Utility of Ultrasound and MRI in Patients with Disorders of Sex Development Undergoing Prophylactic Gonadectomy

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Disclosures

- My co-authors and I have no relevant financial or non-financial relationships to disclose.

Disorders of Sex Development (DSD)

- Defined as atypical development of chromosomal, gonadal, or anatomic sex
  - 46 XX DSD
  - 46 XY DSD
  - Sex Chromosome DSD
- Estimated incidence is 1 in 4,500 births [1]
Prophylactic Gonadectomy

- Indicated for patients with Y chromosome material at risk for developing Germ Cell Tumors (GCTs)
  - Premalignant: Gonadoblastoma (GB), intratubular germ cell neoplasia (ITGCN)
  - Malignant: Dysgerminoma, seminoma, and non-seminoma
- Risk of GCT varies by degree of virilization, location of gonads, and DSD diagnosis

Germ Cell Tumor Risk

<table>
<thead>
<tr>
<th>DSD Diagnosis</th>
<th>Estimated Tumor Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denys Drash Syndrome</td>
<td>40%</td>
</tr>
<tr>
<td>46 XY Gonadal Dysgenesis</td>
<td>30%</td>
</tr>
<tr>
<td>45 X/46 XY DSD</td>
<td>15-40%</td>
</tr>
<tr>
<td>17 β hydroxysteroid dehydrogenase deficiency</td>
<td>17%</td>
</tr>
<tr>
<td>Partial androgen insensitivity syndrome</td>
<td>15%</td>
</tr>
<tr>
<td>Ovotesticular DSD</td>
<td>2.6%</td>
</tr>
<tr>
<td>Complete androgen insensitivity syndrome</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

Pre Operative Evaluation

- No standard diagnostic guidelines for patients undergoing prophylactic gonadectomy
- Unless gonads are easily palpated, imaging is performed to:
  - Evaluate for the presence and type of Mullerian structures
  - Locate gonads
  - Identify any features concerning for malignant transformation
Study Objectives

1. To evaluate ultrasonography (US) and magnetic resonance imaging (MRI) in identifying gonads in patients with Disorders of Sex Development (DSD) undergoing prophylactic gonadectomy
2. To assess the capacity of pre-operative imaging to detect pre-malignant and malignant transformation

Methods

- Retrospective case series at tertiary care academic center
- Chart review of patients with relevant ICD-9 codes seen between January 1998 and August 2014
- Inclusion criteria:
  - Karyotype showing 46 XY or 45 X/46 XY
  - Unilateral or bilateral prophylactic gonadectomy
  - Pre-operative MRI and/or ultrasound
- Exclusion criteria:
  - Incomplete records

Methods

- Data was abstracted from demographic facesheets, outpatient clinic visits, radiology reports, operative reports, and pathology reports
- Proportions were compared with a chi-square test with a statistical significance set at 0.05
- Institutional IRB approval was obtained
Results

- 39 patients met inclusion and exclusion criteria
- Most were non-Hispanic white (77%), English speaking (97%), and had a female gender of rearing (82%)
- Average age at the time of surgery was 8.1 years
  - Bimodal distribution
    - 48% had surgery before age 5
    - 44% had surgery after age 11
- 7 patients (18%) had a family history significant for a first degree relative with a DSD

### DSD Diagnosis, N=39

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Gonadal Dysgenesis</td>
<td>9 (23)</td>
</tr>
<tr>
<td>Partial Gonadal Dysgenesis</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Complete Androgen Insensitivity</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Mosaic Turner/Mixed Gonadal Dysgenesis</td>
<td>10 (26)</td>
</tr>
<tr>
<td>5 Alpha Reductase Deficiency</td>
<td>4 (10)</td>
</tr>
<tr>
<td>17 Beta Hydroxysteroid dehydrogenase Deficiency</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Denys-Drash Syndrome</td>
<td>1 (3)</td>
</tr>
<tr>
<td>46 XY DSD, Unknown Diagnosis</td>
<td>4 (10)</td>
</tr>
</tbody>
</table>

### Germ Cell Tumors, N=39

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonadoblastoma/ITGCN</td>
<td>11 (28)</td>
</tr>
<tr>
<td>Dysgerminoma</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

### Germ Cell Tumor by DSD Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Gonadal Dysgenesis</td>
<td>3/9 (33)*</td>
</tr>
<tr>
<td>Partial Gonadal Dysgenesis</td>
<td>3/4 (75)</td>
</tr>
<tr>
<td>Complete Androgen Insensitivity</td>
<td>1/5 (20)</td>
</tr>
<tr>
<td>Mosaic Turner/Mixed Gonadal Dysgenesis</td>
<td>4/10 (40)</td>
</tr>
<tr>
<td>5 Alpha Reductase Deficiency</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td>17 Beta Hydroxysteroid Dehydrogenase Deficiency</td>
<td>0/2 (0)</td>
</tr>
<tr>
<td>Denys-Drash</td>
<td>0/2 (0)</td>
</tr>
<tr>
<td>46 XY DSD, Unknown Diagnosis</td>
<td>1/4 (25)</td>
</tr>
</tbody>
</table>

* Includes patient with Dysgerminoma
Study Objective #1

- Evaluate ultrasonography and magnetic resonance imaging (MRI) in identifying gonads in patients with Disorders of Sex Development (DSD) undergoing prophylactic gonadectomy.

Results

- 33 patients had pre operative ultrasound
  - 35 out of 65 gonads (54%) were identified
- 14 patients had pre operative MRI
  - 11 out of 27 gonads (41%) were identified

* No significant difference between imaging modalities in identification of gonads (p=0.25)
Study Objective #2

- Assess the capacity of pre-operative imaging to detect pre-malignant and malignant transformation.

Results

- Pre-malignant lesions (gonadoblastoma and ITGCN) were diagnosed in 28% of patients
  - There were no distinguishing characteristics documented on pre-operative imaging
- Dysgerminoma was diagnosed in one patient (2.5%)
  - Described as an ovary with “normal size and echotexture” on both ultrasound and MRI

Streak Gonad vs Dysgerminoma
Results

- No significant difference in pre-malignant gonadal tumors among those gonads that were visualized versus non-visualized on both ultrasound (17% vs 23%, p=0.57) and MRI (9% vs 25%, p=0.62)

Conclusions

- Both ultrasound and MRI were limited in identifying gonads
  - Ultrasound better at identifying dysgenetic gonads
  - Pre-malignant lesions were not identified on either imaging modality
  - The dysgerminoma was mistaken for a normal ovary in a patient expected to have streak gonads

Clinical Implications

- Ultrasound should be considered as the first line imaging modality in DSD patients undergoing prophylactic gonadectomy
- Because pre-malignant lesions cannot be identified on imaging, surveillance of gonads in patients with DSD at low risk for GCT (such as CAIS) is controversial
STRENGTHS AND LIMITATIONS

Strengths
- Thorough chart review
- Adds to limited available data

Weaknesses
- Small heterogeneous patient group
- Retrospective study

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Emily Kobernik
Previous PAG fellows

Questions?

References