Bipolar Disorder
Postpartum Psychosis
Integrative Case Conference
Facilitator's Guide

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Pre-Assessment Learning

- Bergink, V., Rasgon, N., & Wisner, K. L. (2016). Postpartum psychosis: madness, mania, and melancholia in motherhood. *American journal of psychiatry*, *173*(12), 1179-1188.
- Wesseloo R, Kamperman AM, Munk-Olsen T, Pop VJ, Kushner SA, Bergink V. Risk of Postpartum Relapse in Bipolar Disorder and Postpartum Psychosis: A Systematic Review and Meta-Analysis. Am J Psychiatry. 2016 Feb 1;173(2):117-27.

Optional Supplemental Reading

- Bergink, V., Armangue, T., Titulaer, M. J., Markx, S., Dalmau, J., & Kushner, S. A. (2015). Autoimmune encephalitis in postpartum psychosis. American Journal of Psychiatry, 172(9), 901-908.
- Bergink, V., Burgerhout, K. M., Koorengevel, K. M., Kamperman, A. M., Hoogendijk, W. J., Lambregtse-van den Berg, M. P., & Kushner, S. A. (2015). Treatment of psychosis and mania in the postpartum period. American Journal of Psychiatry, 172(2), 115-123.
- Kamperman, AM, Veldman-Hoek, MJ, Wesseloo, R, Robertson Blackmore, E, Bergink, V. Phenotypical characteristics of postpartum psychosis: A clinical cohort study. Bipolar Disord. 2017; 19: 450– 457.

Overview
The goal of this module is to utilize a clinical case presentation to broaden learners' knowledge of Postpartum Psychosis. After completion of this module, learners should have a preliminary understanding of the epidemiology, phenomenology, pathophysiology, diagnostic considerations, prevention, and treatment of post-partum psychosis. This session is designed to last 60 minutes but can be modified for a longer or shorter session. The session is best utilized for psychiatry residents who have some clinical experience with pregnant and/or postpartum patients. Prior to the session, residents should read the articles included in the pre-reading section of this module.

Session
- **Clinical Vignette: read aloud (5 minutes)**
- **Residents divide into small groups and discuss questions 1-5 (15 min)**
- **Each group presents their findings to the large group (15 minutes)**
- **Large group continues with "Case Continued" and discusses questions 6-8 as a large group (15 minutes)**
- **All residents participate in large group discussion led by facilitator (10 minutes)**

Learning Objectives
1.Understand the epidemiology of Postpartum Psychosis.
2. Identify and diagnose Postpartum Psychosis utilizing phenomenology.
3. Understand current theories of etiology.
4. Create a differential diagnosis list based on diagnostic considerations.
5. Provide evidence-supported treatment.
6. Develop prevention strategies to be used with patients and their support networks.

Case Presentation

Mrs. L is a 29-year-old G1P1 female @ 6 days postpartum with no known psychiatric history. She was brought to the Emergency Department by her husband who reported increasingly bizarre behaviors at home.

Mr. L described Mrs. L as a cheerful and friendly person at baseline, with several close friends in different social groups. He reported that her pregnancy had been highly desired and that both her pregnancy and delivery had progressed without complication. Their son was born via SVD at 39 weeks, weighing 7lbs and 3oz. Mr. L reports that Mrs. L seemed to do "fine" in the first couple of days after delivery- she was fatigued and sometimes anxious but seemed enamored with their son and was able to initiate breastfeeding with support from lactation consultants. However, a couple of days after discharge from the hospital (postpartum day 4) he noticed some odd behaviors, such as checking behind counters and under tables for no apparent reason. When he approached her about these incidents, she responded "I just want to make sure our baby is safe."

Over the next 2 days her behavior was increasingly bizarre, and her personal hygiene declined. Her husband found her pacing around the baby's room at night while he was soundly sleeping. When he encouraged her to "get some rest," she appeared confused and disoriented, stating that she wasn't tired and needed to be there for her son. Her husband noticed she had thrown away many of the soaps and lotions that had been given to them as gifts at their baby shower and when he asked her about it she reported they smelled "off," she knew they were contaminated and didn't want to expose their son to "those poisons." On the day of evaluation, the patient's husband was worried about her health, and thought she might need some relief from the stress of caring for their child. He decided to stay home from work to give her some relief. Around noon time, he heard the infant crying on the baby monitor, and went to check on him. When he walked into the room, he saw patient holding a pillow standing by the side of the crib. He immediately attempted to take the pillow from her. She initially resisted his efforts, repeatedly stating "I must save him, what are you doing", but subsequently released the pillow and allowed him to bring her to the Emergency Department.

On exam, she appeared her stated age, her hair was uncombed. She was wearing mismatched socks and a wrinkled shirt with visible food stains. She was calm, and cooperative with the exam, but was guarded, made poor eye contact with the evaluator, and often looked around the room apprehensively. She exhibited psychomotor agitation evidence by repeated rocking motion with her upper torso. Her speech was spontaneous, and was normal in articulation, prosody, and rhythm. Her volume varied from shouting at the evaluator to whispering under her breath. She described her mood as "afraid" and at times appeared irritable; her affect was labile. Her thought process was tangential, at some points she exhibited loose associations. She endorsed an occasional auditory hallucination of a baby crying. She exhibited delusional beliefs that she had "holy powers" and that she and her son were on a "divine mission." She reported she had been "receiving messages" giving her information about this mission and went on to elaborate that the "only way to make sure his soul ends up in the right hands is to send him to heaven myself." She had poor insight and judgement. No illicit substances were detected on initial urine toxicology screen, and blood alcohol level was <10.

Additional history was gathered from patient's husband and her mother (via telephone). Mrs. L's maternal aunt was diagnosed with "manic-depressive" disorder, but details are unclear as she passed away at a young age. Otherwise, the patient's family did not have a history of mental illnesses or substance abuse. There were no suicides in the family. She grew up in a supportive and loving middle class household with both parents and her brother. She excelled academically, and successfully obtained a law degree from their state university. She is currently on maternity leave from her job at a local real estate law firm. She has no psychiatric history; she saw a school counselor several times in high school after a classmate committed suicide, but she did not know this classmate well. She has never taken any psychotropic medications, and does not use tobacco products or drink alcohol. She tried marijuana in college several times, but has had no other illicit substance use since then. She has no medical problems, and her only surgery was a tonsillectomy at age 12. She has no known drug allergies.

Discussion Questions

1. Please describe the epidemiology of postpartum psychosis (PPP). Specifically, how common is PPP and when are women at highest risk? What psychiatric diagnoses are associated with PPP?
Facilitator elicits the following:
• PPP is very rare. According to international data, incidence ranges from incidence ranging from 0.9-2.6 per 1,000 births
• The risk for first onset of affective psychosis is 23 times higher within **4 weeks** after delivery compared with any other period during a woman's life. The majority of PPP cases, however, occur in the first **2 weeks** after birth.
• PPP is often considered a Bipolar **Spectrum Disorder**, although there is thought to be a subset of patients who only have episodes in the context of the postpartum time-period.
• Postpartum psychosis is associated with an increased risk for suicide and infanticide.

2. For this patient, what are the chances she will develop another episode of postpartum psychosis after subsequent births? What about psychiatric symptoms outside of the postpartum period?
Facilitator elicits the following:
• After an incipient postpartum affective psychosis, a woman has 50%-80% chance of developing another serious psychiatric episode, usually within the bipolar spectrum.

3. Please describe the phenomenology of postpartum psychosis. Specifically, when do symptoms usually start? What are common symptoms of PPP? How are symptoms of PPP similar or distinct from affective psychosis in non-perinatal patients? What is the expected duration of symptoms if left untreated?
Facilitator elicits the following:
• The typical time of symptom onset is between 3 to 10 days after birth, and women with bipolar disorder on average have a faster onset of symptoms than women with PPP who do not have bipolar disorder. It should be noted that the onset of symptoms often occurs after a woman has been discharged from the hospital and during a time of a lot of change and uncertainty. This often makes the presentation of PPP a confusing and very distressing experience for both the new mother and the family.
• Early symptoms may include insomnia, mood fluctuation, and irritability.
• Postpartum psychosis is notable for delirium-like appearance, cognitive symptoms such as disorientation, confusion, derealization, and depersonalization may occur.
• Women have a relatively **low incidence** of certain psychotic symptoms including thought insertion, withdrawal or broadcasting, passivity experiences, hallucinatory voices giving running commentary, or social withdrawal.
• Distinct from affective psychosis occurring outside the perinatal period, women may experience mood-incongruent delusions often focused on the newborn (such as developing a delusion that a baby is defective in some way, possessed or otherwise in danger).
• Disorganized, bizarre behaviors and obsessive thoughts regarding the newborn are typical.
• Delusions of altruistic homicide (often with associated maternal suicide) to "save them both from a fate worse than death" may occur. Postpartum psychosis is associated with an increased risk for both suicide and infanticide. The risk of infanticide in the setting of psychosis is estimated at 4%.
• Regarding the duration of symptoms, one cohort study reported episode duration similar to mood episodes seen with bipolar disorder outside the perinatal period (1 month for manic features and 2.5 months for mixed or depressed features).

4. Please describe current theories of postpartum psychosis pathophysiology.
Facilitator elicits the following:
• Childbirth is a clear etiological event that is a trigger for postpartum psychosis, and a significant predictor is primiparity. If a woman's first delivery is not complicated by postpartum psychosis, the likelihood of developing PPP becomes substantially lower after subsequent deliveries.
• There are no specific **genetic** studies in women with first-lifetime onset postpartum psychosis, but vulnerability for postpartum relapse in women with bipolar disorder has been investigated. Current areas of investigation include genetic variants of the serotonin transporter gene (5-HTT) and chromosome 16p13. No estrogen receptor or glucocorticoid receptor gene polymorphisms in relation to postpartum psychosis has been established (see Bergink 2016 study for more information).
• Due to significant fluctuations in **reproductive hormone levels** during and immediately after pregnancy, researchers have postulated different theories linking sensitivity to rapid changes in these hormones to onset of postpartum psychosis, but evidence remains limited.
• Bergink et al. have reported the co-occurrence of postpartum psychosis with thyroiditis and preeclampsia, which have established **autoimmune and inflammatory etiologies**. Investigators have also reported the identification of CNS auto-antibodies in 4% (4/96) of patients with postpartum psychosis, which suggests autoimmune encephalitis may be present in a subset of cases. Two of these patients had anti-NMDA receptor encephalitis.

• **Circadian rhythm disruption** is common in postpartum psychosis. Sleep disruption resulting from labor and delivery may initiate the circadian disruption and contribute to mania or mixed state. The early postpartum period is characterized by more awakenings, a later onset of stage 4 and restorative REM sleep, and sleep loss.
• Of note, there are no consistently identified obstetric risk factors and in contrast to postpartum depression, life stressors are not major risk factors for PPP.

5. What are some differential diagnostic considerations? What diagnostic tests should be considered?
Facilitator elicits the following:
• Differential diagnosis should include: acute infections, peripartum blood loss and anemia, exacerbation of preexisting endocrine and/or autoimmune diseases such as primary hypoparathyroidism, and thyroid disease (there is a well-documented postpartum rebound of thyroid peroxidase antibodies during the first months postpartum, and an initial negative screen immediately postpartum does not rule out thyroid disease). Neurological symptoms should raise concern for anti-N-methyl-D-aspartate (NMDA) receptor encephalitis. However please note that in some cases of NDMA receptor encephalitis, initial clinical presentation was notable for the absence of neurological signs. Patients then went on to develop extrapyramidal symptoms to low dose antipsychotics. Clinicians should consider an autoimmune encephalitis workup in patients with extrapyramidal symptoms to low dose antipsychotics. Late-onset inborn errors of metabolism can present with clinical features similar to postpartum psychosis.
• Diagnostic testing may include: CBC to evaluate infectious processes, UA to assess for cystitis, CMP, TSH, free T4, TPO antibodies, ammonia level (to rule out urea cycle disorders), alcohol and substance use screening to identify toxic or withdrawal syndromes.
• If a patient has neurological symptoms, such as seizures, decreased consciousness, dyskinesia, overt motor symptoms, or extrapyramidal symptoms, the treatment team should consider NMDA receptor autoantibody screening as well as brain imaging (MRI). If the above neurological symptoms are absent, but patients exhibit extrapyramidal symptoms in the setting of low dose antipsychotics, workup for encephalitis should be considered. Observational data from a study by Bergink et al (2016) was notable for cases of NMDA receptor encephalitis in which patients had not demonstrated neurological signs on initial presentation, but went on to experienced extrapyramidal symptoms when treated with low dose Haldol.

Case Presentation Continued

After a thorough assessment and evaluation for underlying causes, you determine that Mrs. L has PPP. You explain the diagnosis to Mr. L, who appears to take comfort in having a diagnosis and asks “So what do we do now? How will she get better?”

Discussion Question

6. Describe potential treatment for Mrs. L. What level of care will she need? What treatment strategies might you suggest?
Facilitator elicits the following:
• Postpartum psychosis is a treatable psychiatric emergency and therefore requires immediate evaluation. **Inpatient psychiatric hospitalization is often indicated to ensure the safety of the patient and her infant, especially when clinical judgement reveals elevated risk for lethality.** In the case of Ms. L, she presents a clear need for inpatient treatment due high risk of harm to herself and her infant.
• The largest evidence base exists for treatment with **lithium**, which is highly efficacious for acute treatment of postpartum psychosis, as well as maintenance treatment. Lithium is the drug of first choice during the acute phase of illness unless contraindicated (due to impaired renal function, or serious side effects).
• **Second generation antipsychotics** and/or **benzodiazepines** might also be considered in the initial phase of treatment.
• **ECT** can be an effective treatment for both depression and mania, and associated risks of adverse effects are low. ECT during pregnancy does require the availability of obstetrical monitoring and support and ideally access to NICU care.

Case Presentation Continued

Upon further discussion with Mr. and Mrs. L, Mrs. L is agreeable to inpatient admission. She expresses relief that she may not have to “feel like this forever.” She does have questions about what to expect. Specifically, she asks the following questions: “Can I continue to breastfeed while I am in the hospital? How long will I need to be on these meds? Won’t being apart from my baby make it hard for us to bond?”

Discussion Question

7. Discuss how you would address Mrs. L's concerns.
Facilitator elicits the following:
• Given the severity of her symptoms, her health and safety should be the first priority. While Ms. L is currently agreeable to inpatient admission, an involuntary admission would likely also be appropriate in this case.
• Mr. and Mrs. L should be informed of both the benefits and risks associated with breastfeeding in this setting. This discussion should also explore Ms. L's wishes about breastfeeding. If she does wish to breastfeed, she should be offered a breast pump and a clean refrigerated space for breastmilk storage. As sleep deprivation due to frequent awakenings may contribute to the onset and maintenance of mania, she might consider pumping during daytime hours only (realizing that this might result in decreased supply).
• In terms of medication exposure, Lithium is not an absolute contraindication to breastfeeding. Lithium exposure through lactation can adversely affect the infant when its elimination is impaired, such as in dehydration or prematurity. It is generally recommended that women on lithium can breastfeed under more advantageous circumstances (full-term infant, illness stability and with a collaborative pediatrician). While hospitalization may preclude Ms. L from continuing to breastfeed in the immediate future, offering her the option to utilize a breast pump to maintain her supply would allow her the option of continuation of breastfeeding once stability is achieved.
• Data on the safety of second-generation antipsychotics is more limited but overall reassuring.
• It is generally recommended that women with PPP without a previous history of bipolar disorder should be maintained on Lithium monotherapy for 9 months after initial stabilization. After 9 months of stabilization, a gradual, monitored taper can be considered.
• While separating mother and baby is potentially a traumatic event for both, Mrs. L should be reassured that this is the best course of action to address immediate safety concerns. Inpatient units vary in terms of policies and procedures around infant visitation, but in an ideal circumstance Mrs. L would be offered supervised and supported visitation with her infant as she is recovering in the hospital when deemed appropriate by her treating psychiatrist. After hospitalization, Mrs. L and her infant may benefit from infant mental health services to provide more ongoing dyadic therapy focused on the mother-child relationship.

Case Presentation Continued

Six months after initial presentation, Mrs. L attends a follow-up appointment with her outpatient psychiatrist. She has been stable since her hospital discharge 5 months ago with good treatment adherence. She states she would like to discuss the idea of her having another baby in the future, perhaps in the next year. She asks you "will the same thing happen again if I have another child?"

Discussion Question

8. Discuss how you would address Mrs. L's question, including information about the risk of recurrence and therapeutic strategies to reduce her risk.
Facilitator elicits the following:
• Mrs. L should be counselled that she is at increased risk for another postpartum mood episode, however there are measures that can be taken to reduce that risk. After an incipient postpartum affective psychosis, a woman has a 50-80% chance of developing another serious psychiatric episode, usually within the bipolar spectrum. (Bergink et al. 2016)
• Women with a history of postpartum psychosis have a 29% risk of postpartum psychosis in subsequent pregnancies. (Wesseloo et al.)
• While postpartum psychosis is often considered a bipolar spectrum illness, it is unclear at this time whether or not Mrs. L will progress to having mood episodes outside of the perinatal period. There does appear to be a subset of patients who experience mood episodes only in the context of postpartum. Ms. L's family history of bipolar disorder may put Ms. L at higher risk of recurrent illness outside the postpartum period.
• The benefits of prophylaxis during pregnancy need to be carefully weighed against the risks to the fetus. The current evidence base indicates that women with a history of psychosis limited to the postpartum period are not at elevated risk of psychiatric episodes during pregnancy. However, for women with evidence outside of the peripartum period of bipolar disorder, there is an increased risk for relapse of illness during and outside of pregnancy for women who discontinue maintenance medication.
• It is important that Mrs. L approach the planning for her next pregnancy in close contact with her psychiatrist. It might be advisable to postpone further pregnancy plans until there is an opportunity to assess her mood and other symptoms off of medication. This plan would entail a slow taper of medications after at least 9 months of stability and then a period of observation of 6-12 months.

• If Mrs. L does show a prolonged period of stability off psychiatric medications, the psychiatrist could consider monitoring her off of medications throughout her next pregnancy, and then starting Lithium prophylaxis at birth. If Mrs. L does have an illness recurrence prior to her next pregnancy, the psychiatrist would need to discuss with her the protective effect that medications are expected to have on her illness vs the risk of Lithium or other mood stabilizer use during pregnancy.
• Other preventative strategies for future pregnancies include stress management, prioritizing sleep and a stable circadian rhythm, psychoeducation for partner and other family, and increasing social supports.