

Case Report

Treatment-resistant depression management in postpartum depression – a case report and literature review

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ABSTRACT

Postpartum depression (PPD) affects approximately 10-15% of women and can cause significant morbidity for mothers, infants, and families. When postpartum depression fails to respond to two adequate trials, it is called as treatment resistant postpartum depression (TRPPD). Treatment of TRPPD is challenging because of breastfeeding, limitation of medication and competing childcare responsibilities. We report the case of a 26-year-old female with a history of anxiety, ADHD, and depressive disorders who developed severe postpartum depression following her two pregnancies. Following her second delivery, she developed severe depressive symptoms within three weeks postpartum, with a PHQ-9 score of 28. Despite multiple sequential pharmacological regimens including desvenlafaxine with bupropion and subsequent dose adjustments, the patient showed only partial and transient improvement. Significant clinical response was achieved after addition of cariprazine along with intensive psychotherapy and structured psychosocial support, including enhanced caregiving assistance. Her PHQ-9 decreased to 5 three weeks after initiation of this regimen. Sustained remission was observed over long-term follow-up continuing to this day. This case demonstrates the complexity of TRPPD and the limitations of monotherapy. Early detection of treatment resistance is crucial in avoiding impaired infant bonding and long-term maternal dysfunction. A multimodal approach comprising psychotherapy, augmentation techniques, antidepressant optimization, and psychosocial support is needed for effective management and long-term remission. TRPPD is a difficult and underdiagnosed disorder that requires individualized, multidisciplinary care. In refractory circumstances, combination medication and targeted psychological therapies may improve effectiveness. More research is required to develop evidence-based treatment approaches and uniform diagnostic standards for TRPPD.

Keywords: Treatment-resistant depression, Postpartum, Treatment-resistant postpartum depression, Psychotherapy, Psychosocial support

INTRODUCTION

Treatment-resistant depression (TRD), a severe and complex form of major depressive disorder (MDD), is characterized by an inability to establish remission after at least two adequate trials of antidepressant medication with distinct pharmacological mechanisms.¹ TRD affects 30-40% of people with depression and has been linked to considerable functional impairment, higher healthcare utilization, poorer quality of life, and an elevated risk of suicide.² The pathophysiology of TRD is multifaceted, encompassing monoaminergic dysregulation, neuroinflammation, and dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis. Empirical research has indicated that TRD impairs neuroplasticity, as evidenced by reduced brain-derived neurotrophic factor (BDNF) levels and altered neural connectivity.³ As a result, TRD continues to be one of the most difficult disorders seen in psychiatric practice and frequently requires novel therapeutic approaches outside of traditional antidepressant therapy.³

One of the most severe postpartum complications is postpartum depression (PPD), a psychiatric disorder that affects 10-15% of women after giving birth.⁴ PPD is characterized by symptoms of anhedonia, sleep disruptions, energy loss, difficulty concentrating, persistent negative feelings or depressive moods, and impaired bond between mother and infant.⁵ Beyond its impacts on the mental health of mothers, PPD can negatively impair the emotional, cognitive, and behavioral development of infants.⁶ These combined effects on both mother and child often disrupt family dynamics, and make it more difficult for mothers to give their children the best care possible.⁶ Although many women with PPD benefit from first-line treatments like psychotherapy and antidepressant drugs, a small percentage of them still suffer from severe depressive symptoms even after receiving appropriate treatment, and therefore meet the diagnostic criteria for treatment-resistant postpartum depression (TRPPD).⁷

The development of TRD during the postpartum period poses unique clinical challenges. Pharmacological symptom management for patients with TRD carries medication safety risks, especially when the newborn infant can be affected by medication through breastfeeding. Hormonal fluctuations during the postpartum period may change the onset and persistence of depressive symptoms, contributing to the variability in PPD presentation in each patient. Other factors, such as sleep deprivation, psychosocial stressors, obstetric difficulties, and previously diagnosed psychiatric problems, may also contribute to the onset of depressive symptoms.⁸

Management of treatment-resistant postpartum depression often requires a multidisciplinary and individualized approach. Some examples of possible therapeutic options are antidepressant optimization, pharmacologic

augmentation procedures, intense psychotherapy interventions, electroconvulsive therapy (ECT), and transcranial magnetic stimulation (rTMS).⁹ Ketamine, esketamine, and neuroactive steroids are examples of rapid-acting agents that have shown promise as treatments for severe or refractory cases.

This study details the case of a young postpartum woman with TRD who continued to experience depressive symptoms despite conventional therapy measures. This case illustrates the necessity of diagnosing and treating TRD during the postpartum period with an individualized treatment plan to give the patient the best possible chance at symptom remission and restoration of maternal function.

CASE REPORT

Our patient is a 26-year-old female, mother of two children aged 3 years and 3 months old, who sought consultation for an almost permanent state of depression since the birth of her youngest son. She had a personal history of an unspecified anxiety disorder, especially related to situations of separation from her home environment, to her academic performance in her teen years, to her duties as a wife and a mother, all without receiving any medication or consistent psychotherapy. Furthermore, the patient had been diagnosed with attention deficit hyperactivity disorder at the age of 10, for which methylphenidate 10 mg daily was prescribed.

The patient's final years of high school and subsequent marriage were described as consistently tense, with frequent episodes of 'severe anxiety' that, by the description presented, corresponded with panic episodes. These episodes were frequently controlled with benzodiazepines provided by family and friends, but at unknown dosages and without consultation. Beside the symptoms of anxiety, the patient was first diagnosed with depression 1 year before becoming pregnant with her first child, and was treated with fluoxetine 10 mg daily and 8 weeks later it was also added bupropion 20 mg daily, with which the patient's symptoms were controlled (PHQ-9 of 7 after 4 weeks of combined treatment) and she remained symptom free throughout her first pregnancy.

Approximately 3 weeks after giving birth to her first child, the patient presented a deep state of sadness, severe difficulties falling asleep, feelings of hopelessness, and being overwhelmed by the duties of motherhood. At the time, hospitalization was not required, and fluoxetine was increased to 30 mg, bupropion was discontinued and venlafaxine 150 mg daily was added. Within 21 days of the new treatment plan the patient showed significant improvement. At the beginning of this episode, her PHQ - 9 score was 21, and by the end of the first month, it went to a score of 7.

For the next 2 years, although no new episode of major depressive disorder, occasional anxiety sadness episodes before were reported by the patient with no regular follow-

up by psychiatric specialists or any other physician, and the patient maintained the same regimen, plus her usual ADHD medication, plus occasional clonazepam 0.5 mg, upon occasions of severe anxiety. Approximately 4 weeks after giving birth to her second child, whose pregnancy was carried out with no major problems or mood episodes from the patient, she started experiencing deep sadness and anxiety; she was unable to fall asleep for almost three days, barely eating and feeling incapable of carrying out her duties, taking care of her newborn.

Her PHQ-9 at the time was reported to be 28, venlafaxine was discontinued and desvenlafaxine 50 mg daily plus bupropion 150 mg were started along with psychotherapy 45 min twice a week, and for the next 4 weeks no major improvement was seen, with the patient not nursing her newborn, nor being able to care for herself, after this point both the doses of desvenlafaxine and bupropion were increased to 100 mg and 200 mg respectively. Four more weeks later, no improvement was evident. To this regime Cariprazine 3 mg daily was added and the patient was moved back to her parents' house, with a nurse who would assist her daily, and psychotherapy was indicated once more, twice a week, for 45 mins.

With this regimen, strictly followed weekly, and contrasted with adherence to her medication, by the end of the second week, the patient was able to get out of her house, cook, and maintain personal hygiene. Her feelings and levels of activity substantially improved, and by the end of the second month of the new treatment, she was, although assisted, able to start taking care of her children, her PHQ-9 only three weeks after the beginning of this new regime decreased to 5 points.

Over the subsequent three years, no episodes of depression of any kind had been reported by the patient, who has been seen regularly every three months, with the same treatment plan established before.

DISCUSSION

Postpartum care and support are a vital part of maternal and infant health.¹⁰ Postpartum is a major transition in the life of a woman and requires support and adjustments on physical, psychological, and social levels.^{4,11} The World Health Organization stresses the importance of intensive care, and post-hospital stay, which is typically 48 hours in America. Despite the confirmation that postpartum support is critical in the prevention of infant and maternal morbidity, there is a lack of research on the effectiveness of certain postpartum care plans.¹² In studies that examined maternal mental health that targeted high-risk women, there are specific interventions that have been seen to benefit this population. Nurse visits combined with case conferencing, 24-hour telephone access after discharge, peer support programs, increasing parenting knowledge, and nurse home visitation have been proven to assist mothers in the postpartum process.¹³

Postpartum depression is defined as a MDD during postpartum, and onset is within 1 month after childbirth.¹³ However, it can start in pregnancy or continue for months after the child is born.^{14,15} The diagnostic criteria of postpartum depression include depressed mood, loss of interest, anhedonia, sleep disturbance, appetite disturbance, impaired concentration, psychomotor disturbance, fatigue, feelings of guilt, feelings of worthlessness, and suicidal thoughts that are present during the same 2-week period and are a change from the patient's previous functioning.¹³ Earlier recognition of PPD is necessary, as the disorder can include thoughts of harming oneself as well as one's child.

PPD is a challenging diagnosis to assess because of the overlapping changes women experience postpartum: sleep, appetite, fatigue, etc. PPD occurs in 10-15% of women who have recently given birth, but fewer than half the cases are recognized.¹⁴ There are risk factors that clinicians should be aware of in the perinatal period: MDD, stressful life events, immigration status, income level, age, poor social support, and marital conflict. While all of the aforementioned factors can impact PPD status, hormonal fluctuations with estrogen and progesterone also contribute to PPD onset. There is a certain level of normal hormonal fluctuations that occur; however, being aware when these fluctuations are atypical is important for early recognition of PPD.¹¹

TRD has many definitional dilemmas, but is generally defined as a minimum of two prior treatment failures with adequate dosage and duration used. Since TRD is a very complex disorder, patients with TRD are twice as likely to require hospitalization, and costs are six times higher for those who are treatment-resistant than for those with typical MDD.¹⁴

TRD can develop in those with PPD, which is referred to as TRPPD. Risk factors for treatment resistance have not been well investigated, specifically for this population of mothers with PPD. One study used a sample of 3,522 women to detect the risk factors for developing TRPPD. They concluded that patients with lower educational attainment, lower household income, active smokers, and being non-cohabitation increased the risk of TRPPD. Characteristics that increased the risk of TRPPD were having three or more births, cesarean delivery, and preterm delivery.¹⁵

Early detection is necessary in cases of PPD for the safety of the mother and child.¹² Misdiagnosis is common, partly because PPD presents with significant variability in symptom severity and course.¹² Stigma against PPD further contributes to under-recognition, diagnosis, and treatment of PPD.¹² While the majority of cases resolve within a few months, 24% of women remained depressed one year after giving birth, and 13% of women experienced persistent depressive moods 2 years after giving birth.¹³ Approximately 40% of women with PPD can relapse during another pregnancy or unrelated to pregnancy.¹³

Additionally, if PPD goes untreated, it can cause recurring depressive episodes and prolonged psychiatric issues for the family.¹³

In the case presented in this study, we observed persistent depression following the birth of the patient's first son. The patient did have certain risk factors, like panic attacks and anxiety disorder, prior to the birth of her son.¹³ Her occasional feelings of sadness continued for 2 years after the birth of her son, and persisted into the birth of her second child. The patient underwent more than 2 treatment regimens of adequate dosage and frequency, yet her improvement was minimal. As a result, she met the diagnostic criteria to be diagnosed with PPD.¹² More recently, while being on the same treatment plan and regular clinical visits, the patient showed an improvement in symptoms. Moreover, the patient expressed a desire to have a third child, thereby necessitating an individualized perspective and treatment plan that can adjust with the patient's desires.¹³

Based on the intrinsic limitations that this study faced, further studies should be conducted in order to fully understand TRPPD.¹⁵ Future research would benefit from a larger, more diverse patient sample with consistent measures of symptom severity. Additionally, the impact of factors such as social support, access to care, comorbid symptoms, or co-occurring disorders should be explored in relation to TRPPD.^{13,15} Constructing a deeper understanding of this disorder is important for psychiatric, obstetric, and psychosocial care.¹³ In this manner, TRPPD will have less of an impact on the daily life of the patient, and help ease the stress or burden on family members, as well as being necessary for the safe functioning of the family unit.¹³

CONCLUSION

TRPPD represents a severe and complex subtype of postpartum mood disorder that requires early recognition and a comprehensive, individualized treatment approach. In the context of pre-existing anxiety, a history of ADHD, and considerable psychosocial stressors, this case emphasizes the difficulties in managing persistent depressive symptoms after numerous adequate treatment attempts. The patient had shown limited response to successive antidepressant and antipsychotic regimens. Only after a multidisciplinary approach combining pharmacological optimization (venlafaxine and cariprazine), structured psychotherapy, and improved psychosocial support was put into place did the patient exhibit significant and long-lasting clinical improvement. This emphasizes the significance of treating biological, psychological, and social aspects of TRPPD holistically instead of focusing only on pharmaceutical adjustments. In order to prevent long-term psychiatric illness, extended maternal dysfunction, and poor mother-infant bonding, early identification of treatment resistance in postpartum depression is essential. Sustained remission and effective recovery require multidisciplinary care that includes

psychiatry, psychotherapy, family support systems, and continuous follow-up. Further research is needed to better define TRPPD, identify predictive risk factors, and establish standardized treatment protocols to improve outcomes for both mothers and their children.

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