Evaluation and Diagnosis of the Dysmorphic Infant

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KEYWORDS

• Aplasia cutis congenita • Holoprosencephaly • Asymmetric crying facies
• Preauricular tags • Cleft lip with or without cleft palate • Congenital heart defects
• Ventral wall defects • Polydactyly

KEY POINTS

- Congenital anomalies are a significant cause of neonatal intensive care unit (NICU) admissions.
- Congenital anomalies may be genetic in etiology or may be the result of teratogenic exposure or multifactorial inheritance (the interaction of both genetic and environmental factors).
- The presence of a particular congenital anomaly may necessitate evaluation for the presence of other specific associated anomalies or genetic syndromes.
- Most genetic syndromes are defined by a specific pattern of congenital anomalies.
- Some congenital anomalies may be inherited within families as an isolated trait, highlighting the importance of taking a family history and of examining parents for similar anomalies, when appropriate.

INTRODUCTION

Congenital anomalies are present in at least 10% of all NICU admissions, many of whom have an underlying genetic condition.[1] Neonatologists are often the first physicians to evaluate these infants and consequently need to be familiar with various physical differences to pursue further screening for occult malformations, perform diagnostic testing, and appropriately counsel families. The purpose of this article is review the dysmorphology examination with particular attention to anomalies that are readily apparent in the neonatal period.

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An anomaly is a structural defect that deviates from the normal standard and can be categorized as major or minor. A major anomaly has surgical, medical, or cosmetic importance and may be a marker for other occult malformations. A minor anomaly has no significant surgical or cosmetic importance; however, many genetic syndromes are recognized based on the pattern of minor anomalies present. Anomalies arise from 1 of 3 mechanisms, each of which has different diagnostic and inheritance implications. The first mechanism is termed a malformation, which is a structural defect arising from an intrinsically abnormal developmental process. Malformations include anomalies like congenital heart defects and cleft lip and palate. These types of anomalies are more likely associated with a genetic condition or predisposition. A deformation is an abnormality arising from prenatal mechanical forces on otherwise normally formed fetal structures. Deformations can include clubfeet, overlapping toes, and unusual head shape (although these disorders may also be malformations). Deformations are rarely genetic and recurrence risks are typically low. Lastly, disruptions are structural defects resulting from the destruction or interruption of intrinsically normal tissue. Examples of disruptive anomalies include limb reduction defects from amniotic band sequence and certain types of intestinal atresias due to vascular insufficiency.[2] Anomalies due to this mechanism are much less likely due to a genetic condition or to recur in a future pregnancy.

BIRTH PARAMETERS

Both increased and decreased birth parameters are associated with multiple genetic and nongenetic etiologies. Fetal macrosomia may be defined as a birth weight greater than 4000 g or more than 2 SDs above the mean of a reference population, whereas fetal-growth restriction is defined as a birth weight less than 2 SDs below the mean for gestational age in a reference population. The differential diagnoses for both fetal macrosomia and fetal growth restriction are broad and include chromosomal abnormalities and teratogenic exposures. Chromosomal abnormalities have varying phenotypes depending on the size of the chromosomal segment involved and the individual genes in that segment. Consequently, it is beneficial to evaluate for congenital anomalies in those who have macrosomia or growth restriction. In both instances, a chromosomal microarray should be considered. If the physical examination indicates features of a well-characterized genetic syndrome, such as a trisomy or Beckwith-Wiedemann syndrome, then testing can be tailored to that particular syndrome (**Tables 1** and **2**).[3–8]

Although abnormal birth parameters in the presence of congenital anomalies frequently indicate a genetic syndrome, this is not always the case. For example, infants of diabetic mothers are commonly macrosomic (although growth restriction can also occur) and may display congenital malformations at a frequency of 2 to 4 times the general population rate. Consequently, it may be difficult to distinguish between diabetic embryopathy and a genetic syndrome.[4] In the absence of confirmed maternal diabetes and one of the more specific anomalies seen in diabetic embryopathy, such as caudal regression syndrome or tibial hemimelia with preaxial polydactyly (**Fig. 1**), this diagnosis should be considered a diagnosis of exclusion and the clinician should consider further genetic testing, such as a chromosomal microarray, to evaluate for a chromosome abnormality.[2,3]

Similarly, fetal growth restriction can be due to nongenetic causes, such as placental insufficiency, maternal hypertension, multiple gestation (ie, twinning), and maternal preeclampsia. Most of these conditions result in asymmetric growth restriction as a result of inadequate nutrient transfer to the fetus.[9] Placental insufficiency has also been associated with an increased risk of hypospadias in male infants[10]; therefore, not all birth