Turner syndrome

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1938
Henry Turner: description of clinical triad:
- short stature
- 'sexual infantilism'
- dysmorphic abnormalities

1959
C.E. Ford: discovery of X chromosomal monosomy

1:2500 life born girls
• short stature (mean 147 cm); growth hormone treatment results in 5-12 cm height gain
• ovarian failure: induction of puberty
• dysmorphias
Dia 4

Turner syndrome

Dia 5

Which girl has Turner syndrome?

1 2 3

Dia 6

Turner oxandrolon studie
Cytogenetics

Lymphocyte karyotyping

- 50% 45,X
- 30-40% mosaicism
- 5-15% structural abnormality X

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45,X</td>
<td>71 (42.5)</td>
</tr>
<tr>
<td>45,X/46,XX</td>
<td>19 (11.4)</td>
</tr>
<tr>
<td>45,X/47,XXX</td>
<td>5 (3.0)</td>
</tr>
<tr>
<td>45,X/46,Xi(Xq)</td>
<td>22 (13.2)</td>
</tr>
<tr>
<td>45,X/46,XY or derivative Y</td>
<td>9 (5.4)</td>
</tr>
<tr>
<td>45,X/46,X,r(X)</td>
<td>6 (3.6)</td>
</tr>
<tr>
<td>46,X,i(Xq)</td>
<td>7 (4.2)</td>
</tr>
<tr>
<td>46,X,del(X)</td>
<td>7 (4.2)</td>
</tr>
<tr>
<td>46,X,del(Xp)</td>
<td>5 (3.0)</td>
</tr>
<tr>
<td>46,X,del(Xq)</td>
<td>11 (6.6)</td>
</tr>
</tbody>
</table>

Genotype/phenotype correlation

- Monosomy 45,X in general more severe phenotype than 45,X/46,XX mosaicism
- 46,X, r(X) mental retardation
- 46,X,i(Xq) autoimmune diseases
- Y chromosome associated with an increased risk of gonadoblastoma: prophylactic gonadectomy
- Tissue mosaicism

Wide range of morbidity

**Cardiovascular morbidity**

Life expectancy - 13 years / cardiovascular mortality x 3

Structural abnormalities heart / aorta

- Congenital: bicuspid aortic valve (15-30%), aortic coarctation (10-15%)
- Acquired: aortic dilation / aneurysm (20%) and dissection

1. Normal aortic valve
2. Bicuspid aortic valve
3. Aortic coarctation

**Cardiovascular morbidity**

Increased risk of atherosclerosis

- Hypertension
  - 50% of young adults
  - Chance of dissection in case of aortic dilation / bicuspid aortic valve (treatment goal SBP < 120 mmHg)
- Diabetes mellitus type 1 x11, type 2 x3.5
- Dyslipidemia 40-50% of young adults

**Osteoporosis and fractures**

- Osteopenia, osteoporosis (50%)*
- Higher tendency to fall
- Increased risk in cortical bone fractures
- Pelvic bone loss due to estrogen deficiency
- Fracture risk 2-3x

*DEXA underestimates BMD in short stature
### Dia 13

**Auto-immune disorders**

- Hypothyrodism in 25-40% <40 years (vs 2% in general population)
- Celiac disease in 5% (vs 1% in general population)
- Most prevalent in X,isoXq karyotype

<table>
<thead>
<tr>
<th>Autoimmune disorder</th>
<th>Pathogenicity</th>
<th>Associated with sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyrodism</td>
<td>45% female</td>
<td>50% male/female</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>5% (male)</td>
<td>1% (female)</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>4% (male)</td>
<td>5% (female)</td>
</tr>
</tbody>
</table>


### Dia 14

**Estrogen deficiency and infertility**

**Hormone replacement therapy**

- Ovarian failure: estradiol/dydrogesteron, biphasic or continuous
- Amenorrhea: MetFormin resistance and menstrual cycle resistant
- Ethinylestradiol/levonorgestrel

**Fertility**

- 2-6% 'spontaneous' pregnancy (46,XX mosaicism)
- Fertility techniques:
  - Ovarian failure
  - Egg preservation (from mother/sister)
- Higher risk of abortion, eclampsia, premature birth, growth retardation, certain diseases (2%)

### Dia 15

**Ear and hearing problems**

- Structural abnormalities external and internal ear
- Conductive loss due to recurrent otitis media during childhood
- Early presbyacusis
Dia 16

**Miscellaneous**

- 23-40% congenital structural renal abnormalities
  (recurrent urinary tract infections)
- 36% liver enzyme abnormalities
  (non alcoholic steatosis hepatis, celiac disease)

Dia 17

**Cognitive and psychological issues**

- Impaired visuo-spatial orientation, planning, and recognition of facial expression
- Low self-esteem, social fear, depression

Dia 18

**Wide range of morbidity**

- Freriks et al. NTVG 2007
Turner clinics for adult patients

Consultations
- endocrinologist
- gynecologist
- cardiologist
- ENT physician
- (psychologist)

Investigations
- lab investigations
- cardiac ultrasound
- MRI aorta
- audiogram
- DEXA

Multidisciplinary meetings
- UMCN
- UMCG
- VUMC
- Erasmus MC

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**Klinische Richtlijn Turner Syndroom**

**TURNER**

Periodische laboropnamen

| Test | to 18 years | after 18 years | Follow-up
|------|-------------|----------------|-----------
| TSH  | x (1-6 pm)  | 1x/3-5 years   | x 1x/year |
| LH    | x (1-6 pm)  | 1x/3-5 years   | x 1x/year |
| KGW   | x (1-6 pm)  | 1x/3-5 years   | x 1x/year |
| FSH   | x (1-6 pm)  | 1x/3-5 years   | x 1x/year |
| AMH   | x (1-6 pm)  | 1x/3-5 years   | x 1x/year |
Conclusions

• Besides short stature and ovarian failure, patients with Turner syndrome are prone to a wide range of morbidity throughout life with a large phenotypic variation.

• This requires multidisciplinary care with standardized screening and careful transition from pediatric into adult medical care.