Surgical Considerations in 22Q11.2 Deletion Syndrome

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KEYWORDS

• 22q11.2 deletion syndrome • Velocardiofacial syndrome • DiGeorge syndrome
• Velopharyngeal dysfunction

KEY POINTS

- The 22q11.2 deletion syndrome comprises the disorders also named DiGeorge syndrome and velocardiofacial syndrome.
- The 22q11.2 deletion syndrome is the syndrome most commonly associated with velopharyngeal dysfunction.
- Speech and language delays are common in patients with 22q11.2 deletion syndrome. The complexity of the associated speech and language disorders requires a multidisciplinary approach to management.
- Optimal surgical management of children with 22q11.2 deletion syndrome requires careful preoperative assessment, including imaging of the velopharyngeal mechanism.
- Functional and anatomic abnormalities of the velopharynx associated with 22q11.2 deletion syndrome demand that the surgical approach be tailored to each patient's individual needs.
- Medical comorbidities associated with 22q11.2 deletion syndrome require rigorous preoperative assessment and postoperative monitoring.

INTRODUCTION AND HISTORICAL PERSPECTIVE

General Overview of 22q11.2 Deletion Syndrome

The 22q11.2 deletion syndrome (22q11DS) is a common genetic disorder typically involving cardiac defects, cognitive-behavioral problems, speech-language disorders, velopharyngeal dysfunction (VPD), and dysmorphic facial appearance.[1–7] 22q11DS occurs in approximately 1 in 4000 births and is recognized as the most frequently occurring syndrome associated with VPD and palatal anomalies.[8–10]

Over the past few decades, the nomenclature associated with this syndrome has varied significantly. In 1955, velofacial hypoplasia (referred to as Sedlackova syndrome) was first described by Sedlackova,[11,12] a Czech phoniatrician, in a group of 26 children with congenital short soft palate, hypernasal speech, facial and ear dysmorphism, and muscle fiber abnormalities. In the late 1960s, Angelo DiGeorge[13] identified a new condition termed the DiGeorge anomalad, which included hypocalcemia, hypoparathyroidism, immune deficiency, and cardiac defects.[7,13–15] Later, in 1978, Shprintzen and colleagues[2] reported on a syndrome with typical facies, including a prominent nose and retruded mandible, cardiovascular anomalies, cleft palate, and learning disabilities, later named velocardiofacial syndrome. It was later discovered that these overlapping phenotypes share a common underlying genomic disorder, 22q11DS, now known to be responsible for most cases with these previously described conditions.[15,16]

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Inheritance of the 22q11.2 deletion is autosomal dominant with incomplete penetrance and variable expressivity, and most cases are de novo.[3,7,9,17] In 2005, it was reported that there was a bimodal distribution of age at diagnosis, with a peak at 6.5 years and remaining cases diagnosed in infancy (92% of which had a cardiac defect). For those children diagnosed after 2 years of age, most presented with a speech-language disorder and developmental delay.[18] At present, the diagnosis of 22q11DS is based on a combination of clinical features and genetic confirmation of the deletion. The presence of the 22q11.2 deletion can be confirmed with fluorescence in situ hybridization (FISH) testing as well as microarray. With advancements in genetic testing, smaller and more specific mutations in the same region of the genome can also be identified (eg, TBX1 mutations).[7,19,20]

More than 90% of children with 22q11DS present with speech and language disorders, VPD, and some degree of developmental delay.[2,5,7,21–23] Other frequent clinical findings include cardiac defects and vascular anomalies, including medial displacement and tortuosity of the internal carotid arteries.[24–31] Chiari malformation and cervical spine anomalies have also been observed.[28] Upper respiratory illnesses and feeding difficulties are frequent in infancy.[32] Typical craniofacial features (**Fig. 1**) include a long midface and vertical maxillary excess, malar flatness, and mandibular retrusion. Prominent nose with a squared nasal root, bulbous nasal tip, and hypoplastic nasal alae are also consistent. Also reported are narrow palpebral fissures, long philtrum and thin upper lip, reduced facial affect, and minor external ear anomalies, such as dysmorphic helices.[2,4,7] Endocrine, immune, and renal abnormalities are common.[8,26,27] Behavioral difficulties, as well as significant psychiatric disorders, are also frequently identified.[21,33,34] For a summary of additional phenotypic features, as well as general medical care guidelines for the syndrome, the reader is referred to Bassett and colleagues.[1]

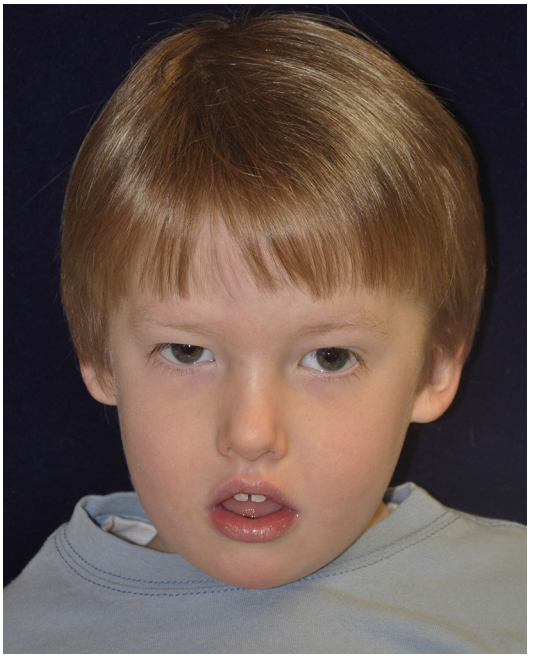

Fig. 1. Typical craniofacial features associated with 22q11DS, including long midface with vertical maxillary excess, malar flatness, prominent nose with squared nasal root and bulbous nasal tip, hypoplastic nasal alae, narrow palpebral fissures, thin upper lip, and mild craniofacial asymmetry.

Speech and Language Disorders in 22q11DS

Generalized speech-language delays are commonly reported in 22q11DS, with many children showing early signs of velopharyngeal (VP) inadequacy.[2,6,23,35,36] In addition to hypernasality, children may have articulation or phonological disorders, with a small percentage displaying motor speech disorders as well.[28,35,37,38,39] Flat affect, reduced emotional expression, fast rate, high pitch, and monotone speech are also observed in many children. A significant proportion of preschool and school-aged children with 22q11DS show glottal stop substitutions, which are the most common compensatory error in the speech of children with cleft palate.[35,36,40] The articulation skills of children with 22q11DS have been shown to be poorer than those of children with nonsyndromic cleft palate/VPD.[41] A comprehensive review of information regarding speech-language disorders in 22q11DS is given by Gorlin and Baylis.[42]

VPD in 22q11DS: Structural and Neuromuscular Considerations

VPD in patients with 22q11DS has a complex causal origin (**Fig. 2**). Although overt palate clefting is uncommon in 22q11DS, studies cite a high incidence of VPD and submucous clefting, as well as palatopharyngeal hypotonia, and obtuse cranial base or deep retropharynx (termed palatopharyngeal disproportion), all of which can compromise VP adequacy for speech.[2,4,7,19,23,43,44] Ruotolo and colleagues[45] reported that the increased pharyngeal depth associated with platybasia combines with increased pharyngeal width in affected patients to produce large increases in