Ovotesticular Disorder of Sex Development (OT- DSD) among Egyptian DSD patients

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Introduction

Ovotesticular disorder of sex development (OT-DSD) is a rare disorder of sexual differentiation characterized by the presence of both testicular and ovarian tissues in the gonads of the same individual. The incidence of OT-DSD ranges from 3% to 10% of all DSD. Patients usually present at birth with ambiguous genitalia, and the majority show a 46,XX karyotype, with absence of the SRY sequence (Matsui et al., 2011; Khadilkar et al., 2015). The etiology may be due to 46,XX/46,XY chimerism as a result of fertilization of the ovum and the polar body or tetragametic fusion, mosaicism with various combinations (46,XX/47,XXX, 45X/46,XY) (Paula et al., 2015) or mutations of autosomal or sex chromosome genes involved in the testis-determining pathway.

Objectives

Clinical, histopathological and Cytogenetic studying of this rare form of Disorders of sex development (DSD) among Egyptian patients.

Patients:

Among 540 DSD patients studied over a period of 5 years (2010-2015) who were referred to the Clinical Genetics and endocrinology Clinic, NRC, Cairo, Egypt, we report 8 patients with OT-DSD. The patients constituted 6% of the patients presenting with ambiguous genitalia and 1.5% of all patients. Seven patients presented with ambiguous genitalia, One male patient presented with pubertal breast development. OT-DSD pathological diagnosis was confirmed in all patients.

Methods:

- Detailed clinical examination
- Anthropometric measurements
- Hormonal assay
- Imaging examinations
- Chromosomal analysis and Fluorescence in situ hybridization (FISH)
- Laparoscopy, laparotomy and gonadal biopsy with gonadal histopathological examination
- FISH on gonadal tissue cells

Results

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex of rearing</th>
<th>Age (year/month)</th>
<th>Laparoscopy</th>
<th>Pathology</th>
<th>Cytogenetic results</th>
<th>FISH on gonadal tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>13.00</td>
<td>Testis like gonad (infraginal region)/ovary, hypoplastic uterus</td>
<td>Right: Dysgenetic tests, left: ovary with some follicular activity</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(40), ins (dic(Y)p11.32)wcpY, XpY, SRY+, DYZ3++</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x[10] (DXZ1)x,1 (DXZ2)x,1 (XY)c (SRY)</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>00.09</td>
<td>Testis like gonad (infraginal region)/ovary, hypoplastic uterus</td>
<td>Both testicular and ovarian tissues within the left gonad. Rt. scrotal epididymal cyst.</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(19), 47,X,idic(Y) (p11.32)X,46,XX(Y)</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x,1 (DXZ1)x,1 (DYZ1)x,1 (DXZ2)x,1 (DXZ1)x,1 (DYZ2)x,1 (XY)c (SRY)</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>11.08</td>
<td>A uterus and a left gonad, right scrotal swelling.</td>
<td>Both testicular and ovarian tissues within the left gonad. Rt. scrotal epididymal cyst.</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(19), 47,X,idic(Y) (p11.32)X,46,XX(Y)</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x,1 (DXZ1)x,1 (DYZ1)x,1 (DYZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (XY)c (SRY)</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>3 years</td>
<td>Prepubertal uterus and bilateral gonads.</td>
<td>Bilateral ovotesticular. Right testicle, ovotesticular left testicle.</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(19), 47,X,idic(Y) (p11.32)X,46,XX(Y)</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (DXZ1)x,1 (DYZ1)x,1 (DXZ2)x,1 (XY)c (SRY)</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>12.00</td>
<td>Prepubertal uterus and no gonadal tissue visualized.</td>
<td>Left testicular, right ovotesticular.</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(19), 47,X,idic(Y) (p11.32)X,46,XX(Y)</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (XY)c (SRY)</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>25.10</td>
<td>Right side Fallopian tube and a small cystic ovary, uterus, left side gonad appeared as testes.</td>
<td>Testicular biopsy: testicular tissue showing small tubules, lined by sertoli cells.</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(19), 47,X,idic(Y) (p11.32)X,46,XX(Y)</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (XY)c (SRY)</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>00.06</td>
<td>Normal size left testis with minimal hydrosalpinx. Right gonad not detected.</td>
<td>Both testicular and ovarian tissues in the left gonad. Rt. Testicular tissue visualized.</td>
<td>46,XX(60)/46,XX, idic(Y) (p11.32)(19), 47,X,idic(Y) (p11.32)X,46,XX(Y)</td>
<td>nuc (DYZ3)x,Ycen (DYZ1)x,2 (DYZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (DXZ1)x,1 (DXZ2)x,1 (XY)c (SRY)</td>
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Conclusions:

- OT DSD should be considered as one of the differential diagnoses in cases of ambiguous genitalia with non palpable or asymmetrical gonads, pubertal gynecomastia, and cyclical hematuria, irrespective of the karyotype or internal genitalia.
- Gonadal biopsy is important in to establish diagnosing cases of sex chromosome mosaicism.
- Chromosome studies carried out on peripheral lymphocytes do not always reflect the proportion of cell lines in the gonads.

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