Common Otolaryngological Congenital Abnormalities

Visual Synopsis of Classic Syndromes and Features

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http://www.explosm.net/comics
Objective

- Highlight typical features of congenital abnormalities evaluated in the otolaryngology practice
- Visual emphasis on classical presentation of commonly encountered syndromes
Down Syndrome
(Trisomy 21)

- Extra chromosome 21
  - Meiotic nondisjunction in gamete formation
  - Mosaicism (1-2%)
  - Robertsonian translocation (2-3%)
  - Duplication (rare)

- Increased risk with advanced maternal age
- Most common cause of intellectual disability
Down Syndrome Features

- Brachycephaly
- Flat nasal bridge and occiput
- Small, low-set ears
- Macroglossia, glossoptosis
- Upslanting palpebral fissures
- Epicanthal folds
- Brushfield spots
- Simian crease
- Sandal gap deformity of feet
- Excessive nuchal folds
- Mental retardation

(courtesy of Dr. Hutchinson via Maria Blazo, M.D.)
Down Syndrome Features

- Simian crease
- Brushfield spots
- Sandal deformity
- Excessive nuchal folds
- Upslanting palpebral fissure
- Brachycephaly
- Flat nasal bridge, hypoplastic maxilla
- Microtic, low-set ears
- Epicanthus
- Macroglossia, glossoptosis

(Dourmishev, 2009)
Down Syndrome

Other Features

- Muscular hypotonia
- Strabismus
- Congenital cataracts
- Atrial or ventricular septal defect
- Gastroesophageal reflux
- Duodenal stenosis or atresia
- Hirschsprung disease or celiac disease
- Seizures
Down Syndrome
Prenatal Ultrasound

- Absent nasal bones
  - First trimester (60-80%)
  - Second trimester (37-41%)

- Hypoplastic nasal bones
  - Not useful as single marker in first trimester
  - Best used with absent nasal bones in second trimester (60-100%)

(Gonçalves, 2004)
Down Syndrome

Otolaryngological Considerations

- Tympanostomy tubes
- Esophageal atresia, tracheoesophageal fistula
- Atlantoaxial instability
- Obstructive sleep apnea
- Hypothyroidism
- Increased risk for malignancy
  - Acute lymphoblastic leukemia
  - Transient myeloproliferative disorder
Crouzon Syndrome
(Craniofacial Dysostosis)

- Autosomal dominant
- Virtually complete penetrance
- Mutation of fibroblast growth factor receptor II (FGFR2) on chromosome 10
- Affects first pharyngeal arch
  - Precursor maxilla and mandible
  - Early fusion of face and skull bones

(courtesy of Dr. Pine)
Crouzon Syndrome

**Features**

- Craniosynostosis
- Exophthalmos
- Hypertelorism
- Strabismus
- Psittichorhina
- Hypoplastic maxilla
- Mandibular prognathism

Caused by a mutation in the fibroblast growth factor receptor II, located on chromosome 10, this syndrome affects the first branchial (or pharyngeal) arch, which is the precursor of the maxilla and mandible. What occurs in the disease is that an infant's skull and facial bones, while in development, fuse early or are unable to expand. Thus, normal bone growth cannot occur. Fusion of different sutures leads to different patterns of growth of the skull.

- **Hypoplastic maxilla**: insufficient growth of the midface
- **Mandibular prognathism**: chin appears to protrude despite normal growth of mandible and gives the effect of the patient having a concave face
- Mental retardation possible if premature closure of the cranial suture lines
- **Psittichorhina**: beak-like nose
Crouzon Syndrome

Features

- Cranial synostosis
- Exophthalmos
- Hypertelorism
- Strabismus
- Psittichorhina
- Mandibular prognathism
- Hypoplastic maxilla

(Jackson, 2009)
Crouzon Syndrome
Otolaryngological Considerations

- Hearing loss in 1/3 of cases
  - Auricular misalignment
  - Ossicular fixation
  - Serous otitis media
  - Sensorineural and mixed hearing losses

- Surgical craniofacial reconstruction

(http://candar.wordpress.com)
Crouzon Syndrome
Otolaryngological Considerations

- Surgical craniofacial reconstruction

(Jackson, 2009)
Apert Syndrome
(Acrocephalosyndactyly)

- Autosomal dominant
  - Craniofacial abnormalities by FGFR2 mutations
  - Syndactyly by keratinocyte growth factor receptor (KGFR) mutations
- Parents pass on to offspring 50% of the time
- Sporadic mutation in 98%
- Affects first pharyngeal arch

(Shah AR, Danahey DG. Distraction Osteogenesis of the Maxilla. eMedicine 11 Feb 2009.)
Apert Syndrome

**Features**

- Craniofacial dysostosis
- Hypoplastic maxilla
- Frontal prominence
- Syndactyly
- Exophthalmos
- Hypertelorism
- Saddle nose, depressed nasal bridge

**Oral cavity**
- High-arched palate, cleft palate
- Dental abnormalities
Apert Syndrome

Features

- Craniofacial dysostosis
- Syndactyly
- Malocclusion
- Ectopic eruption
- Frontal prominence
- Hypoplastic maxilla
- Hypertelorism
- Depressed nasal bridge

(Chen, 2009)
Apert Syndrome
Dr. Hutchinson’s mnemonic

Apert = Crouzon + Syndactyly
Apert Syndrome
Otolaryngological Considerations

- Conductive hearing loss
  - Chronic otitis media
  - Stapes fixation
  - Patent cochlear aqueduct
- Surgical craniofacial reconstruction

(Jackson, 2009)
Treacher Collins Syndrome
(Mandibulofacial Dysostosis)

- Also known as Franceschetti-Zwahlen-Klein syndrome
- Autosomal dominant
  - TCOF1 gene on chromosome 5q
  - New mutation in up to 60%
- Complete penetrance, variable expression
- First and second pharyngeal arches, grooves, and pouches
Treacher Collins Syndrome

**Features**

- Characteristic facial dysmorphia
  - Downward slanting palpebral fissures
  - Hypoplastic supraorbital rims
  - Malar hypoplasia
  - Mandibular hypoplasia
- Auricular and middle ear malformations
- **Lower eyelid coloboma**
- May have cleft palate
- Normal intelligence

(Tolarova, 2009)
Treacher Collins Syndrome

Features

- Downward slanting palpebral fissures
- Malar hypoplasia
- Hypoplastic supraorbital rims
- Lower eyelid colobomas
- Mandibular hypoplasia
- Auricular malformation

(courtesy of Dr. Hutchinson)
Treacher Collins Syndrome

Features

- Downward slanting palpebral fissures
- Lower eyelid colobomas
- Malar hypoplasia
- Hypoplastic supraorbital rims
- Mandibular hypoplasia
- Auricular malformation
- Scant lower eyelashes
Treacher Collins Syndrome
Otolaryngological Considerations

- **Hearing**
  - Conductive hearing loss in 30%
  - Ossicular malformation
  - Microtia and/or canal atresia
  - Mastoid hypoplasia
  - Some sensorineural hearing loss and vestibular dysfunction

- **Upper airway obstruction**

(Tolarova, 2009)
Treacher Collins Syndrome
Otolaryngological Considerations

- Surgical craniofacial reconstruction

(Jackson, 2009)
Goldenhar Syndrome
Oculoauriculovertebral Dysplasia

- Diverse etiologies
  - In utero vascular disruption with hematoma
  - Disturbed neural crest cells at 30-45 days gestation
- No single genetic locus
- First and second branchial arch
- *Hemifacial microsomia* when no internal organ or vertebral disruption
Goldenhar Syndrome

Features

- Hemifacial microsomia
- Mandibular hypoplasia
- Microstomia
- Epibulbar lipodermoids
- Upper eyelid coloboma
- Vertebral anomalies

(Bailey, 2006)
Goldenhar Syndrome

Features

- Hemifacial microsomia
- Epibulbar dermoid
- Mandibular hypoplasia
- Microtia and preauricular tags/pits
- Upper eyelid coloboma
- Epibulbar dermoid
OMENS
- Orbital distortion
- Mandibular hypoplasia
- Ear anomaly
- Nerve (facial) involvement
- Soft-tissue deficiency

“Plus” to include additional anomalies
- Cardiac
- Skeletal, limb
- Pulmonary
- Renal
- Gastrointestinal

Goldenhar Syndrome

Classification Scheme: Mandible

- Normal mandible

(Horgan, 1995)
Goldenhar Syndrome
Classification Scheme: Mandible

- **Type I**
  Smaller mandible but identifiable mandible

(Horgan, 1995)
Goldenhar Syndrome
Classification Scheme: Mandible

Type II
Functioning temporomandibular joint (TMJ) but abnormal shape and glenoid fossa

- Type II A
  Glenoid fossa is in an acceptable position

(Horgan, 1995)
Type II
Functioning temporomandibular joint (TMJ) but abnormal shape and glenoid fossa

- **Type IIB**
  Abnormally placed TMJ cannot be incorporated into surgical reconstruction

(Horgan, 1995)
Goldenhar Syndrome
Classification Scheme: Mandible

- Type III
  Absent ramus and nonexistent glenoid fossa

(Horgan, 1995)
Goldenhar Syndrome
Classification Scheme

- Orbits

- Ear

(Horgan, 1995)
Goldenhar Syndrome
Classification Scheme

- Facial Nerve
  - N0
  - N1
  - N2
  - N3

- Soft tissue defect
  - S0
  - S1
  - S2
  - S3

(Horgan, 1995)
Goldenhar Syndrome
Otolaryngological Considerations

- Hearing loss
  - More conductive than sensorineural
  - Ossicular abnormalities
  - Microtia
- Aberrant facial nerve course
- Surgical craniofacial reconstruction
Pierre Robin Syndrome

- **Sequence** of micrognathia, glossoptosis, and cleft palate
- **Syndrome** reserved for multiple malformations by a single etiology
- Confusing classification, up to 14 definitions (Breugem 2009)
- Possibly due to arrested intrauterine development
  - Mechanical
  - Neurological
  - Ontogenesis

(Tolarova, 2009)
Pierre Robin Syndrome

Features

- Cleft palate
- Glossoptosis
- Retrognathia
- Micrognathia
- MacroGLOSSIA AND ANKLOGLOSSIA UNCOMMON

(Jackson, 2009)
Pierre Robin Syndrome Sequence

- Mandibular hypoplasia
  - Between 7-11 weeks gestation
  - Mandible gets temporarily “stuck” between clavicle and sternum
  - Oligohydramnios
- Tongue remains high in oral cavity
- Cleft palate results from failed closure of palatal shelves
  - U-shaped cleft palate (80%), can have V-shaped (20%)
  - Typically no cleft lip
Pierre Robin Syndrome
Otolaryngological Considerations

- Airway compromise
  - Upper airway obstruction
  - Feeding, aspiration
  - Subglottic stenosis

- Hearing loss
  - Otitis media most common (60%)
  - Auricular malformation
  - Mixed hearing loss

- Associated syndromes
  - Stickler (18-25%)
  - Velocardiofacial (7-15%)
  - Treacher Collins (5%)
  - Hemifacial microsomia (3%)

- Mandibular “catch up” if isolated sequence

(Tolarova, 2009)
Pierre Robin Syndrome
Otolaryngological Considerations

- Distraction osteogenesis
- Intubation, tracheostomy
- Cleft palate repair

(courtesy of Dr. Hutchinson)
Stickler Syndrome

- Autosomal dominant
- Mutations of type II and XI collagen
  - COL2A1 gene on chromosome 12
  - COL11A1 and COL11A2 genes on chromosome 6
  - COL9A1 is rare recessive variant
- Craniofacial, ocular, and arthopathic features
Stickler Syndrome

Features

- “Flattened” face
- Ocular findings
- Musculoskeletal abnormalities
- Cleft palate

(courtesy of Dr. Hutchinson via Maria Blazo, M.D.)
Stickler Syndrome

Features

- Midfacial hypoplasia
- Long philtrum
- Short upturned nose
- Micrognathia

(Tolarova, 2009)

(Poulson, 2004)
Stickler Syndrome

Features

- **Ocular**
  - Myopia
  - Glaucoma
  - Retinal detachment
  - Cataracts

- **Musculoskeletal**
  - Osteoarthritis
  - Joint hypermobility
  - Abnormal epiphyseal development
  - Vertebral abnormalities
  - Scoliosis
Stickler Syndrome

**Otolaryngological Considerations**

- **Hearing loss**
  - Mild to moderate sensorineural hearing loss (SNHL) in 80%
  - Significant SNHL or mixed hearing loss in 15%
  - Conductive component secondary to eustachian tube dysfunction from cleft palate
  - Ossicular abnormalities may be present

- **Pierre Robin sequence**
  - Present in 25% of Stickler syndrome
  - Cleft palate
  - Micrognathia

(courtesy of Dr. Hutchinson via Maria Blazo, M.D.)
Waardenburg Syndrome

- Autosomal dominant
- Multiple genes
  - PAX3 (Types 1 and 3)
  - MITF, SNAI2 (Type 2)
  - EDN3, EDNRB, SOX10 (Type 4)
  - Autosomal recessive for Type 4
- Variable penetrance
  - Hearing loss
  - Dystopia canthorum
  - Pigmentary abnormalities
Waardenburg Syndrome

Features

- Dystopia canthorum
- Flat nasal root
- Hypoplastic nasal alae
- Synophyrs
- Heterochromia irides
- Isohypochromia irides
- White forelock
- Vitiligo
- Cleft lip and palate (10%) (Schwartz, 2010)
Waardenburg Syndrome

Features

- White forelock
- Hypoplastic alae
- Short philtrum
- Heterochromia irides
- Dystopia canthorum
- Isohypochoromia irides
- Flat nasal root
- Synophyrs

(courtesy of Dr. Hutchinson)
**Waardenburg Syndrome**

**Features**

- **Major**
  - Heterochromia irides
  - White forelock
  - Dystopia canthorum
  - Congenital sensorineural hearing loss
  - Affected first-degree relative

- **Minor**
  - Congenital leucoderma
  - Synophyrs
  - Broad high nasal root
  - Hypoplastic nasal alae
  - Premature graying hair
Waardenburg Syndrome

Diagnosis

- Major
  - Heterochromia irides
  - White forelock
  - Dystopia canthorum
  - Congenital sensorineural hearing loss
  - Affected first-degree relative

- Minor
  - Congenital leucoderma
  - Synophyrs
  - Broad high nasal root
  - Hypoplastic nasal alae
  - Premature graying hair

**Diagnosis**

- 2 major features
- 1 major feature + 2 minor features
Waardenburg Syndrome

Subtypes

- Type 1
  - Full symptomatology
  - Facial asymmetry, dysmorphic facies

- Type 2
  - No dystopia canthorum, white forelock less common
  - Sensorineural hearing loss, heterochromia irides

- Type 3 (Klein-Waardenburg syndrome)
  - Similar to Type 1 but with skeletal anomalies and mental retardation
  - Rib aplasia, cystic sacrum, cutaneous syndactyly

- Type 4 (Shah-Waardenburg syndrome)
  - Association with Hirschsprung disease

(Schwartz, 2010)
Waardenburg Syndrome

Subtypes

- **Type 1**
  - Full symptomatology
  - Facial asymmetry, abnormal facies

- **Type 2**
  - No dystopia canthorum, white forelock less common
  - Sensorineural hearing loss, heterochromia irides

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(courtesy of Dr. Hutchinson)
Waardenburg Syndrome

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Waardenburg Syndrome

Subtypes

- **Type 1**
  - Full symptomatology
  - Facial asymmetry, abnormal facies

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  - Sensorineural hearing loss, heterochromia iridum

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  - Rib aplasia, cystic sacrum, cutaneous syndactyly

- **Type 4** (Shah-Waardenburg syndrome)
  - Association with Hirschsprung disease
Waardenburg Syndrome
Otolaryngological Considerations

- Congenital sensorineural deafness
  - Typically not progressive
  - Hearing amplification
  - Cochlear implantation
- Cleft lip or palate repair
- Cosmetic considerations
Beckwith-Wiedemann Syndrome

- Imprinting defect at chromosome 11p15
  - Most cases are sporadic
  - Autosomal dominant familial inheritance in 15%
- Most common overgrowth syndrome in infancy

(courtesy of Dr. Hutchinson)
Beckwith-Wiedemann Syndrome

- Imprinting defect at chromosome 11p15
  - Most cases are sporadic
  - Autosomal dominant familial inheritance in 15%
- Most common overgrowth syndrome in infancy
- Five common features
  - Macroglossia
  - Macrosomia
  - Midline abdominal wall defect
  - Ear pits/creases
  - Neonatal hypoglycemia
Beckwith-Wiedemann Features

- Macroglossia
- Macrosomia
- Midline abdominal defect
- Ear pits/creases

(courtesy of Dr. Hutchinson via Maria Blazo, M.D.)
Beckwith-Wiedemann Features

- Major
  - Midline abdominal defect
  - Macroglossia
  - Macrosomia
  - Ear pits/creases
  - Adrenocortical cytomegaly
  - Renal abnormalities
  - Embryonal tumors
  - Cleft palate (rare)
  - Hemihyperplasia
Beckwith-Wiedemann Features

- **Major**
  - Midline abdominal defect
  - Macroglossia
  - Macrosomia
  - Ear pits/creases
  - Adrenocortical cytomegaly
  - Renal abnormalities
  - Embryonal tumors
  - Cleft palate (rare)
  - Hemihyperplasia

- **Minor**
  - Neonatal hypoglycemia
  - Polyhydramnios
  - Prematurity
  - Facial nevus flammeus
  - Hemangioma
  - Characteristic facies (i.e. midface hypoplasia)
  - Cardiac anomalies
  - Diastasis recti
  - Advanced bone age
Beckwith-Wiedemann
Diagnosis

**Major**
- Midline abdominal defect
- Macroglossia
- Macrosomia
- Ear pits/creases
- Adrenocortical cytomegaly
- Renal abnormalities
- Embryonal tumors
- Cleft palate (rare)
- Hemihyperplasia

**Minor**
- Neonatal hypoglycemia
- Polyhydramnios
- Prematurity
- Facial nevus flammeus
- Hemangioma
- Characteristic facies (i.e. midface hypoplasia)
- Cardiac anomalies
- Diastasis recti
- Advanced bone age

**Diagnosis**
- At least 2 common features
- 3 major features
- 2 major features + 3 minor features
Beckwith-Wiedemann
Otolaryngological Considerations

- **Macroglossia**
  - Airway obstruction, feeding difficulty
  - Less noticeable with age

- **Increased risk of malignancy**
  - Wilms’ tumor
  - Hepatoblastoma
  - Surveillance
    - Abdominal ultrasound every 3 months until 8 years
    - Alpha-fetoprotein every 6 weeks until 4 years
Neurofibromatosis
Type 1 (von Recklinghausen)

- *Peripheral* neurofibromatosis
- Autosomal dominant
  - Neurofibromin gene (NF1) on chromosome 17
  - Half result from *de novo* mutation
- Variable expression
- Better prognosis than Neurofibromatosis Type 2

(courtesy of Dr. Hutchinson via Maria Blazo, M.D.)

(Dahl, 2010)
Neurofibromatosis, Type 1

Features

- Café au lait spots
- Cutaneous neurofibromas
- Plexiform neuromas
- Lisch nodules
- Axillary or perineum freckling (Crowe sign)
- Optic gliomas
- Bone abnormalities
Neurofibromatosis, Type 1

Features

- Cutaneous neurofibomas
- Café au lait spots
- Axillary freckling
- Plexiform neuroma
- Optic glioma
- Lisch nodules
- Long bone bowing

(courtesy of Dr. Hutchinson via Maria Blazo, M.D.)

(Dahl, 2010)
Neurofibromatosis, Type 1

Diagnosis

- Six or more café au lait macules
  - Diameter larger than 5mm in prepubescent
  - Diameter larger than 15mm in adults
- Two or more neurofibromas or one plexiform neurofibroma
- Axillary or inguinal freckling
- Optic glioma
- Two or more Lisch nodules
- Distinctive osseous lesion
- First-degree relative with condition

(Nazareth, 2010)
Neurofibromatosis Type 2

- Central neurofibromatosis
- Autosomal dominant
  - NF2 (Merlin) gene on chromosome 22
  - Approximately 10% of all individuals with neurofibromatosis
- Significant morbidity, decreased lifespan
- Paucity of café au lait spots and Crowe sign

(Pletcher, 2010)
Neurofibromatosis, Type 2

Features

- Café au lait spots
- Schwannomas
  - Bilateral acoustic neuromas
  - Spinal cord
  - Nonvestibular
- Subcapsular cataracts
- Meningiomas
Neurofibromatosis, Type 2

Diagnosis

- Bilateral vestibular schwannomas
- Presumptive
  - Affected first-degree relative
  - Unilateral vestibular schwannoma
  - Or two of the following:
    - Meningioma
    - Glioma
    - Schwannoma
    - Juvenile posterior subcapsular or cortical cataract
- Suggestive
  - Unilateral vestibular schwannoma
  - Two of the following:
    - Meningioma
    - Glioma
    - Schwannoma
    - Juvenile posterior subcapsular or cortical cataract
  - Or multiple meningiomas
Klippel-Feil Syndrome
(Brevicollis, Wildervanck)

- Cervical vertebral fusion
  - Type I – single level
  - Type II – multiple, noncontiguous segments
  - Type III – multiple, contiguous segments
- Short, webbed neck and low hairline
- Unclear etiology
- Associated abnormalities
  - Sprengel deformity
  - Scoliosis
  - Facial asymmetry
  - Renal abnormalities

(Sullivan, 2009)
Other Syndromes
Without Craniofacial Features

- **Usher**
  - Hearing loss with defective inner ear
    - Type I – deafness and vestibular dysfunction
    - Type II – nonprogressive hearing loss and normal vestibular function
    - Type III – progressive hearing loss and half vestibular function
  - Progressive vision loss from retinitis pigmentosa

- **Pendred**
  - Sensorineural hearing loss
  - Thyroid goiter

- **Jervell and Lange-Neilsen**
  - Defective potassium channel from KCNQ1 and KCNE1 mutations
  - Sensorineural hearing loss and palpitations (long QT syndrome)
Conclusion

- Many syndromes will present to the otolaryngologist
  - Warrant otolaryngological intervention
  - Attention to coexisting conditions
- Many affected individuals are aware of the social stigma related to their condition

http://www.explosm.net/comics


References


References


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