Common Genetic and Epigenetic Syndromes

Darius J. Adams, MD[a,b,*], David A. Clark, MD[b]

KEYWORDS

• Syndrome • Genetic • Microdeletion • Epigenetic • Imprinting

KEY POINTS

- Cytogenetic anomalies should be considered in individuals with multiple congenital anomalies.
- DNA methylation analysis is the most sensitive initial test in evaluating for Prader-Willi and Angelman syndromes.
- The timely identification of cytogenetic anomalies allows for prompt initiation of early intervention services to maximize the potential of every individual as they grow older.
- Although many of these conditions are rare, keeping them in mind can have a profound impact on the clinical course of affected individuals.

Newborns with large genomic anomalies tend to have a pattern of malformations. If an isolated anomaly is noted, it is less likely a large genomic anomaly but could still be related to single gene mutations. There are exceptions as in the case of Turner syndrome; the only presenting sign at birth in some cases is lymphedema. The common large-scale chromosomal and genomic anomalies are reviewed.

LARGE-SCALE GENOMIC ANOMALIES

Down Syndrome

Down syndrome is one of the most common large-scale genomic anomalies with a prevalence of approximately 1 in 700 births.[1–5] Infants born with Down syndrome are typically hypotonic and consequently have feeding difficulties. Cardiac anomalies are present in approximately 40% of individuals with Down syndrome. Most commonly, an atrioventricular canal or endocardial cushion defect is noted; however, isolated ventricular septal defects, auricular septal defect, and aberrant subclavian arteries have also been noted less frequently. Additional findings include the following:

- Low-set ears
- Up-slanting palpebral fissures

Disclosure statement: Speakers Bureau/grants from BioMarin.
[a] Atlantic Health System, Morristown, NJ, USA; [b] Albany Medical Center, Albany, NY, USA
* Corresponding author. 100 Madison Avenue, Morristown, NJ 07690.
E-mail address: Darius.adams@atlantichealth.org

Pediatr Clin N Am 62 (2015) 411–426
http://dx.doi.org/10.1016/j.pcl.2014.11.005 **pediatric.theclinics.com**
0031-3955/15/$ – see front matter

- Brushfield spots
- Flat facial profile
- Short neck
- Hypotonia/poor Moro reflex
- Mental retardation (Figs. 1–4)

Early intervention services can be beneficial and can help maximize potential. An increased risk of leukemia and Alzheimer disease has been noted in older individuals.

Trisomy 13 (Patau Syndrome)

Trisomy 13 has a prevalence of approximately 1 in 7000 births.[6] This condition can present on the holoprosencephaly spectrum, with some individuals having severe midline anomalies of the brain and other structures including a single nostril and pronounced hypotelorism (closely set eyes). Additional findings are as follows (Figs. 5 and 6):

- Cutis aplasia (usually of posterior scalp)
- Polydactyly
- Microphthalmia, coloboma of iris
- Cleft lip and/or palate
- Abnormal ears that are low set
- Cardiac anomalies
- Severe neurologic involvement

Life span is typically limited to weeks or months; however, there have been cases that have been described with individuals living years. Individuals with mosaicism can have milder manifestations and live much longer.

Trisomy 18 (Edwards Syndrome)

Trisomy 18 has a prevalence of approximately 1 in 4500 births.[6] Individuals with this syndrome have a characteristic clenched hand appearance with a tendency for overlapping of the index finger over the third digit and the fifth finger over the fourth digit. Additional findings include the following:

- Short sternum
- Low-set malformed ears
- Micrognathia
- Clenched hands with overlapping fingers (Fig. 7)

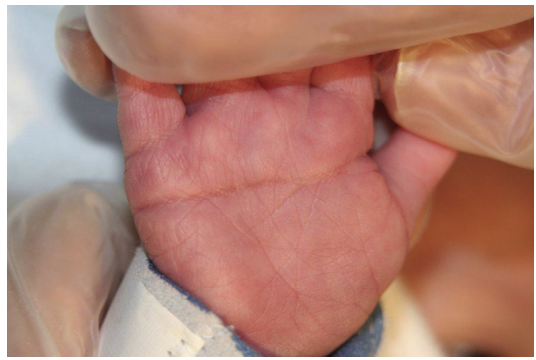

Fig. 1. Single transverse palmar crease noted in trisomy 21. (*Courtesy of* D. Clark, MD, Albany, NY.)