CHROMOSOMAL MICROARRAY ANALYSIS FOR DEVELOPMENTAL DELAY/INTELLECTUAL DISABILITY, AUTISM SPECTRUM DISORDER, OR CONGENITAL ANOMALIES

I. Chromosomal microarray analysis for developmental delay, intellectual disability, autism spectrum disorder, or congenital anomalies (81228, 81229, S3870) is considered **medically necessary** when:

   A. The member has developmental delay and/or intellectual disability, excluding isolated speech/language delay (see below), **OR**

   B. The member has autism spectrum disorder, **OR**

   C. The member has multiple congenital anomalies not specific to a well-delineated genetic syndrome, **OR**

   D. The member has short stature.

II. Chromosomal microarray analysis for developmental delay, intellectual disability, autism spectrum disorder, or congenital anomalies (81228, 81229, S3870,) is considered **investigational** for all other conditions of delayed development, including:

   A. Isolated speech/language delay*.

*See Background and Rationale section for more information about this exclusion.

DEFINITIONS

1. **Autism spectrum disorders**: Defined in the DSM V as persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history:
   a. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth

conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.

b. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
c. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

2. **Multiple congenital anomalies:** According to ACMG, multiple anomalies are not specific to a well-delineated genetic syndrome. These anomalies are structural or functional abnormalities usually evident at birth, or shortly thereafter, and can be consequential to an individual's life expectancy, health status, physical or social functioning, and typically require medical intervention.

3. **Developmental delay (DD)**: Slow-to-meet or not reaching milestones in one or more of the areas of development (communication, motor, cognition, social-emotional, or adaptive skills) in the expected way for a child's age

4. **Intellectual disability (ID)**: Defined by the DSM V as an individual with all of the following:

    a. Deficits in intellectual functions, such as reasoning, problem solving, planning, abstract thinking, judgment, academic learning, and learning from experience, confirmed by both clinical assessment and individualized, standardized intelligence testing.

    b. Deficits in adaptive functioning that result in failure to meet developmental and sociocultural standards for personal independence and social responsibility. Without ongoing support, the adaptive deficits limit functioning in one or more activities of daily life, such as communication, social participation, and independent living, across multiple environments, such as home, school, work, and community.

    c. Onset of intellectual and adaptive deficits during the developmental period.

BACKGROUND AND RATIONALE

Chromosomal Microarray Analysis for Developmental Delay/Intellectual Disability, Autism Spectrum Disorder, or Congenital Anomalies

American Academy of Pediatrics

The American Academy of Pediatrics (2014, reaffirmed 2020) issued a clinical report on the optimal medical genetics evaluation of a child with developmental delays (DD) or intellectual disability (ID), which stated “CMA [chromosome microarray analysis] now should be considered a first-tier diagnostic test in all children with [global] GDD/ID for whom the causal diagnosis is not known…. CMA is now the standard for diagnosis of patients with GDD/ID, as well as other conditions, such as autism spectrum disorders or multiple congenital anomalies.” (p. e905)

American College of Medical Genetics and Genomics (ACMG)

The ACMG (2010, reaffirmed 2020) published a Clinical Practice Resource on array-based technologies and their clinical utilization for detecting chromosomal abnormalities. CMA testing for copy number variants was recommended as a first-line test in the initial postnatal evaluation of individuals with the following:

- Multiple anomalies not specific to a well-delineated genetic syndrome
- Apparently nonsyndromic DD/ID
- ASD [autism spectrum disorder]

A 2021 focused revision to the ACMG practice resource “Genetic evaluation of short stature” states: “Chromosomal microarray…should be part of the initial genetic work-up for idiopathic short stature (ISS) and small for gestational age (SGA) with persistent short stature as well as syndromic short stature…” (p. 813)

CMA is considered investigational for all other indications, including members with isolated speech/language delay (AAP 2014 Clinical Report, page e905), as diagnostic yield in this clinical situation is thought to be low.

REFERENCES

1. Moeschler JB, Shevell M; Committee on Genetics. Comprehensive evaluation of the child with intellectual disability or global developmental delays. Pediatrics. 2014, reaffirmed March 2020;134(3):e903-e918. doi:10.1542/peds.2014-1839
2. Manning M, Hudgins L; Professional Practice and Guidelines Committee. Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities. Genet Med. 2010, reaffirmed April 27 2020;12(11):742-745. doi:10.1097/GIM.0b013e3181f8baad
3. Manning M, Hudgins L; American College of Medical Genetics and Genomics (ACMG) Professional Practice and Guidelines Committee. Addendum: Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities [published online ahead of print, 2020 Jun 8]. Genet Med. 2020;10.1038/s41436-020-0848-8. doi:10.1038/s41436-020-0848-8
4. Mintz CS, Seaver LH, Irons M, Grimberg A, Lozano R, ACMG Professional Practice and Guidelines Committee. Focused Revision: ACMG practice resource: Genetic evaluation of short stature. Genet Med. 2021;23(5):813-815.