HHV-6 and Schizophrenia:
An Unusual Presentation or an Unproven Etiology?

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Human herpesvirus-6 (HHV-6) is the etiologic agent of roseola infantum, a self-limited acute febrile illness of childhood. Infections in immunocompetent patients are rare and pose diagnostic challenges.[1] Prior studies[2,3] have suggested that central nervous system inflammation from an immune response to infectious agents can produce symptoms closely resembling schizophrenia. Further, studies[4] have demonstrated a genetic co-susceptibility to some viral infections and schizophrenia. The potential medical causes of psychosis (secondary psychosis) are broad and are prone to be overlooked. Further complicating this situation is the lack of clinical practice guidelines for treating psychiatric symptoms of a specific secondary etiology. We present a case of HHV-6 infection with an unusual neuropsychiatric presentation in an immunocompetent patient.

Case Report

A 44-year-old Black man, who was an active military member, presented to the emergency department with a 1-day history of left-sided weakness and pain, severe intermittent headache, double vision, fever, and auditory hallucinations. He reported a history of auditory hallucinations resulting in a psychiatric inpatient hospitalization 3 months prior. While hospitalized, he was diagnosed with schizophrenia and stabilized on an unknown dose of haloperidol. He was informed of a potential medical cause; however, no further workup was completed. After discharge, he continued to experience waxing and waning symptoms but did not take the haloperidol. At the presenting visit, a lumbar puncture was performed and revealed neutrophilic pleocytosis. A provisional diagnosis of meningoencephalitis was made, and treatment was initiated with empirical antibiotics and an antiviral. The psychiatry department was consulted for concern of psychosis. Six days later, CSF PCR (cerebrospinal fluid polymerase chain reaction) came back positive for HHV-6. Since this is usually a self-limiting disease, the infectious disease consultant recommended discontinuation of antibiotics and the antiviral. He improved over the next few days with supportive treatment and was discharged with haloperidol 5 mg nightly and 2 mg daily as needed for auditory hallucinations. He was advised to follow up with the psychiatry department; however, he did not attend his follow-up appointment.

Discussion

This case illustrates behavioral symptoms that can present with an underlying infection and the difficulties in diagnosing such a possible etiology. Interestingly, Niebuhr et al[3] found a correlation between HHV-6 and schizophrenia among medically discharged military personnel. A large-scale genomic study by Nudel et al[4] found evidence of the presence of a genetic risk for acquiring infections and a genetic correlation with mental disorders, as well as a high degree of comorbidity between them. Despite preliminary case-control and genomic studies suggesting an association between infection and schizophrenia, there remains a paucity of clinical information on how best to manage these cases. In our patient, HHV-6 was suspected as the etiology of symptoms that were originally diagnosed as schizophrenia. Given the severity of this diagnosis, patients would benefit from further exploration of this association to prevent misdiagnosis with a serious mental illness.

Primary psychosis is the result of an underlying psychiatric disorder, while secondary psychosis is due to a medical cause. In delineating the 2 disorders, history of the presenting problem, mental status examination, and collateral information are paramount.[5] Primary disorders are likely to present in the adolescent and young adult population.[6] A first break in a middle-aged or geriatric patient is suspicious for secondary causes. A subacute presentation would be suggestive of a medical cause.[6] Our patient was older and exhibited a subacute presentation. Finally, his symptoms presented with nonpsychiatric symptoms, which should greatly raise the suspicion for secondary psychosis. Psychiatric diagnoses often indicate lifelong medication use. Given the inherent risks of medications and the potential for a medical etiology being left unexplored, it is imperative that a thorough workup for an underlying medical cause be completed when warranted.

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