



Response to Washington Post May 1, 2021 article “Doctors said the boy was suffering from teenage psychosis. What he really had was a rare genetic condition.”

Presenting information on complex disorders in leading national newspapers can greatly benefit the public. Such presentations, illustrated with one or more individuals with the disorder of focus, can enhance the understanding of the clinical presentation and inform about potential treatment approaches. Unfortunately, the above article did not convey medical information accurately on the link between genetic disorders and neuropsychiatric disorders and is misleading regarding the established standards of care.

The individuals described have chromosome 22q11.2 Deletion Syndrome (also known as Velocardiofacial Syndrome; VCFS), which impacts multiple organ systems including the brain. The effects on the brain are often associated with neuropsychiatric symptoms and diagnosable illnesses. Importantly, such neuropsychiatric manifestations are indistinguishable in presentation and course from those observed in the general population. They have the same developmental pattern: for example, anxiety and attention deficit disorders are common in childhood, and schizophrenia spectrum disorders in late adolescence and early adulthood.

Because 22q11.2 Deletion Syndrome provides a window into understanding associated neuropsychiatric conditions, there have been global efforts of scientists and clinicians working collaboratively so that large samples can be examined systematically. The National Institute of Mental Health (NIMH) of the National Institutes of Health (NIH) has supported this research, recognizing its potential contributions to advance the understanding and treatment of brain disorders such as schizophrenia, which is about 20 times more common in 22q11.2 Deletion Syndrome than in the general population. As part of these efforts, the International Brain Behavior Consortium (IBBC) included 22 international sites documenting the clinical presentation of schizophrenia and associated neurobehavioral and neuroimaging patterns in 22q11.2 Deletion Syndrome. These were found to be the same as those established in schizophrenia in the general population. Current research efforts have expanded to include other genetic disorders associated with major neuropsychiatric manifestations, spearheaded by the NIMH-supported Genes to Mental Health (G2MH) Network. The 22q11.2 deletion is known to be a major contributor to schizophrenia, and ongoing research aims to reveal the multiple genetic and other contributors that increase or decrease risk for this important psychiatric illness, and so could identify new strategies for prevention and management.

The Washington Post article is conceptually misleading in its assumption that because a psychiatric disorder occurs in association with a genetic disorder then somehow it is no longer a psychiatric disorder. This would be like saying, when a person with a known genetic risk factor for breast cancer meets criteria for breast cancer, that the person did not have breast cancer. It has been recognized for several decades that the 22q11.2 Deletion Syndrome is associated with schizophrenia. Avoiding the

diagnosis of this serious mental illness may further reinforce stigma and ignores the vast literature on schizophrenia in 22q11.2 Deletion Syndrome.

Avoiding the psychiatric diagnosis may also lead to inappropriate treatment. Metyrosine has not met the bar for evidence as an appropriate intervention and does not meet recognized standards of treatment for schizophrenia in the general population, or in 22q11.2 Deletion Syndrome. There are no published randomized clinical trials, which are necessary to establish the safety and efficacy of a treatment.

Diagnosis of complex disorders requires multidisciplinary expertise and recognition that there are multiple pathways to specific disorders. It is very helpful to know from clinical genetic testing that an individual has the 22q11.2 Deletion Syndrome. For those presenting with psychotic features such as hallucinations, expert psychiatric care to ensure accurate psychiatric diagnosis and implementation of optimal treatment that follows standard clinical practice guidelines remain the essence of evidence-based medicine.

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