Recognizable Syndromes in the Newborn Period

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KEYWORDS

• Newborn period • Syndrome recognition • Dysmorphology • Birth defects

KEY POINTS

- Many syndromes have a different presentation in the newborn period compared with childhood or adult life, and recognition early in life is frequently based on a characteristic pattern of dysmorphic features and/or malformations that can vary from the classic presentation seen in childhood.
- Early recognition of syndromes is increasingly important, as for many of them there are professional guidelines for treatment and surveillance.
- Genetic testing with next-generation sequencing will increasingly be performed for diagnosis in the newborn period and will expand our understanding of the clinical variability within syndromes.

INTRODUCTION

The primary goals of the assessment of an infant with congenital anomalies in the neonatal period are to establish a diagnosis, identify associated abnormalities, develop a management plan, and assess the natural history and prognosis. The correct diagnosis enables parents and clinicians to obtain accurate information, plan for appropriate surveillance, determine recurrence risks and access support and advocacy groups. Standard tools for the diagnostic assessment in the newborn period include a pregnancy history, birth history and family history, physical examination, and investigations to delineate the presence of additional anomalies, including cranial ultrasound, chest radiograph, echocardiogram, abdominal or renal ultrasound, skeletal survey, and ophthalmologic examination. If the baby is stable, more detailed imaging or invasive testing, such as magnetic resonance imaging (MRI) scan of the brain or other relevant regions, can be considered.

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Chromosome testing with array comparative genomic hybridization (aCGH) is the standard of care in the investigation of many infants with multiple congenital anomalies, birth defects, or neurologic signs. Chromosomal aneuploidies and chromosomal deletions and duplications are identified in an estimated 7.5% of infants with multiple congenital anomalies. A growing number of infants also undergo gene panel sequencing or genomic testing with exome sequencing. Despite the increased testing options now available, an accurate knowledge of the presentation of syndromes in the neonatal period is often needed to obtain the correct diagnosis.

One of the most important initial decisions is whether an infant's presentation is syndromic, as opposed to an isolated birth defect or sequence that is less likely to be associated with additional malformations or an easily discernible underlying genetic cause. A syndrome can be defined as a set of developmental anomalies or pattern of defects occurring together in a recognizable and consistent pattern that is caused by a single cause.[1] Many syndromes are associated with dysmorphic features and a recognizable facial gestalt that enables a clinical diagnosis. Imaging or other investigations to determine the extent of phenotypic involvement and chromosomal, biochemical, and/or molecular genetic testing are usually performed to confirm the syndrome diagnosis. It is important to be aware that, just as the appearance and physiology of typically developing infants alters with time, the manifestations of syndromes can be specific to different developmental time periods. In the neonatal period, syndromes may either be more straightforward or more difficult to recognize. It is vital for clinicians to be aware of these differences, so that an age-appropriate differential diagnosis is considered at the baby's bedside.

This review describes a selection of the syndromes most frequently encountered in the newborn period, with an emphasis on the physical findings that present shortly after birth. The authors have focused on syndromes that are frequently encountered and that differ significantly in presentation in the newborn period compared with later in childhood, and on syndromes that are frequently encountered and for which early recognition is helpful because it prompts surveillance or more timely treatment. Space limitations have prevented the coverage of many conditions, and the craniosynostoses and disorders of sexual development that may present in the neonatal period are not included.

TEXT

Table 1 provides a summary of common syndromes that are recognizable in the newborn period based on cardinal symptoms and signs. Syndromes with causative genes have been grouped into body systems; syndromes caused by chromosome aberrations, metabolic conditions, and conditions with multifactorial or an unknown cause are listed separately. Genetic confirmation should be performed for those conditions for which it is available (Table 2), and it is important to remember that many chromosomal abnormalities can be phenocopies of Mendelian genetic syndromes. In the following text, the authors discuss selected conditions that have specific neonatal presentations, listing clinical features and reasons that an early diagnosis may be helpful.

CRANIOFACIAL SYNDROMES

The diagnosis of Van der Woude syndrome (MIM 119300) is a good example of the utility of a thorough examination, as the small lip pits that are pathognomonic for this condition in association with cleft lip/palate (CL/P) can sometimes be missed