Congenital and Acquired Disorders Presenting as Psychosis in Children and Young Adults

Sheldon Benjamin, MD[a,*], Margo D. Lauterbach, MD[d,e], Aimee L. Stanislawski, MD[b,c]

KEYWORDS

• Psychosis • Congenital disorders • Inherited disorders • Genetic disorders
• Differential diagnosis

KEY POINTS

FOR EVALUATING CHILDREN AND ADOLESCENTS WITH PSYCHOTIC SYMPTOMS

- Perform a standard medical and laboratory evaluation, then examine for the presence of dysmorphic features, major neurologic signs, and major organ system problems.
- In a child without dysmorphic features, intellectual disability, or family history of psychotic disorder, perform a comprehensive neurologic and medical evaluation.
- Become familiar with the 7 more common, easily missed, congenital disorders that can include psychosis (acute intermittent porphyria, Asperger disorder, Gilbert syndrome, glucose-6-phosphate dehydrogenase deficiency, Huntington disease, neurofibromatosis type 1, XXX karyotype).

INTRODUCTION

Psychiatrists, neurologists, and pediatricians are often called on to evaluate youth with psychotic symptoms for possible medical, neurologic, or neurodevelopmental causes. The diagnosis of acquired neurologic disorders, although not always straightforward, is most familiar to general psychiatric practitioners and is briefly reviewed. In contrast, a bewildering array of rare congenital neuropsychiatric conditions that

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[a] Departments of Psychiatry and Neurology, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655, USA; [b] Behavioral Health, VA Western NY Healthcare System, 3495 Bailey Avenue, Buffalo, NY 14215, USA; [c] Department of Psychiatry, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, Buffalo, NY 14215, USA; [d] Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD, USA; [e] Neuropsychiatry Program, Sheppard Pratt Health System, 6501 North Charles Street, PO Box 6815, Baltimore, MD 21285-6815, USA
* Corresponding author.
E-mail address: sheldon.benjamin@umassmed.edu

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include psychosis has been described. Although some reviews of congenital disorders that include psychosis have been published,[1–5] clear guidance on the neuropsychiatric evaluation and differential diagnosis of these conditions can be difficult to find.

To address this dearth of information, in a previous publication,[6] we described the congenital disorders that may include psychosis, and proposed a straightforward neuropsychiatric approach to their differential diagnosis based on major associated signs and relative prevalence of the disorders. In this article, we update the diagnostic guide using similar methodology, searching PubMed using the term psychosis paired with the terms metabolic, genetic, congenital, or neurodevelopmental. Disorders were included if they were heritable or congenital, typically present by young adulthood, included at least 3 case reports, and contained adequate description of psychotic symptoms. Descriptors of psychotic symptoms included such terms as hallucinations, delusions, schizophrenialike, and schizophreniform, as well as known psychotic syndromes such as Capgras. Standard neurology textbooks were consulted for additional information.[7–11] Disorders were categorized by the presence of 1 or more of 20 prominent groups of associated signs with an emphasis on those of neurologic significance that occur most commonly in each disorder. Epidemiologic information gathered via OMIM (Online Mendelian Inheritance in Man),[12] GeneTests,[13] and orphanet[14] was used to classify disorders into more common (prevalence greater than 1/10,000), rare (prevalence 1/10,000 to 1/50,000), and extremely rare (prevalence less than 1/50,000) groups. Guidance on laboratory and neurodiagnostic evaluation is offered for each disorder, along with a list of known genetic loci.

CLINICAL APPROACH

The evaluation of children and adolescents with new-onset psychosis begins with a thorough personal, psychosocial, medication (prescription and over-the-counter), and family history, followed by physical and neurologic examination. Although secondary psychotic symptoms can occur in any child, the absence of dysmorphic features, intellectual disability, or family history of psychosis should increase suspicion of an acquired medical or neurologic cause. The list of acquired disorders reported to present with psychosis is extensive.[15,16] There is no gold standard laboratory evaluation, but a screening examination including complete blood count, hepatic and renal function tests, serum electrolytes and glucose, vitamin B_{12} and folate, thyroid-stimulating hormone, erythrocyte sedimentation rate, and antinuclear antibody, along with urinalysis, is typically recommended, with testing for the human immunodeficiency virus if risk factors are present, serum ceruloplasmin in the presence of a movement disorder, and serum or urine toxicology if ingestion or drug abuse was possible. A history of seizures or brief stereotyped behavioral episodes is evaluated with a sleep-deprived electroencephalogram. Focal findings or a history of traumatic brain injury are followed up with cranial magnetic resonance imaging (MRI). Evidence of delirium, seizures, or catatonia indicates expansion of laboratory evaluation to include toxicologic screening, cerebrospinal fluid (CSF) analysis, and anti-*N*-methyl-D-aspartate (NMDA) receptor antibodies, the most frequent causes of such presentations being infection-related, drug-induced, traumatic, autoimmune, and metabolic.[17] The subacute development of psychosis, variable memory impairment, followed by either delirium or variable consciousness, seizures, catatonia, involuntary movement disorder, or autonomic instability may indicate the presence of autoimmune limbic encephalitis. This constellation is an indication for MRI (to seek evidence of limbic hyperintensities on fluid-attenuated inversion recovery