Postpartum Psychosis or Something Else?

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ABSTRACT

Psychosis is a psychiatric emergency that affects up to 1 in 500 women postpartum and can result from various etiologies. We present a case vignette and review of the relevant literature to highlight the broad differential diagnosis of postpartum psychosis with atypical features. Recommendations for evaluation, diagnosis, and treatment of patients with complex neuropsychiatric symptoms in the postpartum period are discussed. This case of postpartum psychosis with malignant catatonia highlights the role of immunology in the development and treatment of postpartum psychosis and the need for future research to more accurately define the etiology and best tailor treatment.

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Postpartum psychosis is a severe psychiatric illness that occurs after 0.89 to 2.6 per 1,000 births and is considered a psychiatric emergency due to its association with suicide and infanticide.[1–3] Diagnosing and managing postpartum psychosis can be challenging as there are no diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*), symptoms are often atypical, and there are no consensus guidelines for management.[4–6] We describe a case of first-episode psychosis in an adolescent female with malignant catatonia presenting immediately after delivery and discuss the diagnosis and treatment of complex neuropsychiatric symptoms during the postpartum period.

CASE VIGNETTE

Ms A, a primigravida, unmarried, 18-year-old female with a past psychiatric history of anxiety and no reported history of trauma, presented to the hospital at 39 weeks gestation with contractions. She had received routine prenatal care, and her pregnancy was complicated by anemia and gestational hypertension in the third trimester without symptoms of preeclampsia. After 5 hours of labor, she delivered a healthy baby boy with normal Apgar scores via a spontaneous vaginal delivery. Her labor was complicated by an asymptomatic elevation of maternal heart rate to 190 beats per minute (bpm), but it immediately decreased to 120 bpm after delivery, with minimal blood loss.

On postpartum day 2, Ms A was found in the bathroom making generalized convulsive movements and was unresponsive to voice for less than 1 minute. Upon evaluation from the Obstetrics team, she was altered, disoriented to time, and unable to follow 2-step commands. Her blood pressure was found to be elevated to 142/82 mm Hg, and she was given labetalol 20 mg IV once and then maintained on nifedipine 10 mg daily until her hypertension resolved at postpartum day 10. Given her history of gestational hypertension, she was treated empirically for eclampsia with magnesium 4 g once intravenously. The Neurology team was consulted, and examination results were unremarkable. As recommended by Neurology, Psychiatry was consulted to evaluate for non-epileptic seizure as her mental status remained altered.

Upon initial psychiatric evaluation, Ms A was withdrawn, disoriented to time, and unable to answer most questions. Her family reported that she had not slept during the 2 days prior to delivery and that on the day after delivery she had visual hallucinations of many people in her hospital room, including her baby who was in the nursery. Ms A expressed concern to her family that the baby did not love her and was not her own. On postpartum day 3, Ms A displayed symptoms of catatonia, which included mutism, upper extremity rigidity, staring, and minimal responsiveness to stimuli, resulting in a Bush-Francis Catatonia Rating Scale[7] score of 15, along

Clinical Points

- Postpartum psychosis has a broad differential including autoimmune encephalitis.
- A thorough workup, including input from the Psychiatry, Neurology, and Medicine teams, is essential to determining the etiology of psychosis in the postpartum period.
- Immune system dysfunction is common in the postpartum period and may play a role in the treatment of psychosis.

with a fluctuating level of consciousness. She was started on intravenous (IV) lorazepam, which was titrated up to 2 mg every 8 hours. The next day, she exhibited symptoms of dysautonomia, with systolic blood pressure to 170 mm Hg, heart rate to 138 bpm, and fever to 101 °F. Given the severity of her symptoms and concern for malignant catatonia, she was transferred to the medical intensive care unit.

The diagnostic workup for Ms A's neuropsychiatric symptoms was focused on delirium due to occult medical etiology, such as thyroiditis, urea cycle disorder or infection, or autonomic encephalitis, versus catatonia due to a primary medical or psychiatric etiology. Laboratory results were notable for elevated white blood cell count (13.9 K/μL), elevated lactic dehydrogenase (336 U/L), low serum iron (57 μg/dL) and percent saturation (15%), with normal total iron binding capacity, elevated erythrocyte sedimentation rate (32 mm/h), elevated C-reactive protein (1.9 mg/dL), and decreased immunoglobulin G (502 mg/dL). Comprehensive metabolic panel, amylase, lipase, thyroid stimulating hormone, free T_4, thyroid peroxidase antibody, vitamin deficiency tests, ammonia, ferritin, transferrin, and creatine kinase were all unremarkable. Rheumatologic studies such as double stranded DNA, nuclear antibody screen, serum anti–*N*-methyl-D-aspartic acid (NMDA) receptor antibody test, glutamic acid decarboxylase antibody, and immunoglobulin A were within normal limits. Infectious diseases such as Lyme disease, human immunodeficiency virus, hepatitis, chlamydia, gonorrhea, and syphilis were also ruled out. Urine drug screen was negative. Urinalysis was notable for a urinary tract infection showing elevated white blood cells and nitrites, which was treated with ampicillin. Imaging studies including computed tomography of the head (CTH), magnetic resonance venography of the head, magnetic resonance imaging (MRI) of the brain, chest x-ray, and pelvic ultrasound were all unremarkable. Her pelvic examination was negative for uterine tenderness, bleeding, or foul-smelling lochia, ruling out endometritis. The patient had normal continuous EEG and CSF studies, including CSF glucose, oligoclonal bands, protein, and cell count, and serum autoantibodies were negative.

The team awaited her paraneoplastic autoantibody CSF evaluation, but started empiric treatment for autoimmune encephalitis. Ms A received a 5-day course of IV methylprednisolone 250 mg every 6 hours for empiric treatment of NMDA encephalitis along with IV lorazepam 2 mg every 8 hours for treatment of catatonia, which in concert led to an improvement in her vital signs, catatonic symptoms, and general mental status. She then became more engaged in psychiatric evaluation and reported having symptoms of depression that started during pregnancy. She was initiated on aripiprazole 5 mg oral daily for treatment of mood and psychotic symptoms, and lorazepam was tapered off. She was eventually discharged home on aripiprazole 5 mg.

DISCUSSION

What Is the Differential Diagnosis for Psychotic Symptoms During the Postpartum Period and What Does the Workup Entail?

The differential diagnosis for new onset psychotic symptoms in a postpartum patient is broad, and thorough medical, psychiatric, and neurologic histories and examinations should be completed.[2] Autoimmune diseases such as hyperthyroidism, systemic lupus erythematous, and autoimmune encephalitis can be triggered during the postpartum period and present with psychosis. Infections, electrolyte abnormalities, vitamin deficiencies, and metabolic problems such as urea cycle disorders may also present with delirium and psychotic symptoms during this period. Obstetrical complications like postpartum hemorrhage, eclampsia, and endometritis should be considered.[2] Other psychiatric diagnoses such as postpartum depression, generalized anxiety disorder, obsessive-compulsive disorder, and acute stress reaction related to a traumatic birth should remain on the differential. Substance use must also be ruled out before diagnosing postpartum psychosis.

Laboratory studies should include complete blood count and comprehensive metabolic panel, urine drug screen and urinalysis, ammonia level, thyroid function tests, inflammatory markers, vitamin levels, and rheumatologic and infectious panels. Brain imaging, including CTH and MRI, as well as a lumbar puncture may also be indicated, particularly with new-onset psychotic symptoms or co-occurring neurologic symptoms such as in the patient described.[2]

What Is Postpartum Psychosis?

Postpartum psychosis is generally considered a presentation of bipolar spectrum disorder rather than a primary psychotic illness such as schizophrenia.[2] Risk factors include young age, primigravida, a history of bipolar disease or inflammatory disorders such as preeclampsia or thyroiditis, pregnancy- or delivery-related medical complications or psychosocial stressors, and a family history of psychosis or perinatal mental illness.[2,8,9] The initial presentation of postpartum psychosis may include primarily nonpsychotic symptoms such as irritability, anxiety, dysphoria, and insomnia. As symptoms progress, paranoia, bizarre behavior, delusions, depersonalization, derealization, and cognitive dysfunction often arise. Delirium with impaired cognitive functioning is a unique

feature of postpartum psychosis present in up to 25% of cases. Catatonia has been seen in 5% of cases.[5] Delusions concerning the child or childbirth are a major concern, and a thorough risk assessment is vital given the 5% risk of suicide and 4% risk of infanticide associated with this illness.[1,5,10] Treatment recommendations include the use of mood stabilizers, particularly lithium, and antipsychotics. Benzodiazepines may be used if there is concern for catatonia, and electroconvulsive therapy should be considered in cases that are refractory to medications.[2]

What Is the Etiology of Delirium With Dysautonomia in This Patient?

Due to Ms A's neuropsychiatric symptoms with autonomic dysfunction, there was concern for malignant catatonia with underlying postpartum psychosis or autoimmune encephalitis.[11] Her autonomic instability and altered mental status resolved with a 5-day course of methylprednisolone 1 g daily and lorazepam 6 g daily. Response to both of these agents suggests that autoimmune encephalitis may have been the underlying etiology; however, laboratory findings did not confirm this diagnosis. Eclampsia cannot be fully ruled out as EEG was not performed until after her shaking episode, and she was treated with magnesium along with antihypertensives. Furthermore, eclampsia, postpartum psychosis, and autoimmune encephalitis can be comorbid.

The major immunologic and hormonal changes that occur in women after birth make the postpartum period a uniquely sensitive time to develop autoimmune disorders. Immunologic changes during pregnancy and postpartum often lead to immune dysfunction, and studies have shown that women with postpartum psychosis display increased monocytes, decreased T-cells, and an up-regulation in immune-related genes compared to controls.[12] Similarly, immune dysfunction also increases susceptibility to autoimmune conditions and infections during the postpartum period.[13] Hormonal fluctuations are ubiquitous in pregnancy with the rise in progesterone and estrogen during pregnancy to prepare the body for growth and maturation of the fetus, and a dramatic decrease during the postpartum period.[2,14] Estrogen modulates dopaminergic activity in the hypothalamus, and it has been hypothesized that the acute estrogen withdrawal after delivery can lead to psychotic symptoms due to the increased sensitivity of dopamine receptors postpartum.[15]

There is significant overlap between autoimmune encephalitis and psychosis in general, and autoimmune encephalitis may be the underlying etiology for postpartum psychosis in a certain subset of patients.[16] Anti-NMDA receptor encephalitis, the most well-characterized autoimmune encephalitis in which autoantibodies attack the glutamate receptor, is of particular interest in postpartum psychosis, and commonly causes autonomic dysfunction and catatonia.[11] In one study of 96 patients diagnosed with postpartum psychosis who were screened for anti-NMDA receptor encephalitis, about 4% of woman were found to have anti-NMDA antibodies. Interestingly, regardless of whether these patients had the antibody, all patients improved on both a mood stabilizer and antipsychotic.[17] Testing for anti-NMDA receptor encephalitis includes CSF analysis, serum studies (antibody testing, lactate, erythrocyte sedimentation rate, C-reactive protein, complete blood count), EEG, and MRI brain.[18–20] MRI findings are notable in only 50% of cases, and even when findings are present, the pattern is often variable depending on the autoantibody involved.[11,21] While CSF autoantibodies are highly predictive of the disease, they often take weeks to yield a result, and results may be negative in milder forms of the illness.[18] Recent studies now show that brain 18F-FDG positron emission tomography scans have high detection sensitivity for autoimmune encephalitis and can be a useful diagnostic tool.[22] Treatment for NMDA encephalitis may include corticosteroids, plasmapheresis, and intravenous immunoglobulin, and refractory cases can respond to B cell depleting drugs such as rituximab.[23] Additionally, there are other types of autoimmune encephalitis that can present without changes in the CSF cell counts and there are likely many subtypes that have yet to be discovered.[24]

Case Vignette Continued

Four days after her discharge, Ms A presented to the emergency room for insomnia, paranoia, and delusions. She was admitted to the inpatient psychiatric unit with a diagnosis of postpartum psychosis as results of her CSF autoimmune panel had been negative. Over the next month, she was stabilized, and she was discharged home on oral lorazepam 2.5 mg, olanzapine 20 mg, lithium 1,200 mg, sertraline 100 mg, and benztropine 3 mg daily. She was scheduled for outpatient psychiatric follow-up 5 days after discharge. The psychiatry team recommended that Ms A participate in an intensive outpatient program after discharge, yet the patient declined this level of care. Ms A missed her outpatient appointment, so the team conducted outreach calls to both the patient and her mother but were unable to make contact. At a postpartum obstetrics visit 2 weeks later, Ms A's mental status was stable, and she consented to starting medroxyprogesterone acetate injections for contraception.

One month later at 3 months postpartum, Ms A returned to the emergency room with worsening insomnia, labile mood, intermittent agitation, restlessness, paranoia, and disorganized thought process without autonomic or neurologic symptoms. She was admitted to the psychiatry unit again and restarted on benzodiazepines, lithium, and olanzapine. She quickly had significant weight gain and hypertriglyceridemia from olanzapine and was then switched to aripiprazole. Her symptoms improved after 2 weeks, and she was discharged on lithium 1,200 mg oral daily and aripiprazole 400 mg injection monthly with close supervision from her family.

SUMMARY

In conclusion, this case of atypical postpartum psychosis with malignant catatonia highlights diagnostic and

treatment difficulties in the postpartum period. While the diagnosis of postpartum psychosis due to underlying bipolar disorder was ultimately most likely given her re-presentation with manic and psychotic symptoms, and improvement with psychotropic medications, it remains unclear as to the role of the immune system in precipitating and perpetuating her symptoms. The patient benefited from both immunologic and psychotropic medications and may require another trial of immunologic treatment if she has refractory symptoms in the future.[20] Her case demonstrates how many patients with postpartum psychosis may require both types of therapy and that differentiating between immunologic and psychiatric illness may not be as straightforward as previously thought.

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