Dysmorphology Assessment

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The speaker has signed a disclosure form and indicated she has no significant financial interest or relationship with the companies or the manufacturer(s) of any commercial product and/or service that will be discussed as part of this presentation.

Session Summary

This session will cover a head-to-toe evaluation of a newborn for micro-signs of dysmorphic features, including correct terms for describing dysmorphic features, and formulas and references for normal measurements.

Session Objectives

Upon completion of this presentation, the participant will be able to:

- define the terms: trigonocephaly, brachycephaly, plagiocephaly and scaphocephaly, hypertelorism, hypotelorism;
- correctly measure the inner canthus, outer canthus and inter-pupillary distances;
- label a diagram of the ear with the root, upper helix, and lobe;
- correctly write the formula for determining if the nipples are wide-spaced;
- write the three main palmar creases and name the two creases that make up a single transverse palmar crease (when it is present);
- identify the best genetic test to diagnose a major trisomy (13, 18 or 21);
- identify the best genetic test to order for multiple dysmorphic features where no clear syndrome or major trisomy is suspected.

References

www.genetests.org

Session Outline

See presentation handout on the following pages.
Dysmorphology Assessment

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Definition of Dysmorphology

- The term “dysmorphology” was coined by Dr. David Smith in the 1960s
- Denotes human congenital defects and abnormalities of body structure that originate before birth
- Used to describe individuals whose physical features are not usually found in others of the same age or ethnic background
- “dys” (Greek) – disordered or abnormal
- “morph” - shape

General Evaluation

- Comparison to normal milestones
- Muscle tone: Hyper vs hypotonia, jittery, spastic?
- Facial expression: Bright vs dull? Do the eyes fix, focus and follow?
- General appearance: proportionate or asymmetric
- Growth parameters off the curve?
  - Ht, Wt, HC plotted on growth curve
  - Overgrowth versus failure to thrive
  - Macro versus microcephaly

Head Shape and Size

Look down from the top of the head:
- Fontanelles
- Sutures
- Ear placement

Anterior fontanel

1p36 deletion

Source: www.ggc.org
888-442-4363
Anterior fontanel

Huge AF cause unknown at present

Description of Head Shapes

• Normocephalic
• Trigonocephaly
• Brachycephaly
• Plagiocephaly
• Scaphocephaly

Head Length

• Brachycephaly - short anterior to posterior measurement
• Scaphocephaly - long anterior to posterior measurement
• Occiput - prominent or flat?

Scaphocephaly

Scaphocephaly - sagittal synostosis

Craniosynostosis – all sutures

22q11.2 deletion
- **Brachycephaly**
  - coronal synostosis
  - positional – short gut
- **Hair whorls in unusual places**
  - CHARGE
  - Chromosome abnormality
- **Microcephaly**
  - Prenatal Depakote
- **Maternal PKU – Powerful Teratogen**
  - Microcephaly, Coarc Aorta, Multiple VSDs
- **Head Profile**
  - Nasal bridge
    - flat vs prominent
  - Flat mid-face?
  - Chin development
    - micrognathia - small
    - prognathia - prominent chin
  - Ears - posteriorly rotated?
**Head Profile**

Flat Nasal Bridge
Low set ears
Posteriorly rotated ears

+21 Down syndrome

**Head Width**

- Bi-temporal narrowing
- Eyebrows: uniform, thick, medial flare
- Eye lids: colobomas, hooded, epicanthi
- Eye lashes: thick, sparse
- Iris: colobomas or small globes
- Coarse facies

**Face**

- Coarse facial features
- Depressed nasal bridge
- Corneal clouding
- Up turned nares
- Thick lips
- Exotropia

Hurler syndrome - Mucopolysaccharidosis

**Face**

- Up slanting palpebral fissures
- Bilateral epicanthal folds
- Depressed nasal bridge
- Flat facial profile
- Open mouth - hypotonia

Down syndrome

**Hair color: Is it consistent with parents phenotype, sparse, wiry?**

Angelman 15q11-q13 deletion

**Face**

- Ptosis of eyelids
- Broad nasal tip
- Microcephaly
- Narrow frontal area
- Strabismus

Smith-Lemli-Opitz Syndrome
Canthal Measurements

- Inner canthus
- Outer canthus
- Telecanthus versus hypertelorism

Interpupillary Measurement

- Hypertelorism - eyes too far apart
- Hypotelorism - eyes too close together

Interpupillary Measurements

Face

Hypotelorism
Short, narrow palpebral fissures
Absent columella
Central cleft lip and palate
Single Central Incisor
Holoprosencephaly

Face: Hypertelorism

- Noonan syndrome
- Reiger syndrome (also proptosis)
**Palpebral fissure length**
- Distance from inner to outer canthus
- Short or long palpebral fissures
- Narrow palpebral fissures
- Up slanting
- Down slanting

**Face: Coloboma of the eyelid, malar hypoplasia, partial total absence of lashes**
- Treacher Collins syndrome

**Eyes**
- Coloboma of the iris or retina
- 46,XXY

**Eyes:**
- Hooded eyelids
- Short and narrow palpebral fissures

**Eyes**
- Ankyloblepharon
- Hay-Wells Ankyloblepharon with clefting
Ear Shape

- Root
- Helix: over folded or cupped
- Lobe: absent or creased
- Size: large or small
- Preauricular area: pits or tags

Ears

- Deficient upper helix
- Over-folded helix
- Small ear
- C-shaped ear

22q11.2 deletion

CHARGE syndrome

- Triangular Crus
- Underdeveloped
- Upper helix
- Over folded
- Upper helix
- Moderate to severe hearing loss

Ears: pits, tags, absent lobes

Hemifacial microsomia
Microtia
Asymmetric mouth
Narrow palpebral fissures
Hooded eyelids

Goldenhar syndrome

Ear Position

- Measure from inner canthi across to the root
- Low set
- High set
- Posteriorly rotated
Microtia and low set ears

Mouth: Philtrum Length

- Philtrum:
  - short, long, smooth
- Mid-face:
  - flat, long
- Nasal area:
  - short or long nose
  - laterally built up nose
  - alae nasi formation

Mouth: Smooth Philtrum

Fetal Alcohol syndrome

Smooth philtrum, thin upper lip

FAS as child and teenager

Midface: Long vertical maxillary excess

22q11.2 deletion inherited from mom

Midface

- Long vertical maxillary excess
- Bulbous nose with hypoplastic alae nasi
- Microstomia

22q11.2 deletion
Mandible: Evaluation for micrognathia

Normal mandible placement  4p34 deletion

Williams syndrome - 7q11.23 deletion

Mouth
- Microcephaly
- Wide mouth
- Hoarse voice
- Moderate MR
- Growth retardation
- Outgoing friendly personality
- SVAS

Mandible
- Prognathia
- Short and narrow palpebral fissures
- Deep set eyes
- Hypotelorism
- Long straight eyebrows
- Laterally built up nose
- Short nose
- Thin lips

Whole Family
Mom also affected
Williams syndrome 7q11.23 deletion

Mouth
Bilateral cleft lip and palate
Lip pits
Van der Woude syndrome

Mouth: Cleft lip
Oral-Facial-Digital Syndrome, Type 1
Cleft palate (unknown etiology)

Mouth: Uvula

- Bifid uvula?
- Absent uvula?
- Minimal cleft where uvula should be?

Mouth

- Hypodontia
- Malformed teeth

Reiger syndrome

Mouth: Macroglossia

- Pompe Disease
- Beckwith-Wiedemann syndrome

Neck:

- Cutis gyrata
- Webbed neck
- Micrognathia

45,X Turner syndrome

Trunk Measurements

- Inter nipple distance
- Chest circumference
- IN/CC x 100 = ___%
- if > 25% the nipples are wide spaced
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<thead>
<tr>
<th>Chest</th>
<th>Family history: 3 generations with Noonan syndrome</th>
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<tr>
<td>Wide spaced nipples</td>
<td>Noonan syndrome in dad and daughter</td>
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<td>Pulmonary stenosis</td>
<td>Family history: 3 generations with Noonan syndrome</td>
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<td>Short stature</td>
<td>Noonan syndrome in dad and daughter</td>
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<td>Short webbed neck</td>
<td>Noonan syndrome in dad and daughter</td>
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<th>Family history: 3 generations with Noonan syndrome</th>
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<tr>
<td>Short stature, low posterior hairline, short neck, shield chest, midline surgical scars</td>
<td>Noonan syndrome in dad and daughter</td>
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<th>Chest</th>
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<td>Noonan syndrome in 3 generations. The infant daughter died of heart disease</td>
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<td>Abdomen: hepatomegaly, splenomegaly</td>
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<td>Pericardium defect</td>
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<td>Abdominal wall defect</td>
<td>Abdomen</td>
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<tr>
<td>Diaphragmatic defect</td>
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<td>Intracardiac defects - ectopia cordis, TGA</td>
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Genitalia: learn the Tanner stages, note anal placement

CHARGE - hypogonadism

Ambiguous Genitalia

- Congenital Adrenal Hyperplasia
- Fused labia
- Penile clitoris

Ambiguous Genitalia

- Mosaicism
  - 45,X [70%]
  - 46,XY [30%]

Ambiguous Genitalia - Family Issues

- What to tell the parents and family
  - Full and honest disclosure
  - Review sexual differentiation with diagrams
  - Emphasize “unfinished” not “abnormal”
  - Reassure with appropriate concern and a plan for the future
  - Avoid terms like “hermaphrodite”
  - “Intersex” is becoming more acceptable.

Ambiguous Genitalia - Hospital Issues

- Use “baby” or “infant” and the last name
- Respect the families’ confidentiality
- If healthy, encourage rooming-in
- Refer to a pediatric tertiary center
- Avoid unnecessary genital examinations
Sex Assignment

- Consider the nature of the diagnosis… not just functionality of the phallus
- Primary concern is how will patient prefer to live after puberty

Sex Assignment

As Nature Made Him
The Boy Who Was Raised As A Girl
by John Colapinto

Extremities

- Roberts Phocomelia
  - Autosomal Recessive
- hypomelia
- tetraphocomelia
- amelia

Extremities – absent radius

Palmar Creases:
Three main creases in the general population
1. Proximal transverse
2. Distal transverse
3. Thenar crease

Single transverse palmer crease: occurs when the proximal transverse crease and the distal transverse crease merge into one

Palmar creases and finger creases

Bridge crease
+21 Down Syndrome
Single palmar crease
+21 Down Syndrome
Typical Fetal Alcohol Syndrome crease

Distal transverse crease exits between fingers 2 and 3

Long Tapering Fingers

22q11.2 deletion

Hypoplastic thumb

Finger-like thumb (Triphalangeal)

Fanconi anemia

13q deletion

Overlapping fingers

Also look at nail formation: hypoplastic versus absent

+18

Lymphedema

Hypoplastic finger nails

45, X Turner syndrome

Pre-axial polydactyly
**Post-axial polydactyly**

- Usually no major creases
- Deep plantar creases are sometimes associated with chromosome defects
- Gap between toes 1 and 2? Common in Down synd.
- Prominent heels, rocker bottom feet? Common in trisomy 18

**Pre-axial and Post-axial Polydactyly**

**Oral-Facial-Digital Syndrome, Type 1**

**Ectrodactyly**

+4 mosaic

Unknown

**Arachnodactyly**

Marfan syndrome

**Camptodactyly**

Reiger syndrome
Overlapping toes

Syndactyly

Syndactyly of toes 2 and 3
Syndactyly of toes 2 and 3 and toes 4 and 5

Gap between toes 1 and 2

Preaxial polydactyly of the toes

Deep plantar furrows, overlapping toes or gap between toes

4q34 deletion

Smith-Lemil-Opitz syndrome

+21 Down Syndrome

Infant of Diabetic Mother

Unknown

Rocker Bottom feet
Hypoplastic Great toe
Hypoplastic toe nail

Lymphedema of the dorsum of foot and hypoplastic toe nails

Caudal Regression

Infants of Diabetic Mothers

Sirenomelia

Spine
Thoracolumbar gibbus secondary to anterior vertebral wedging
Short neck
Joint stiffness
Fine body hair
Hirsutism
Hepatomegaly
Splenomegaly

Skin: café au lait spots, hyper or hypo pigmented areas, gluteal folds
Neurofibromatosis and 22q11.2 deletion
Hypomelanosis of ITO
Skin

Sturge-Webber syndrome

Hemihypertrophy

- Beckwith-Wiedemann syndrome
- Increased risk for Wilms Tumor

Hypotonia

Alagille syndrome

Hypotonia - MCAD

Hypotonia: Myotonic Dystrophy

Hypotonia: Spinal Muscular Atrophy - SMA
Hypotonia

When to Refer to Genetics

Rule of Thumb

1 major or 2 minor birth defects
Development delay of unknown cause
2 or more dysmorphic features

What do you see?

17p11.2 deletion
Smith-Magenis syndrome

Picked up by nurse in delivery room in Columbus, Ga. and doctor ran the chromosomal microarray.

Neither the nurse or doctor knew what the diagnosis would be…. But they knew something was not right.

Smith-Magenis syndrome - 17p11.2 deletion

- Infantile Hypotonia
- Brachycephaly with flat midface
- Prominent forehead, broad nasal bridge
- Cardiac and renal defects
- Self Destructive Behavior when Older
  - Onychotillomania (pulling out finger/toe nails)
  - Polyembolokoiamania (inserting foreign objects into body orifices)
- Progressive obesity
- Sleep Disorders – awake at night

Huge advantage to knowing this diagnosis early….
What do you see?

Beauty is in the eye of the beholder.....

Rick Guidotti
Positive exposure


Resources

- www.emory.genetics.edu/ Emory University Department of Human Genetics
- www.kumc.edu/gec/support/ Genetic Conditions and Rare Conditions
- Smith’s Recognizable Patterns of Human Malformation by Kenneth Jones
- www.genetests.org Excellent reviews for physicians and other healthcare professionals