Genetic etiologies and gender outcomes of patients with disorders of sex development presenting with asymmetric gonads

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Introduction

- Individuals with mixed gonadal dysgenesis (MGD) present a 45,X/46,XY karyotype with a testis on one side and a streak on the other side. In contrast, ovotesticular disorder of sex development (DSD) is applied to an individual who has both well-developed ovarian and testicular tissues.
- Patients with MGD and ovotesticular DSD can present with asymmetric gonads. A differential diagnosis between the two conditions has important clinical implications for gender assignment.
- Differential diagnosis of these conditions is based on karyotype and pathological findings of gonads. However, it is difficult to differentiate without a knowledge of histological findings of the gonads and determine sex of rearing and to predict long-term outcomes.

Objectives

- This study investigated the clinical features, karyotype, sex of rearing, and pubertal outcomes of patients with MGD and ovotesticular DSD.

Methods

- This study included 25 patients with DSD who presented with asymmetric gonads. Presenting features, karyotype, sex of rearing, and pubertal outcomes were reviewed retrospectively.

Results

Clinical characteristics at presentation

- All 25 patients presented with ambiguous genitalia at median age of 1 month (range, 1 day to 1.6 years). Eleven of 14 patients with ovotesticular DSD (78.6%) and 10 of 11 patients with MGD (90.9%) presented with asymmetric gonads.
- They manifested labioscrotal deformity (60%), hypospadias (60%), clitoromegaly (36%), cryptorchidism (28%), and microopenis (20%).
- Mullerian duct remnants were found in 17 of 25 patients (68%).

Sex of rearing and clinical course

- Eight of 11 patients with MGD (72.7%) were raised as males, while 8 of 14 patients with ovotesticular DSD (57.1%) were assigned as males.
- Among 8 male-assigned patients with ovotesticular DSD, unilateral gonadectomy was performed in 6 patients. In 6 female-assigned patients, three patients underwent bilateral gonadectomy, while the other three underwent unilateral gonadectomy.

- Seven male-assigned patients with MGD underwent unilateral gonadectomy. Three female-assigned patients underwent bilateral (n = 1) or unilateral (n = 2) gonadectomy.

Fig. 2. Sex of rearing of patients with ovotesticular DSD and MGD

Table 1. Clinical and cytogenetic features of patients with ovotesticular DSD

<table>
<thead>
<tr>
<th>Patient</th>
<th>Karyotype</th>
<th>Mullerian duct remnants</th>
<th>Gonadectomy</th>
<th>Sex of rearing</th>
<th>EMS</th>
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<td>Unilateral gonadectomy</td>
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Fig. 1. Clinical presentation of patients with ovotesticular DSD and MGD

Diagnosis by pathological findings

- Gonadectomy or biopsy was performed at median age of 2.9 years (range, 1 month to 15.1 years). Subsequently, 11 patients were diagnosed with MGD, whereas 14 patients were ovotesticular DSD.
- In 14 patients with ovotesticular DSD, karyotype was 46,XX in 10 (71.4%), 45,X/46,XY in 3 (21.4%) patients, and 46,XX/46,XY in one patient (7.1%).
- In 11 patients with MGD, karyotype was 45,X/46,XY in 6 (54.5%), 46,XY in two patients (18.2%), and other mosaicisms in three patients (27.3%); 45,X/46,XY,del(Y)(q11.23), 45,X/46,XY,add(Y)(p11.3), and 45,X/47,XY,del(Y)(q12).

- Two patients with MGD and seven with ovotesticular DSD reached pubertal age. Among them, one phenotypic male with MGD and five patients with ovotesticular DSD showed spontaneous puberty.
- One male-assigned patient with ovotesticular DSD (Subject 7) showed gender identity problems and gender dysphoria at age 20 years and changed gender as female.
- The one female with MGD showed hypergonadotropic hypogonadism and has been treated with estrogen replacement therapy since 11 years of age.

Conclusions

- Patients who presented with asymmetric gonads have a wide clinical, cytogenetic, and histopathological spectrum.
- Pathological findings of gonads are necessary for differential diagnosis of MGD and ovotesticular DSD.
- Further studies are needed to establish appropriate treatment strategies and gender outcomes.

References


Disclosure statement

The authors have nothing to disclose.