Presented at:
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

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.

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

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 minor pathogenic evidence according to the ACMG classification