Ovarian follicles of young patients with Turner Syndrome contain normal oocytes but monosomic 45,X granulosa cells

Ronald Peek1, Myra Schleedoorn1, Dominique Smeets2, Guillaume van de Zande2, Freek Groenman3, Didi Braat1, Janiene van der Velden4 and Kathrin Fleischer1

1 Department of Obstetrics and Gynecology, Radboud University Medical Center, PO Box 9101, 6500 HB Nijmegen, The Netherlands
2 Department of Human Genetics, Radboud University Medical Center, PO Box 9101, 6500 HB Nijmegen, The Netherlands
3 Amsterdam UMC, Vrije Universiteit Amsterdam, Obstetrics and Gynecology, Amsterdam Reproduction and Development, De Boelelaan 1117 Amsterdam, The Netherlands
4 Amalia Children’s Hospital, Radboud University Medical Center, PO Box 9101, 6500 HB Nijmegen, The Netherlands

INTRODUCTION

- Most women with Turner Syndrome (TS) experience a premature follicular depletion and gonadal dysgenesis due to an accelerated loss of gametes and impaired folliculogenesis.
- Very little is known about the X chromosomal content of ovarian follicular and stromal cells in TS women.
- This information, however, is essential for understanding the mechanisms of premature follicular depletion and gonadal dysgenesis in this specific group of patients and, hence, to evaluate if ovarian tissue cryopreservation is a realistic option to preserve their fertility.

STUDY QUESTION

What is the X chromosomal content of oocytes and granulosa cells of primordial/primary (small) follicles and stromal cells in ovaries of young patients with Turner Syndrome (TS)?

METHODS

Participants

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Cell Lines (lymphocytes and buccal cells)</th>
<th>Number of follicles per mm² tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8</td>
<td>45,X/46,X,46,XX</td>
<td>11</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>45,X,46,XX</td>
<td>64</td>
</tr>
<tr>
<td>C</td>
<td>15</td>
<td>45,XX/46,X</td>
<td>45</td>
</tr>
<tr>
<td>D</td>
<td>16</td>
<td>45,XX</td>
<td>6</td>
</tr>
<tr>
<td>E</td>
<td>15</td>
<td>45,XX</td>
<td>3</td>
</tr>
<tr>
<td>F</td>
<td>14</td>
<td>45,X</td>
<td>0</td>
</tr>
<tr>
<td>G</td>
<td>9</td>
<td>45,X</td>
<td>0</td>
</tr>
<tr>
<td>H</td>
<td>13</td>
<td>45,X</td>
<td>0</td>
</tr>
<tr>
<td>I</td>
<td>3</td>
<td>45,X</td>
<td>0</td>
</tr>
<tr>
<td>J</td>
<td>17</td>
<td>45,X</td>
<td>0</td>
</tr>
</tbody>
</table>

In this study 37 patients with Turner’s syndrome and numerical abnormalities of the X chromosome were included.

Study design

- After unilateral ovariectomy, ovarian cortex fragments were prepared and cryopreserved (A–B).
- One fragment from each patient was thawed and enzymatically digested to obtain stromal cells and primordial/primary follicles (D, G, H).
- Stromal cells, granulosa cells, oocytes and extra-ovarian cells (lymphocytes, buccal cells and urine cells) were analysed by FISH using an X chromosome-specific probe (E, I, K).

RESULTS

- Ovarian follicles were detected in 5 of the 10 patients studied.
- X chromosome analysis revealed that 42 of the 46 oocytes (91%) that were analysed had a normal X chromosomal content.
- Granulosa cells were largely 45,X but showed different levels of X chromosome mosaicism between patients and between follicles of the same patient.
- Despite the presence of a low percentage (10–45%) of 46,XX ovarian cortex stromal cells, normal macroscopic ovarian morphology was observed.
- The level of mosaicism in lymphocytes, buccal cells or urine derived cells was not predictive for mosaicism in ovarian cells.

CONCLUSION AND DISCUSSION

- The majority of oocytes in females with TS have a normal X chromosomal content.
- Follicles from the same patient can differ with respect to the level of mosaicism of their granulosa cells.
- The results are based on a small number (n =5) of TS patient samples.
- The functional consequences of these observations require further investigation.

Contact: myra.schleedoorn@radboudumc.nl

Poster presented at: