Isolated microgastria as a single sonographic finding representing CHARGE syndrome.

Hadar Rosen\textsuperscript{1,3}, Reli Hershkowitz \textsuperscript{2,3}, Arie Koifman\textsuperscript{1,3}

\textsuperscript{1}Assuta University Medical Center Ashdod Israel \textsuperscript{2}Department of Obstetrics and Gynecology Soroka Medical Center \textsuperscript{3}Beer Sheva Ben Gurion University of the Negev, Beer-Sheva Israel

<table>
<thead>
<tr>
<th>Case Description</th>
<th>Genetic testing</th>
<th>Discussion</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 year old G1P0 Referred for genetic consultation due to Ambiguous Genitalia</td>
<td>Fetal DNA was obtained from cultured amniotic fluid. Parental DNAs were obtained from cultured peripheral blood cells. CMA demonstrated: Maternally inherited 3 Mb duplication on Xp21.3 encompassing NR0B1/DAX1 gene. NORB1/DAX1 maps to Xp21.3 The NR0B1 gene encodes an orphan member of the nuclear receptor superfamily that maps to Xp21 The human protein is designated DAX1, which stands for dosage sensitive sex-reversal (DSS), adrenal hypoplasia congenita (AHC) locus on the X chromosome, gene 1 pregnancy was terminated. Abortus presented with genital ambiguity small penis grade 3 hypospadias cryptorchidism. No Other external abnormality was noted.</td>
<td>Embryonic development needed to the determination of a sexual phenotype, which initially commit the bipotential gonad to either a testis or an ovary and direct normal morphogenesis of external genitalia, is complex. Disorders of sexual development (DSD), range from genital abnormalities to complete sex reversal, are a result of various abnormalities in those processes. Molecular basis underlying the pathology of DSD is far from complete. Chromosomal aneuploidy, overt and cryptic rearrangements, copy number variants (CNV’s), point mutations and even epigenetic alternation were all reported as possible ethology of DSD. Microdeletions and microduplications in the genome of children born with urogenital disorders and established de novo germline rearrangements are significant risk factors for developmental defects of human urogenital tract.</td>
<td>Our findings suggest that a sonographic finding suggestive of urogenital abnormality should prompt a comprehensive genetic investigation including karyotype, CMA, as well as specific gene mutations (as been previously described for DAX1). The maternal inheritance points to the important role of gene dosage in urogenital system development.</td>
</tr>
</tbody>
</table>

Case Description

- Ambiguous Genitalia:
  - Couple: Healthy
  - Non consanguineous
  - Caucasian
- Pregnancy:
  - Spontaneous
  - Basic anatomy at 23 weeks
  - Micropenis
- Repeat anatomy at 32 weeks
  - “Tulip sign”

Discussion