PROPOSED GUIDELINES

Based on frequencies found in literature review

Major Features

- Dysphagia / Feeding difficulty / Gastrostomy tube (g-tube) (95%)
- Postnatal short stature (97%)
- Characteristic facial features (98%)
- Thick lips (95%)
- Loose skin (94%)
- Abnormal palmar skin creases (99%)
- DD (developmental delay) / MR (mental retardation) (100%)

Unique Features

- * Congenital heart problems (65%) including pulmonic stenosis (20%), hypertrophic cardiomyopathy (40%) and atrial tachycardia (30%)
- * Benign (44%) and malignant tumors (15%)
- * Characteristic facial features with large mouth (78%)
- Stretchy skin with hyperpigmentation
- Kyphoscoliosis
- Engaging personality
- Curly hair
- Normal head circumference

Other Features

- Polyhydramnios (62%)
- Birth weight >50%
- Hernias (50%)
- Vision problems – ptosis, nystagmus and strabismus

* When added to Major Features will greatly increase

Costello Syndrome Diagnostic Guidelines

Defining the criteria to diagnose a multiple congenital anomaly syndrome takes many years, many patients and remains largely unscientific, often relying on the "gestalt" (overall impression) of a syndrome to make the final diagnosis.

Costello's first reports in 1971 and 1977 were expanded by der Kaloustian (1991), and Martin and Jones (1991). Recent review articles characterize over 100 patients (Hennekam, 2003), and summarize neurological and behavioral issues (Kawame et al., 2003; Axelrad et al., 2004, Delrue et al., 2003), cardiac complications (Lin et al., 2002), orthopedic problems (Yassir et al., 2003), malignancies (Gripp et al, 2003), and the adult appearance (White et al., 2005).

A clinical diagnosis of Costello syndrome can now be confirmed by testing for specific mutations in the HRAS gene.

For additional information or copies of this brochure contact:

International Costello Syndrome Support Group:
www.costellokids.org.uk

Costello Syndrome Family Network:
http://www.costellosyndromeusa.org/

WEB LINKS:

Online Mendelian Inheritance in Man:
http://omim.org/entry/218040

GeneReviews for Costello syndrokme:
http://www.ncbi.nlm.nih.gov/books/NBK1507/

RASopathiesNet
http://rasopathiesnet.org

This document was developed by Medical Geneticist V.K. Proud and parent, Lisa Schoyer with assistance from Angela Lin and Karen Gripp, Costello Syndrome Professional Advisory Committee.

In loving memory of V.K. Proud.

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Costello Syndrome

Guidelines

for Clinical Diagnosis

Clinical Geneticists have been working since 1995 with families and the International Costello Syndrome Support Group (ICSSG) and the Costello Syndrome Family Network (CSFN) to better understand this disorder. For the 4th International Costello Syndrome Conference in St. Louis, Missouri, we presented diagnostic guidelines for Costello syndrome.

NATURAL HISTORY

Infants (<1year)

Polyhydramnios
Fetal distress
C-section (Cesarean section)
LGA (large for gestational age)
Feeding problems and hypotonia
Gastrostomy tube (g-tube) in the first 4 years
FTT (failure to thrive)
Growth delay in weight and length but with normal head circumference
Motor delays

Toddlers (1-3 years)

Distinctive facial features, broad mouth
Loose, lax skin, soft, deep wrinkles, abnormal creases in palms and soles, stretchy skin, loose joints
Hernias
Hypertrophic cardiomyopathy
Arrhythmia, especially atrial tachycardia
Strabismus, ptosis
Malignancy
DD (developmental delay)

Children (4-12 years)

Short stature
Distinctive facial features with broad mouth and thick lips
Kyphoscoliosis, cervical kyphosis
Remarkably pleasant, sociable, humorous and easy-going personality

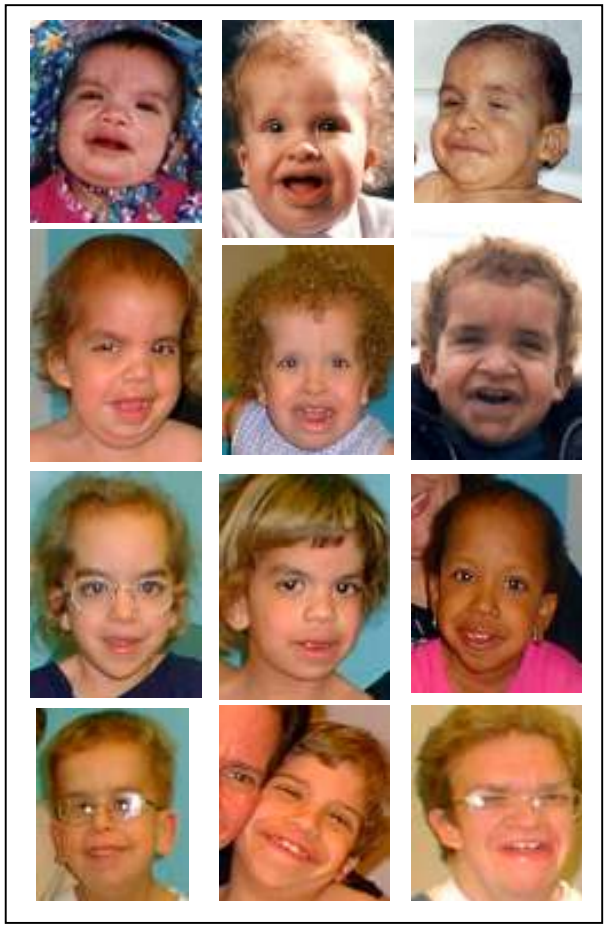
Adolescents/Adults

Coarse classic facial features
Thicker, often curly hair
Nasal fibromata
Breast papilloma
Hyperkeratosis, hyperpigmentation
Short stature
Skeletal and orthopedic problems
DD (developmental delay) / MR (mental retardation)

KEY FEATURES

The faces of these individuals, who range in age from infancy to adulthood, illustrate the distinctive appearance of Costello syndrome.

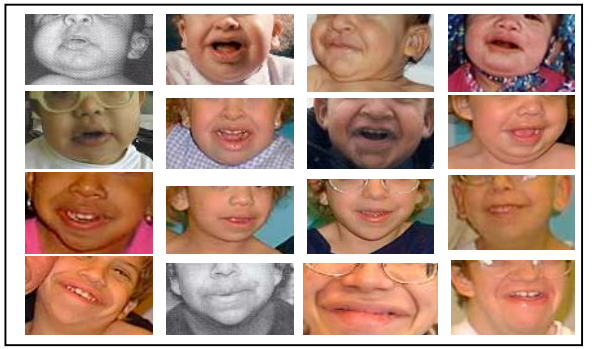
Distinctive facial features



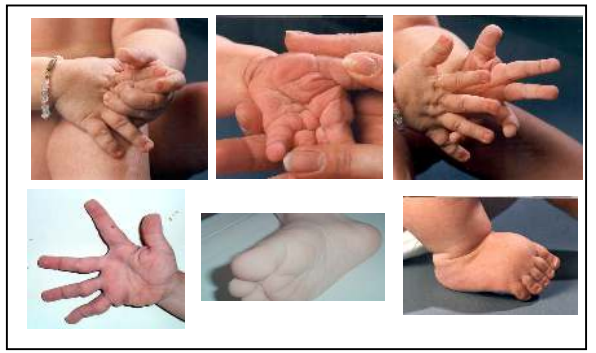
KEY FEATURES

continued

Large mouth and thick lips



Loose skin / deep creases



Life-threatening complications

Cardiac arrhythmia
Hypertrophic cardiomyopathy
Malignancy

Photo credits go to the parents of the above children and adults and, for the fourth image on the first panel, Rick Guidotti/Positive Exposure.