Medical Workup in Patients with Newly Diagnosed Autism Spectrum Disorder (ASD)

Children and adults with diagnoses of both intellectual disability (ID) and ASD based on DSM-V criteria with no previous medical workup should undergo the following:

Syndromic Appearance

If the patient’s appearance and history are consistent with a known genetic syndrome, consider referral to genetics and/or obtaining syndrome-specific labs. Consider obtaining a microarray if appearance is syndromic even if age is >21 years.

No Syndromic Appearance

Routine

Genetic testing should be discussed with patients and their caregivers in patients with ASD who are 21 years old or younger. They should understand that: 1) the testing may not identify an underlying cause for their ASD/ID, 2) the testing may reveal genetic abnormalities not related to ASD/ID, 3) the testing may confirm a genetic cause of ASD/ID that can help us be vigilant about other potential issues related to that genetic problem, 4) testing may not change the approach to clinical care.

If the patient and caretakers choose to proceed with testing:

- Obtain chromosomal microarray (CMA)
- If the above are abnormal, consider referral to a genetics counselor

Specific Risks

Genetic testing:

- In a patient who has had 2 or more miscarriages, consider adding a karyotype
- If concern for Rhett syndrome (girls with a history of significant developmental regression), and CMA / fragile X testing was normal, consider obtaining *MECP2* Rhett mutation
- If comorbid macrocephaly (head circumference >2.5 SD above mean for age and sex), consider obtaining *PTEN* testing to rule out hamartomatous tumor syndromes

Metabolic Testing

- Testing for problems with metabolism is indicated in pediatric patients who have:
  - Lethargy, limited endurance
  - Hypotonia
  - Recurrent vomiting and dehydration
  - Early seizure
  - Dysmorphic or coarse features
Developmental regression outside of the typical ASD speech regression at 18 – 24 months
- Hearing impairment
- Vision impairment
- Unusual odors
- Specific food intolerance (eg, protein)
- Inadequate or questionable adequate newborn screen
- Poor growth, microcephaly

- If indicated, obtain:
  - Serum – total homocysteine, acyl-carnitine profile, and amino acids
  - Urine – organic acids, glycosaminoglycans, oligosaccharides, purines, pyrimidines, guanidinoacetate/creatine metabolites

*Rarely*

- MRI is NOT typically indicated
  - Consider MRI if there are neurologic deficits on clinical exam, or in the presence of specific indicators (e.g., microcephaly, regression, seizures, and history of stupor/coma)
- EEG is NOT typically indicated
  - Consider EEG in patients with seizure-like episodes
  - Consider EEG in patients with a significant developmental regression that takes place after the age of 3 to evaluate for potential Landau-Kleffner syndrome, Electrical Status Epilepticus in Sleep (ESES), etc.

- Lead testing should be based on risk factors for lead exposure (e.g. living in an older home with potential lead paint), but is NOT routinely done as part of the ASD workup

*Not Indicated*

- Tests with little evidence that should NOT be done include: tests for heavy metals (other than lead), yeast metabolites, gut permeability micronutrients, trace elements, and immune abnormalities

References: