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Adult-Onset Psychosis and Clinical Genetics: A Case of Phelan-McDermid Syndrome

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To the Editor

Psychiatric presentation of Phelan-McDermid Syndrome (22q13.3 deletion) is not well characterized.[1] We present the case of a patient whose worsening symptoms led to psychiatric evaluation, with subsequent genetic testing and diagnosis.

Case Report

The patient is a 38-year-old woman previously diagnosed with cerebral palsy, major depressive disorder with psychotic features, general anxiety disorder, and schizophrenia with catatonia. She has a history of developmental delay, hypotonia, and seizure-like activity since childhood. Although she has moderate mental retardation (IQ: 51) she is verbal, friendly, and completed high school (special education). General functioning, mood, and behavior were stable into adulthood until her first psychiatric hospitalization at age 32. She began having behavioral regression and decline in skills including bathing, dressing, and feeding. For periods of weeks she became nonverbal, confused, detached, and incontinent. She would often stare at her hands, at times shaking or screaming, and refuse to eat.

Dysmorphology examination was notable for multiple anomalies, including striking bilateral lateral eyelid fullness and ptosis. Chromosomal microarray revealed a 22q13.33 deletion diagnostic for Phelan-McDermid syndrome (OMIM#606232). Treatment was optimized with quetiapine titrated to 300 mg twice daily. Approximately 2 weeks after treatment initiation, her family reported significant improvements in the patient's affect, speech, and level of independence, with resolution of psychotic symptoms and normalization of sleep/wake cycle. At 10 months later, she continues to struggle with depression, although her psychosis is improved.

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Discussion

Patients with 22q13 deletion are haplo-insufficient for the SHANK3/PROSAP2 protein affecting excitatory synapse formation.[2] Affected children often display stereotyped repetitive movements and struggle with sleep and socialization. Some are diagnosed with autistic spectrum disorder. Adults may develop psychotic symptoms, including catatonia.[3] Our patient's symptoms responded poorly to SSRI or benzodiazepine monotherapy, but relatively quickly to quetiapine. One previous case report showed a similar response to risperidone,[2] and, together, these cases may build evidence for new approaches to treatment of these catatonic episodes specific to SHANK3 deletion.

Although a constellation of findings—facial gestalt, hypotonia, developmental and speech delay—are consistently seen in this syndrome, no clinical criteria are diagnostic; therefore, genetic testing is necessary. Caveats to genetic testing in psychiatry exist,[3] but attention to behavioral regression, unexplained developmental delay, or unusual physical exam findings should prompt genetics consultation.

This case highlights the emerging role of genetic testing in psychiatry. This patient and her family now have an explanation for her lifelong diagnostic odyssey and valuable information regarding recurrence risk. A plan to screening for known medical comorbidities has been implemented, and the family has access to peer groups.[4] Molecular evaluation in other people with similar presentation may lead to improved treatment strategies.

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