KABUKI SYNDROME

OVERVIEW:

Kabuki Syndrome is a rare genetic syndrome, affecting between 1 and 10,000 and 1 in 32,000 people. Kabuki Syndrome is found equally among males and females. In 1968, Dr. Yoshikazu Kuroki and colleagues examined a boy in Fukuoka, Japan who possessed a unique set of malformations that did not fit any known syndromes at that time. Another child who had similar characteristics was examined in Kanagawa ten years later, followed by three others in the next two years. Around the same time, in 1967, Dr. Norio Niikawa and colleagues discovered a female infant who possessed an unusual set of characteristics that again, did not fit any known syndromes at that time. They discovered four other individuals from Hokkaido, Japan. In 1981, the findings of these individuals were presented as a new malformation syndrome and given the name, "Kabuki make-up." This name was chosen because of the facial resemblance to the makeup of actors in Kabuki, which is traditional Japanese theatre. This syndrome has also been referred to as Niikawa-Kuroki syndrome, but is now more commonly referred to as Kabuki Syndrome.

CAUSES:

In 2010, researchers at the University of Washington announced the discovery that a MLL2 gene mutation is responsible for about two-thirds of individuals with Kabuki Syndrome, thus making it possible to definitively diagnose some children. It is suspected that there are many gene mutations responsible for Kabuki Syndrome, leading researchers to further investigate the genetic causes.

DIAGNOSIS:

DIAGNOSTIC CRITERIA: An individual must possess four out of five of the main characteristics, with the distinct facial features being very important:

- Facial features: long palpebral fissures with eversion of outer third, arched eyebrows with sparse outer half, prominent eyelashes, prominent and/or misshapen ears, and depressed nasal tip
- Skeletal abnormalities
- Dermatoglyphic abnormalities
- Intellectual disability (mild to moderate)
- Postnatal short stature

ASSOCIATED FEATURES: There are co-existing conditions that may support diagnosis, but are not considered to be key characteristics. These associated conditions vary in number and degree and each individual may demonstrate unique features:

- Hyptonia
- Feeding difficulties
- Recurrent infections
- Congenital heart defects
- Renal (kidney/urinary tract anomalies)
- Small mouth, micrognathia (smallness of the jaws), cleft or high arched palate
- Hypodontia (missing teeth), unusually shaped teeth, and misalignment
- Birth - normal weight; infancy & childhood - underweight; pre-teen onward - possible obesity
- Early breast development in girls
- Hearing impaired and/or inner ear malformations

HEALTH ISSUES:

- **Facial characteristics**: long palpebral fissures, lower palpebral eversion, arched eyebrows with sparse outer lateral half, long eyelashes, blue sclera, ptosis, depressed nasal tip, prominent broad philtrum, cleft lip/palate or arched palate, dysmorphic ears, preauricular pits, abnormal dentition
- **Musculoskeletal characteristics:** short fingers, short middle phalanx of fifth finger, syndactyly - mild webbing between fingers, cranial abnormalities, vertebral abnormalities, rib anomalies, scoliosis, hypotonia, joint laxity, dislocations of hip, patella and shoulders
- **Neurological issues**: hypotonia (can impact motor development and feeding) microcephaly and seizures
- **Growth:** delay often starts during the first year of life- adult with Kabuki will be shorter than the norm
- **Cardiac:** cardiovascular malformation (congenital, during the formation of the heart); most common: juxtaductal coarctation of the aorta, ventricular septal defect, and atrial septal defect
- **Hearing:** hearing loss is common (possibly due to recurrent infections); conductive hearing loss is most common
- **Vision:** many children with Kabuki have optical anomalies, more common: blue sclerae, strabismus, coloboma, ptosis, and micropthalmia
- **Sensory/Behavior:** Many individuals with Kabuki syndrome have sensory processing disorder; more common reported sensory issues include, need for oral stimulation, tactile defensiveness towards various sensations and stimuli, panic-like reactions to

certain noises, and aversion to textures and/or smells of select foods. Anxiety, obsessive/compulsive traits and autistic-type behaviors may be present

- **Gastrointestinal:** Gastroesophageal reflux; Undiagnosed diarrhea and/or constipation is commonly reported
- **Endocrine and Genito-Urinary:** Renal tract infections can occur. Common renal anomalies include: renal dysplasia, renal agenesis, horseshoe kidney, and ectopic kidney; Ureter abnormalities include obstruction, reflux, and duplication.
- **Immune/Blood:** susceptible to recurrent ear infections in their early childhood years. typical toddler has approximately 11 upper respiratory infections a year
- **Ectodermal:** hyperelastic skin; hands feel soft and are short with short fingers; Persistent fetal fingertip pads is highly characteristic; abnormalities with the nails, hair and skin. Nails can be absent, incompletely formed and fragile.

LIFESPAN:

Current research on Kabuki Syndrome does not indicate a shortened life span. There is no cure for this syndrome, but many of the associated features can be corrected or lessened with appropriate intervention.

LIVING WITH KABUKI SYNDROME:

Kabuki Syndrome is a life-long disability. It is not a progressive disorder, however, new conditions may occur over time due to complications caused by Kabuki. The ability to live an independent life will vary from person to person depending on their abilities and resources available. The majority of individuals with Kabuki syndrome will need a supervised home or work setting, however, many people will have a mixed degree of independence and assistance, and some people may be able to function independently at work and home.

DEVELOPMENT AND THERAPIES:

Individuals with KS often experience delays in multiple areas of development. Evaluation as part of an early intervention is extremely important. During school years, children with Kabuki will benefit from various therapies to enhance learning.

Early Intervention - Identify needs, develop plan to provide therapeutic services, and track progression
Physical - Develop gross motor skills to improve strength, and assess need of supports for various settings
Occupational - Develop fine motor skills, strength, and dexterity. Assess need of supports for various settings
Speech - Improve articulation, oral motor control, develop language and, introduce sign language (if needed)

Sensory Integration - Improve sensorimotor, self-regulation, environmental settings, social skills, and self-esteem issues of sensory integration dysfunction
Music – an area of interest that can enhance and motivate learning in

RESOURCES:

Kabuki Syndrome Network: http://kabukisyndrome.com/