22q11.2 Deletion Syndrome: Role of the SLP in Diagnosis, Assessment and Treatment

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22q11.2 Deletion Syndrome: Role of the SLP in diagnosis, assessment and treatment

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Overview

• Overview of the 22q11.2 deletion syndrome (22q)
• Speech-language and developmental profiles of children with 22q
• Assessment and treatment guidelines

History of the 22q11.2 Deletion Syndrome

• DiGeorge sequence/anomaly (DiGeorge, 1965)
  - Hypoparathyroidism, Thymic Hypoplasia, Interrupted Aortic Arch
• Velocardiofacial syndrome (Shprintzen et al., 1978)
• Sedlackova syndrome (Sedlackova, 1955) (R. Gorlin, personal account)
  - Hypenasality, facial dysmorphism
• Other names: Conoctrunal anomaly face, Opitz G/BBB, and Cayler cardiofacial syndromes
• 22q11.2 deletion syndrome (Scambler et al., 1992)
• Same Name Campaign (http://www.22q.org/news.php)
22q11.2 Deletion Syndrome

- 1/4000 births
- 2nd leading cause of congenital heart defects (after Down syndrome)
- Autosomal dominant inheritance
  - the majority of cases are de novo
- Males and females equally affected
- Variable expressivity
  (Devriendt et al., 1998; McDonald-McGinn et al., 1999)

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22q11.2 Deletion Syndrome

- Age at diagnosis (Oskarsdottir et al., 2005)
  - Median 6.5 years
  - 26% diagnosed in infancy (92% of which had cardiac defects)
  - 74% diagnosed >2 years of age, primarily due to speech-language delay/VPD, developmental delay, or recurrent infections, or milder presentation of “medical” problems
- The majority of children are diagnosed through cardiology, immunology, and Cleft Palate clinics

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22q Phenotype

- Developmental delay, learning disabilities, and/or mental retardation are present in >90% of patients with 22q11DS (Gerbes et al., 1999; Moss et al., 1999; Niklasson et al., 2001; Sastri et al., 1997)
  - 22q11DS is one of the most common causes of developmental delay, accounting for 2.4% of individuals with developmental disabilities (Rauch et al., 2006)
- 90% show motor delays from birth and the majority of children show signs of hypotonia and poor balance
  - Average age at walking is 18 months (Oskarsdottir et al., 2005)
22q Phenotype

- Cardiac/vascular anomalies in 70-80%
  - VSD, TOF, IAA, tortuous carotids
- Palatal anomalies/dysfunction in 75-85%
  - Cleft palate, SMCP, VPD
- Immune deficiency and frequent infections
- Renal anomalies in 30%

(McDonald-McGinn et al., 1999)

22q Phenotype

- Feeding/swallowing problems, related to:
  - Clefting/VPD
  - Gastroesophageal reflux
  - Hypotonia
  - Cardiac complications
  - Laryngeal anomalies
  - GI malformations
  - Airway obstruction (15% have Pierre Robin sequence)

(Eicher et al., 2000)

22q Phenotype

- Speech-language disorders
- Endocrine abnormalities
  - Hypocalcemia, hypoparathyroidism
- Neurologic/neuromuscular problems
  - Seizures, structural brain abnormalities
- C-spine abnormalities
- Short stature, growth hormone deficiency

(McDonald-McGinn et al., 1999)
22q Phenotype

• Hearing loss and ear anomalies
  – External ear dysmorphology
  – Middle and inner ear anomalies
  – ~50% have mild fluctuating conductive hearing loss secondary to chronic otitis media
  – ~15% have sensorineural hearing loss
  – Importance of early screening and placement of ventilation tubes

  (Digilio et al., 1999; Devriendt et al., 2004)

22q Phenotype

• Significant variability in degree of developmental delay and cognitive impairment, varies with age (Gorlin et al., 1999; Moss et al., 1995; Niklasson et al., 2001; Swobon et al., 1997)
  – Average IQ ~73 in children, PIQ>VIQ, lower IQ in familial cases (DeSmedt et al., 2007)

• Developmental, cognitive, and psychiatric findings appear to be independent of cardiac history

• Mathematical and visual-spatial deficits are common
  – Relative strengths seen in vocabulary, reading skills, rote/factual tasks (Simon et al., 2005)

22q Phenotype

• High prevalence of a range of behavioral and psychiatric disorders:
  – Generalized social skill deficits
  – Some children exhibit features of autism
  – ADHD
  – Depression and anxiety disorders
  – Psychotic disorders including schizophrenia and bipolar disorder
    • 22q11.2 deletion is one of the highest known risk factors for schizophrenia

  (Niklasson et al., 2001; Goldberg et al., 1993; Shprintzen et al., 1992; Bassett et al., 1996; Murphy et al., 1999; Papoutsis et al., 1998; Green et al., 2009)
Facial Phenotype

- Ethnic variation
- Long midface
- Prominent nose
- Broad nasal root
- Bulbous nasal tip
- Narrow palpebral fissures
- Ear dysmorphology
- Decreased facial affect and/or facial hypotonia
- Facial nerve and muscular asymmetry (asymmetrical lip function—depressor anguli may even be missing)

(Garito and Tapia, 2008)

Genetic Testing

- Karyotype ("chromosomes"): Occasionally detects large deletions (~25%) but often "overlooks" the deletion
- Fluorescence in situ hybridization (FISH) for 22q11.2 deletion (Ornseth et al., 1992; Scambler et al., 1992)
  - Up to 20% of cases missed by FISH testing alone
- Microarray comparative genomic hybridization (array-CGH) and oligoarray
- Multiplex ligation-probe amplification (MLPA)

Speech-Language Disorders in 22q
Speech-Language Profile in 22q

- Speech-language delays
- Hypernasality / VPD
- Articulation disorders
- Voice disorders (+/- laryngeal anomalies)
- Motor speech disorders
- Language disorders
- Social skills deficits

(Gorlin and Baylis, 2009)

Early Speech-Language Profile

- Speech-language delay and various communication disorders present in >90% of children and adolescents with 22q11DS
  - ~70% of children virtually nonverbal at 2 years of age
  - Language delays often exceed that expected for cognitive level
  - Expressive language tends to be more impacted than receptive

- Many have early signs of VPD
  - Missed diagnosis of glottal stops/articulation disorder may result in inappropriate treatment planning and delayed management of VPD

(Golding-Kushner, 2005; McDonald-McGinn et al., 1997; Scherer et al., 1999; Shprintzen et al., 1978; Solot et al., 2000; Carneol et al., 1999; Golding-Kushner et al., 1985)

Language Profiles Vary by Age

- Younger children with 22q11DS typically exhibit:
  - Reduced vocabulary size
  - Reduced speech output and restricted variety of sounds
  - Shortened length of sentences
  - Immature grammar
- Older children show:
  - Impaired comprehension
  - Impaired pragmatic/social language skills
  - Difficulties with figurative language, abstract concepts, temporal-spatial concepts
  - Difficulties with interpretation of nonverbal cues

(Carneol et al., 1999; Golding-Kushner et al., 1985; Scherer et al., 1999; Scherer et al., 2001; Woodin et al., 2001; Glaser et al. 2002; Persson et al., 2003)
Language Profiles

- For a minority of children, language difficulties may first become "visible" in school-age years as language demands and complexity increases.

- Majority show deficits in social interaction and pragmatics skills, which may be independent of cognitive status:
  - Difficulties with nonverbal cues
  - Difficulties with peer relationships

Voice Disorders

Voice disorders

- Hoarseness, breathy voice, reduced loudness, high-pitched, monotone
  - Vocal fold paralysis/paresis (+/- history of CHD surgery), laryngeal web

- Rough/hoarse quality may be masking underlying VPD

Articulation

- Most younger children have poor speech intelligibility
- 75% have articulation disorders and/or late acquisition and achievement of accuracy of speech sounds
- If VPD, increased risk for articulation disorder
  - Tend to use glottal stop substitutions more than other children with cleft palate
  - Will also display weak pressure consonants and audible nasal emission
- Many children also display errors independent of VPD
Articulation

Children with 22q have been shown to display:
• Significantly lower phonetic accuracy than children with cleft palate;
• More severe limitations in phonetic inventory and early vocabulary development than children with cleft palate;
• A higher percentage of glottal stops than children with cleft palate, regardless of severity of VPD; and
• Poorer articulation and expressive language than children with Down Syndrome and that expected given their IQ,
• regardless of age.

(Baylis et al., 2008; Scherer et al., 1999; Scherer et al., 2001; D’Antonio et al., 2001)

Motor Speech Disorders

Motor speech disorders have also been reported
• Dysarthria and/or Childhood apraxia of speech (Kummer et al., 2007; Hultman et al., 2000; Solot et al., 2000; Carneol et al., 1999; D’Antonio et al., 2001)
• Abnormalities of brain morphology and neurotransmitters (Bish et al., 2004; Simon et al., 2005)

Motor Speech Deficits in 22q

• Apraxia
  – Difficult differential diagnosis in the presence of VPD
  – Perceptual confusion of omissions vs glottal stops, decreased movement of mouth
  – Younger children show limited phonetic inventory and poor intelligibility

• Dysarthria
  – Older children show articulatory imprecision
  – Evidence of CN involvement with asymmetrical palatal and facial/lip motion
  – Voice and resonance disorders more typical of dysarthria
  – Cases of patients with 22q with Parkinson’s

Brain and neurotransmitter abnormalities
### Velopharyngeal Dysfunction in 22q

- 75-85% of children with 22q exhibit velopharyngeal dysfunction with hypernasal speech (Haapanen and Somer, 1993; Nayak and Sell, 1998; Rommel et al., 1999).
  - A minority of patients with 22q have a cleft palate, but most will have more subtle indicators of a submucous cleft palate or a "normal" appearing palate with VPD.

### VPD in 22q

- Severity of VPD/hypernasality tends to be more severe than children with nonsyndromic cleft palate.
- Tend to have less optimal surgical outcomes compared to children with nonsyndromic cleft palate.
  
  *(D’Antonio et al., 2001; Milczuk et al., 2007)*

### Other Factors Influencing VPD in 22q

- Abnormal position of the levator veli palatini (anteriorly displaced)
- Hypoplasia and hypotonia of the levator veli palatini and pharyngeal constrictors
- Palato-pharyngeal disproportion
  - Obtuse cranial base angle, wide pharynx
- Cranial nerve abnormalities leading to limited or asymmetric VP function.
- Abnormal VP closure timing
  
  *(Ruotolo et al., 2006; Hultman et al., 2000; Arystan and Shprintzen, 2004; Kuehn, 2003; Zim et al., 2003; Baylis et al., 2009)*
Complicating Matters

Treatment of VPD in 22q

- Need for presurgical nasopharyngoscopy, as well as MRI/MRA of head/neck and C-spine x-ray (D’Antonio and March, 1987; Hultman, 2000; Mackenzie-Stepner et al., 1987; Mitnick et al., 1996; Tatum et al., 2002)
- Tend to have a higher risk for persisting symptoms of VPD after surgery than other children with VPD (Mehendale et al., 2004; Losken et al., 2006)
  - But have more severe degree of hypernasality pre-operatively than other populations
- Tend to require wider pharyngeal flaps for best speech outcome (Tatum, 2002; Kirschner et al., 2005)
Assessment and Treatment Guidelines for the SLP

Role of SLP in Diagnosis

“Because of the high incidence of speech/resonance disorders and learning disabilities among this population, the SLP may be the most likely (and sometimes the first) professional to interface with these individuals.”

(Carneol, Marks, Weik et al., 1999)

If 22q is suspected...

- The SLP may initiate a conversation with the family about the concern that there may be an underlying explanation for the child’s speech, learning, palate, etc., problems that should be investigated, as this information will be important for treatment planning.

- The SLP may refer the patient to their local 22q Center, or even their local Cleft Palate Team for assessment, which should include a genetics evaluation and possible testing; or, the family may self-refer or be referred to a center/team by their primary care doctor.

- Coordinated care is critical (Bassett et al., 2011)
Implications for Assessment

All children with 22q should undergo:
1. Comprehensive developmental assessment and referral to an early intervention program
2. Assessment of palate and velopharyngeal function as part of a Cleft Lip and Palate / 22q Center Team evaluation
3. Hearing testing (in addition to newborn screening)
4. Comprehensive speech-language evaluation
5. Neuropsychological, psychological, and/or cognitive-behavioral assessment in the preschool years (ages 3+), at school-age and adolescence
6. Additional medical screenings/tests for children with 22q (echo, labs, renal ultrasound, C-spine, etc.)—coordinated through NCH 22q Center

(Carneal et al., 2008; Bassett et al., 2011)

Implications for Assessment

• Speech-language evaluation guidelines (profile/needs may change over time)
  – Articulation testing
  – Receptive and expressive language testing
  – Assessment of speech and VPC with Cleft Palate Team / 22q Center SLP
  – Assessment of pragmatics/social skills
  – Assessment of feeding/swallowing, as indicated
  – Oral exam
  – Updated testing every 1-3 years, depending on needs

Implications for Treatment

• Earlier assessment and intervention is better
  – Referral at time of diagnosis and frequent monitoring is preferred over a wait-and-see approach
  – Individualized treatment plan blending traditional early intervention approaches to stimulate language with cleft-related intervention approaches that emphasize early sound production (e.g., Scherer et al., 2008)
Implications for Treatment

• Children with 22q11DS benefit most from frequent, individualized and intensive therapies
  – Include focus on both language and speech sound production
  – 1:1 setting is best given attention deficits, developmental delay, and high frequency of compensatory articulation errors which require cleft-type therapy strategies

Implications for Treatment

• Address compensatory errors (e.g., glottal stops) first, using placement approaches similar to the cleft palate population (e.g., Trost-Cardamone et al., 2006)
• Language therapy needs may vary over the years, tend to persist for most children, goals should be individualized
• Many children with 22q will benefit from a social skills group in late schoolage and adolescence
• Attention, behavior, and cognitive problems can all impact progress with therapy

What is a 22q Team?

• Multidisciplinary team of experts that have experience in the diagnosis, assessment and treatment of children with 22q, and coordinates the care across the involved disciplines
  – Genetics, Cardiology, Plastic Surgery, Speech Pathology, Developmental Pediatrics, Dentistry, Immunology, Neuropsychology, Psychiatry, Audiology, Otolaryngology, Endocrinology, Hematology, Neurology, Orthopedics, Urology, Nephrology