Prodromal symptoms of schizophrenia: What to look for

Badari Birur, MD, Bradley G. Burk, PharmD, BCPP, and Rachel E. Fargason, MD

Dr. Birur is Associate Professor, Department of Psychiatry and Behavioral Neurobiology, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama. Dr. Burk is Clinical Pharmacist, University of Alabama at Birmingham, Birmingham, Alabama. Dr. Fargason is the Patrick H. Linton Professor and Medical Quality Officer, Senior Associate Director of Strategic Planning, Department of Psychiatry and Behavioral Neurobiology, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama.

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Schizophrenia is characterized by psychotic symptoms that typically follow a prodromal period of premonitory signs and symptoms that appear before the manifestation of the full-blown syndrome. Signs and symptoms during the prodromal phase are subsyndromal, which implies a lower degree of intensity, duration, or frequency than observed when the patient meets the full criteria for the syndrome. Early detection of prodromal symptoms can improve prognosis, but these subtle symptoms may go unrecognized.

In schizophrenia, a patient may exhibit prodromal signs and symptoms before the appearance of pathognomonic symptoms, such as delusions, hallucinations, and disorganization. The schizophrenia prodrome can be conceptualized as a period of prepsychotic disturbances depicting an alteration in the individual's behavior and perception. Prodromal symptoms can last from weeks to years before the psychotic illness clinically manifests.[1] The prodromal symptom cluster typically becomes evident during adolescence and young adulthood.[2]

In the mid-1990s, investigators tried to identify a "putative prodrome" for psychosis. The term "at-risk mental state" (ARMS) for psychosis is based on retrospective reports of prodromal symptoms in first-episode psychosis. Over the next 2 decades, scales such as the Comprehensive Assessment of ARMS (CAARMS)[3] and the Structured Interview for Prodromal Syndrome[4] were designed to enhance the objectivity and diagnostic accuracy of the ARMS. These scales have reasonable interrater reliability.[5]

Researchers also have attempted to stage the severity of ARMS.[6] Key symptom group predictors were studied to determine which individual symptoms or cluster of symptoms are most associated with poor outcomes and progression to psychosis. Raballo et al[7] found the severity of the CAARMS disorganization dimension was the strongest predictor of transition to frank psychosis. Other research suggests that approximately one-third of ARMS patients transition to psychosis within 3 years, another one-third have persistent attenuated psychotic symptoms, and the remaining one-third experience symptom remission.[8,9]

Despite multiple studies and meta-analyses, current scales and clinical predictors continue to be imperfect.[8] Efforts to identify specific biological markers and predictors of transition to clinical psychosis have not been successful for ARMS.[10,11] The ***Table***[8,9,12,13] (***page 47***) summarizes diagnostic criteria that have been developed to more clearly identify which ARMS patients face the highest imminent risk for transition to psychosis; these have been referred to as ultra high-risk (UHR) criteria.[14] These UHR criteria depict 3 categories of clinical presentation believed to confer risk of transition to psychosis: attenuated psychotic symptoms, transient psychotic symptoms, and genetic

Table

Clinical screening of patients at risk for developing schizophrenia

Ultra high-risk diagnostic criteria[a]	Key additional symptom clusters that confer a high risk for transition to psychosis
A. Attenuated psychotic symptoms The presence of ≥1 of the following attenuated psychotic symptoms lasting ≥1 week and present within the past year and no longer than 5 years: • Paranoid ideation • Ideas of reference • Odd beliefs or magical thinking • Odd thinking and speech • Unusual perceptual experiences	**A. Low global functioning** • Functional decline • Long duration of symptoms • Low educational attainment • Poor social functioning
B. Transient psychotic symptoms The presence of ≥1 brief limited intermittent psychotic symptoms that last <1 week and resolve spontaneously: • Delusions • Hallucinations • Disorganized thought process	**B. Alterations in cognition and thinking** • Poor attention • Disorganization • Highly unusual thought content • Bizarre thinking
C. Genetic predisposition Genetic and phenotypic trait vulnerability (schizotypal personality disorder in the patent or having a first-degree relative with a psychotic disorder) plus recent significant decline in psychosocial functioning	**C. Positive psychotic symptoms** **D. Negative symptoms** **E. Sleep disturbance** **F. Affective instability**

[a]A, B, or C in the context of drop in function or ongoing poor functioning satisfies ultra high-risk criteria

Source: References 8,9,12,13

predisposition. Subsequent research found that certain additional symptom variables, as well as combinations of specific symptom clusters, conferred increased risk and improved the positive predictive sensitivity to as high as 83%.[15] In addition to the UHR criteria, the ***Table***[8,9,12,13] also lists these additional variables shown to confer a high positive predictive value (PPV) of transition, alone or in combination with the UHR criterion. Thompson et al[16] provide more detailed information on these later variables and their relative PPV.

What about treatment?

While discussion of the optimal treatment options for patients with prodromal symptoms of schizophrenia is beyond the scope of this article, early interventions can focus on preventing the biological, psychological, and social disruption that results from such symptoms. Establishing a therapeutic alliance with the patient while they retain insight and engaging supportive family members is a key starting point. Case management, cognitive-behavioral or supportive therapy, and treatment of comorbid mood, anxiety, or substance use disorders are helpful. There is no clear consensus on the utility of pharmacotherapy in the prodromal stage of psychosis. While scales and structured interviews can guide assessment, clinical judgment is the key driver of the appropriateness of initiating pharmacologic treatment to address symptoms. Because up to two-thirds of patients who satisfy UHR criteria do not go on to develop schizophrenia,[16] clinicians should be thoughtful about the risks and benefits of antipsychotics.

Approximately one-third of patients with 'at-risk mental state' transition to psychosis within 3 years

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