COL2A1 Gene Abnormality and Kabuki Syndrome: Possible Risk Factors for Catatonia and Psychosis in an Adolescent Female

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Introduction. The COL2A1 gene, among other collagen genes, is fundamental in the composition of the extracellular matrix (ECM). Dysfunction in ECM contributes to disruption of synapse connectivity, neuronal mutation and abnormalities of neurotransmission, including GABAergic, glutamatergic, dopaminergic systems, and neural inflammatory processes. The COL2A1 gene and KMT2D (pathogenic variant in Kabuki Syndrome) have been theorized to play a role in the development of schizophrenia, though neither has been described as increasing risk of catatonia.

Case Report. A 16-year-old female, with Kabuki Syndrome (without known pathogenic variants), intellectual disability, craniofacial dysmorphism, sensorineural hearing loss, periventricular leukomalacia, and heterozygous COL2A1 gene abnormality presented with abrupt change in baseline for one month. The examination was consistent with catatonia, including poor oral intake, incontinence, slowed movements, catalepsy, disorientation, agitation, mutism, insomnia, stereotypic movements, autonomic abnormalities, and visual and auditory hallucinations. Medical workup including neuroimaging, EEG, lumbar puncture, and encephalitis panel were negative. Benzodiazepines resolved catatonia symptoms but caused behavioral disinhibition. Low dose Valproate and Olanzapine led to rapid and complete resolution of symptoms with return to baseline.

Discussion. To our knowledge, this is the first description of catatonia and psychosis in a patient with COL2A1 genetic variant and Kabuki Syndrome. GABA, glutamate, and dopamine dysfunction, as well as neuroinflammation, are all identified risk factors for catatonia, and the COL2A1 gene is known to affect these processes. More studies are required to establish the relationship between the Kabuki Syndrome phenotype, COL2A1 gene, and potential increased risk for psychosis and catatonia in these populations.