000G and ExAC databases and are predicted to be **pathogenic** by various bioinformatics software **(Table 1).**

CONCLUSIONS

- **we presented two new Egyptian families with PMDS having novel mutations in the AMHR2 and AMH genes.**
- **Our results, *expands the mutational pattern* of this rare disorder and emphasize that persistent mullerian ducts should be included in *differential diagnosis of cryptorchidism.***

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Gonads & DSD

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