Genetics and the mouth

Caren Spencer
Medical Geneticist
University of Pretoria

Overview

- Overview of terminology
- Lips
- Tongue
- Clefts – palate and lip
**Terminology**

- **Size** = eg full, thin
- **Shape** = eg everted, cupid’s bow
- **Colouration** = eg freckling
- **Additional structure** = eg lip pits

**Lips**

- **Size** = eg full, thin
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- **Colouration** = eg freckling
- **Additional structure** = eg lip pits
Full lips

- Coffin-Lowry syndrome – X-linked intellectual disability syndrome. Down-slanted palpebral fissures, bulbous nose, tapering fingers
- Coffin-Siris syndrome – hypoplastic 5th finger, coarse facies and hirsutism with ID. Mostly dominant inheritance
- X-linked α-thalassemia – X-linked intellectual disability with characteristic facies and genital abnormalities. HbH detected
- Costello syndrome - RAS-opathies spectrum with macrocephaly, coarse facies, loose skin over hands and feet
- FG syndrome – X-linked intellectual disability syndrome with imperforate anus, hypotonia and prominent forehead
- MPS.....
Additional features:
• Development
• Personality
• Cardiovascular lesions
• Urinary malformations
• Calcium disturbances

Diagnosis:
• FISH
• MLPA

Treatment:

Recurrence:
• Autosomal dominant


Full lips
• Williams syndrome – microdeletion syndrome involving 7q11.23. Distinctive facial features, hoarse voice, cardiovascular abnormality.
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• MPS…..
Additional features:
• Development
• Dental manifestations
• Skeletal abnormalities
• Radiological features
• Cardiac

Diagnosis:
• *RPS6KA3* in 50%
• Clinical and X-rays

Management:
• Recent article
  [http://www.nature.com/ejhg/journal/v18/n6/full/ejhg2009189a.html](http://www.nature.com/ejhg/journal/v18/n6/full/ejhg2009189a.html)

Inheritance
• X-linked dominant

Full lips

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Colouration

- Freckling

Peutz-Jegher syndrome
Lip pits

- Van der Woude syndrome – lower lip pits, cleft lip and missing second premolars
- Popliteal pterygium syndrome – popliteal webs, cleft palate and lip pits
- Branchio-oculo-facial syndrome – branchial defects, lacrimal duct obstruction, pseudocleft upper lip
- Kabuki syndrome – large palpebral fissures, eversion lower eye lid, persistent fetal fingerpads
• Additional features
  Cleft palate
• Diagnosis
  IRF6

Clinical
• Inheritance:
  Autosomal dominant (variable expression)
Lip pits

- Van der Woude syndrome – lower lip pits, cleft lip and missing second premolars
- Popliteal pterygium syndrome – popliteal webs, cleft palate and lip pits
- Branchio-ocular-facial syndrome – branchial defects, lacrimal duct obstruction, pseudocleft upper lip
- Kabuki syndrome – large palpebral fissures, eversion lower eye lid, persistent fetal fingerpads
- Oral-facial-digital syndrome – see later

- Additional features:
  - Intellectual disability
  - Cardiac abnormalities
  - Skeletal abnormalities
  - Cleft palate
- Diagnosis:
  - MLL2 (KMT2D) gene (KDM6A)

www.KabukiSyndrome.com
Tongue

- Size – microglossia or macroglossia
- Shape – lobulated

Macroglossia

- Beckwith-Wiedeman syndrome – macrosomia, large tongue, anterior abdominal defect, ear creases
- MPS
- Simpson-Golabi-Behmel syndrome - X-linked, multiple congenital abnormality, intellectual disability syndrome
- X-linked thalassemia
• Beckwith-Wiedemann syndrome – macrosomia, large tongue, anterior abdominal defect, ear creases
• MPS
• Simpson-Golabi-Behmel syndrome
• X-linked thalassemia

Beckwith-Wiedemann syndrome (European Journal Human Genetics 2009)
http://atlasgeneticsoncology.org/Kprones/BeckwithWiedemann-ID10037.html
• Additional features:
Major findings-fam hx, macrosomia, macroglossia, ear creases/pits, omphalocele, visceromegaly, embryonal tumour, hemihyperplasia, cytomegaly fetal adrenal cortex, renal abn, cleft palate, placental mesenchymal dysplasia, cardiomegaly, cardiomyopathy
Minor findings- antenatal, hypoglycaemia, naevus flammeus, cardiac abn, facial features, diastasis recti, advanced bone age
• Diagnosis
Molecular not available in SA.
Multiple different mechanisms.
• Management:
Large newborn
Tumour surveillance
• Inheritance:
Mostly sporadic but few familial

Cleft lip and palate
• 1 in 700
• M:F 2:1 for cleft lip and 1:2 for cleft palate
• 70% of CL/P is non-syndromic
• 50% CP is non-syndromic
Etiology

<table>
<thead>
<tr>
<th>Syndromic</th>
<th>Non-syndromic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosomal – trisomy 13, 4p-</td>
<td>Environmental – smoking, infections, medication, temperature, alcohol</td>
</tr>
<tr>
<td>Single gene disorders – van der woude syndrome, Stickler syndrome, 22q deletion syndrome, Treacher-Collins syndrome, Kabuki syndrome, Opitz syndrome</td>
<td>Single genes – IRF6, MSXI</td>
</tr>
<tr>
<td>Multifactorial – family history and combination of susceptibility genes</td>
<td></td>
</tr>
</tbody>
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Recurrence risk

- Dependent on the cause
- Multifactorial:

<table>
<thead>
<tr>
<th>Relationship to index case</th>
<th>Recurrence risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibling with unilateral CL</td>
<td>2-3%</td>
</tr>
<tr>
<td>Sibling with unilateral CL/P</td>
<td>4%</td>
</tr>
<tr>
<td>Sibling with bilateral CL/P</td>
<td>5-6%</td>
</tr>
<tr>
<td>Two affected siblings</td>
<td>10%</td>
</tr>
<tr>
<td>Affected sibling and parent</td>
<td>10% (excluding dominant)</td>
</tr>
<tr>
<td>Affected parent</td>
<td>4%</td>
</tr>
</tbody>
</table>

- Folic acid!!
• Very brief overview of some oral manifestations genetic syndromes
• Recognition and literature reviews

• Thank you