46,XY DSD due to biallelic *DHX37* gene mutations

P2-432

Mehmet Eltan[1], Didem Helvacioglu[1], Esra Arslan Ates[2], Zehra Yavas Abali[1], Serap Turan[1], Abdullah Bereket[1], Tulay Guran[1]

[1]Department of Pediatric Endocrinology and Diabetes, Marmara University School of Medicine, Istanbul, Turkey
[2] Department of Medical Genetics, Marmara University School of Medicine, Istanbul, Turkey

Case presentation

A 4.5-year-old boy

History

referred by pediatric urology due to penoscrotal hypospadias and bilateral cryptorchidism

- Uncomplicated pregnancy
- Birth weight 1115 g (-3.0 SDS) at 32 GW
- First cousin parents
- Neurodevelopmental milestones

  Walking at 2 years old, first words at 3 years old
- Severe myopia, operation for cleft palate
- Mild secundum ASD and muscular VSD

Physical examination

Height	116.0 cm	(-0.19 SDS)
Weight	15.7 kg	(-0.92 SDS)
Head circumference	48.0 cm	(-2.28 SDS)

Dysmorphic features

- micro-retrognathia
- anteverted ears
- long philtrum

- Penoscrotal hypospadias and bilateral cryptorchidism

  Stretched penile length: 3.8x0.8 cm

Clinical features

- Small for gestational age
- Mild neurodevelopmental delay
- Secundum ASD and muscular VSD
- Severe myopia
- Microcephaly
- Anteverted ears
- Long philtrum
- Cleft palate
- Micro-retrognathia
- Penoscrotal hypospadias
- Bilateral cryptorchidism
- Mild micropenis

Scrotal ultrasonography testes in the inguinal canal bilaterally

Laboratory

FSH	2.0 U/L
LH	< 0.2 U/L
AMH	36.9 ng/mL (8.9-109 ng/mL)

Total testosterone (hCG stimulation test)

Before	<0.07 µg/L
After	1.74 µg/L

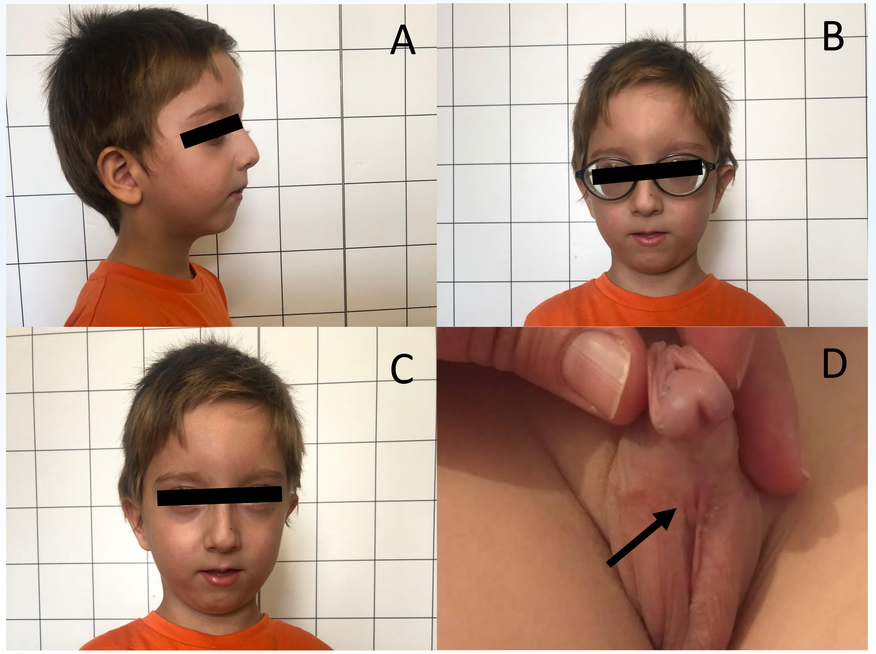

Figure A, B and C. Phenotypical appearance of the index

D. Black arrow demonstrates the penoscrotal hypospadias in the patient

*The parents gave their written informed consent to publish these images.

Genetic analyses

✓Karyotype analysis: 46, XY

✓Targeted next generation sequencing analysis: compound heterozygous for **c.703G>A (p.Val235Ile)/c.632C>T (p.Pro211Leu)** in the ***DHX37*** gene

✓Both variations were observed to be VUS with minör pathogenic evidence according to the ACMG classification

Learning Points:

✓Although monoallelic *DHX37* gene mutations are associated with 46,XY DSD, biallelic *DHX37* mutations may also cause 46,XY DSD in addition to concomitant neurodevelopmental disorders.