Common Otolaryngological Congenital Abnormalities

Visual Synopsis of Classic Syndromes and Features

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All clinical photos are presented solely for educational purposes

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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

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

(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

(Jackson, 2009)
Crouzon Syndrome

Features

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

(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

[Link](http://candar.wordpress.com)
Crouzon Syndrome

Otolaryngological Considerations

- Surgical craniofacial reconstruction

Otolaryngological Congenital Abnormalities: Visual Synopsis

(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

(courtesy of Dr. Hutchinson)
Apert Syndrome

Features

Craniofacial dysostosis
Frontal prominence
Hypoplastic maxilla
Hypertelorism

Syndactyly

Malocclusion
Ectopic eruption
Depressed nasal bridge
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
- Lower eyelid colobomas
- Malar hypoplasia
- Mandibular hypoplasia
- Hypoplastic supraorbital rims
- Auricular malformation

(courtesy of Dr. Hutchinson)
Treacher Collins Syndrome

Features

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

(courtesy of Dr. Hutchinson)
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
- Microtia and preauricular tags/pits
- Epibulbar dermoid
- Upper eyelid coloboma
- Mandibular hypoplasia
Goldenhar Syndrome Classification Scheme

- **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 IIA
  Glenoid fossa is in an acceptable position

(Horgan, 1995)
Goldenhar Syndrome
Classification Scheme: Mandible

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

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

- Soft tissue defect

(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
- Retrognathia
- Macroglossia and ankloglossia uncommon
- Glossoptosis
- Micrognathia

(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)

(Tolarova, 2009)
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)
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

(courtesy of Dr. Hutchinson)
Waardenburg Syndrome

Features

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

Features

- White forelock
- Hypoplastic alae
- Short philtrum
- Heterochromia irides
- Dystopia canthorum
- Isohypochromia irides
- Flat nasal root
- Synophrys

(courtesy of Dr. Hutchinson)

(Schwartz, 2010)
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
  o Full symptomatology
  o Facial asymmetry, dysmorphic facies

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

■ Type 3 (Klein-Waardenburg syndrome)
  o Similar to Type 1 but with skeletal anomalies and mental retardation
  o Rib aplasia, cleft palate, and skeletal anomalies

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

(Schwartz, 2010)

(courtesy of Dr. Hutchinson)
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

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

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

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

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

Subtypes

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

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

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

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

■ Congenital sensorineural deafness
  o Typically not progressive
  o Hearing amplification
  o 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
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

(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


References


