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Premenstrual Psychosis in A Patient with Polycystic Ovary Syndrome: A Case Report

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Abstract

Periodic psychosis in relation to the menstrual cycle phases has been reported but its pathogenesis is not yet known. We report the case of a 28-year old female who had developed schizoaffective disorder over the preceding 10 years. She was diagnosed with polycystic ovary syndrome (PCOS) 3 years later and was noted to have distinct psychotic episodes that coincided acutely with her premenstrual period. Peculiarly she exhibited delusions of pregnancy during her psychotic episodes. This was followed by near resolution with the end of menstruation. This case sheds light on the atypical presentation of psychosis in female patients and the importance of eliciting psychotic symptoms in relation to the menstrual cycle. Considering the potential role of anovulatory cycles and oestrogen in perimenstrual psychoses, psychiatrists should also be aware of the use of antipsychotics that may exacerbate anovulation via hyperprolactinaemia.

Keywords: *Periodic, psychosis, menstrual, oestrogen, case report.*

List of abbreviations

PCOS: Polycystic ovary syndrome
CNS: Central nervous system

Background

Periodic psychosis related to the menstrual cycle was described as early as the mid-19th century by the French psychiatrist, Brière de Boismont, who reported 4 cases of premenstrual insanity [1, 2]. This unique presentation of psychosis was further expounded upon by von Krafft-Ebbing in 1902 [3], and later by Jolly in 1914 [4] who developed a temporal classification of the disorder in relation to the stage of reproductive life [5]. Since then, there have been between 80 to 280 reported cases worldwide [6, 7]. More recently, Brockington has further refined the subclassification of menstrual psychoses by timing within the menstrual cycle [6]:

1. **Premenstrual:** psychosis starts during the second half of the cycle, and sometimes ends with abrupt recovery at the onset of menstrual bleeding
2. **Catamenial:** psychoses which begin with the onset of menstrual flow
3. **Paramenstrual:** psychosis occurs at variable timing, always in harmony with the menstrual cycle
4. **Mid-cycle:** onset almost mid-way between the beginning of menstrual bleeding
5. **Epochal:** bipolar psychoses lasting for the complete cycle, with switches linked to menstruation

These cases raise the possibility of a hormonal role in the manifestation of psychosis in a subgroup of female patients. Despite such works, this concept remains relatively unrecognised and forgotten. Particularly in Singapore, there have been no reported cases of menstrual psychosis. A literature review revealed only 2 cases of menstrual psychosis in association with PCOS reported worldwide [8, 9]. We report a case of periodic psychosis associated with the premenstrual phase of the menstrual cycle presenting with prominent delusions of pregnancy in a patient with PCOS. Through this case, the authors hope to explore a possible aetiology behind premenstrual psychosis in relation to PCOS, as well as an explanation for their patient's delusions of pregnancy.

Case presentation

A 28 year old Chinese female was admitted to an inpatient psychiatric facility after she had presented to the hospital's emergency department with the intention to deliver her unborn child. She was convinced that she was 5 months pregnant and stated that she had abdominal pain and had

missed her menstruations. She had been diagnosed as having schizoaffective disorder since she was 18 years old and has had 6 previous psychiatric admissions during which she had exhibited similar features of delusions of pregnancy. She did not have any family history of psychiatric illness. Her past medical history was characterised by Type 2 diabetes mellitus, PCOS and obesity. Prior to admission, she was on olanzapine 15mg every night and aripiprazole 20mg every morning.

During the admission, she reported her last menstrual period to be 5 months ago and held the belief that she had been impregnated by a celebrity. Physical examination was unremarkable apart from prominent central adiposity. Both urine and serum beta-hCG were negative. Corroborative history from her parents revealed a distinct pattern, in which the patient exhibited episodes of psychosis that coincided with her premenstrual period. The exacerbation of her psychotic symptoms came on in the few days leading up to her menses with gradual resolution as menstrual bleeding ceased. In between these episodes, in the intermenstrual period, she remained relatively well, with no overt positive symptoms of psychosis. She continued to have meaningful friendships and engaged in social activities. However, she had shown an overall decline in function over the 10 years since her diagnosis, demonstrated by her inability to sustain employment and dependence on her mother to administer her insulin.

A review of her past psychotropics showed that she had fared poorly on risperidone and had experienced hyperprolactinaemia as a side effect of the medication leading to oligomenorrhoea. Risperidone was ceased. Since 2017, she has remained relatively stable on a combination of olanzapine and aripiprazole.

Within a few days of her admission, and with gradual uptitration of olanzapine from 15mg to 20mg every night, she no longer held the belief that she was pregnant and had achieved euthymia. She was discharged well and at baseline with no issues with compliance to medication. Outpatient follow-up was carried out at 2 and 6 months post-discharge and psychiatric assessment via history-taking from patient and mother and mental state examination revealed no signs of a relapse of her illness.

Discussion and Conclusions

An underlying hormonal aetiology in relation to PCOS in premenstrual psychosis

Oestrogen has been hypothesised to exert a protective effect against psychosis [10]. Supporting this, conditions associated with oestrogen withdrawal and hypoestrogenic states have been reported to precipitate or exacerbate psychotic symptoms [11]. This has been demonstrated by various reports of acute psychosis with withdrawal of oestrogen such as cases of psychosis occurring post-abortion, with cessation of exogenous oestrogen (e.g. oral contraceptive pills) and administration of oestrogen receptor antagonists (e.g. clomiphene, Tamoxifen) [12].

Oestrogen is known to have a neuromodulatory effect on the central nervous system (CNS) and has been shown to block dopamine receptors [13]. A period of high and sustained oestrogen levels, as with anovulatory cycles, leads to the upregulation of dopaminergic receptors and hence increased sensitivity. This has been demonstrated in studies using both human and animal models, that showed increased dopaminergic receptor sensitivity in the luteal phase of the menstrual cycle [14, 15]. The subsequent oestrogen cascade that happens in the luteal phase preceding menstruation can lead to dopaminergic overactivity giving rise to psychotic symptoms [16].

PCOS is characterised by anovulatory cycles, during which there is relatively unopposed estrogenic stimulation, priming the CNS for a premenstrual fall in oestrogen at the next ovulatory period [9]. This pathogenetic mechanism may explain the clinical picture of our patient with PCOS, who exhibits a clear exacerbation of her psychotic symptoms in the premenstrual phase.

Early treatments for such cases of periodic psychoses associated with the menstrual cycle were aimed at interrupting menstruation via means like ovariectomy and artificial induction of menopause [5]. However, these proved to be unsuccessful. Conventional psychotropics have also been demonstrated to be inadequate in interrupting the periodic nature of this illness [7]. More recent literature has reported the successful use of alternative treatment strategies targeting the hypothalamic-pituitary-ovarian axis [17]. These include hormone replacement, in the form of combined oral contraceptive pills [18] or a GnRH agonist [19], and metformin, in the setting of PCOS to restore normal ovulation [8].

Possible theories behind the delusions of pregnancy

A secondary finding in our patient was the manifestation of her psychotic symptoms in the form of delusions of pregnancy. It is our hypothesis that antipsychotic-induced metabolic syndrome, hyperprolactinaemia and high oestrogen levels in the early luteal phase each played a part in her delusion of pregnancy by causing symptoms akin to the somatic experience of pregnancy. Due to a lack of detailed physical examination and conclusive laboraotry tests, we were not able to definitively confirm these postulations.

Hyperprolactinaemia is a known side effect of most first generation and some second-generation antipsychotics. The high oestrogen levels in the anovulatory cycles of PCOS also lead to dopamine blockade and a consequent increase in prolactin, compounding the effect of antipsychotic use. This resulting hyperprolactinaemia may serve to trigger or

strengthen delusional beliefs of pregnancy through its symptoms of galactorrhoea and amenorrhoea [20]. There have been various cases in the literature documenting a temporal association between hyperprolactinaemia and delusions of pregnancy that resolved with normalisation of prolactin levels and change in antipsychotic agent [21]. We were unable to establish such a temporal association between a rise in prolactin and estrogen levels and our patient's delusion of pregnancy as laboratory tests were not performed in a timely manner due to the retrospective nature of this article. However, hyperprolactinaemia has been documented in our patient in 2013 while she was being treated with risperidone, with a level of 1884 ng/L. At that time, she did not exhibit delusions of pregnancy.

Antipsychotic-induced metabolic syndrome also gives rise to features that may further fuel this delusion, such as widening abdominal girth and breast tenderness/engorgement [22]. The high oestrogen levels in the early luteal phase of the menstrual cycle similarly result in such effects on the body. With her medical history of hypertension, hyperlipidaemia, type 2 diabetes mellitus and obesity, our patient meets the criteria for metabolic syndrome. However, we were not able to confirm this hypothesis as serial measurements of her abdominal girth were not performed and history taking revealed no breast symptoms.

Therefore, a combination of adverse effects from antipsychotic use and elevated oestrogen levels, gives rise to bodily symptoms that together may precipitate and reinforce delusions of pregnancy by mimicking its symptoms.

Limitations

The main limitation of this case is its retrospective nature. We were unable to determine the exact dates in relation to her menstrual cycle during which psychotic symptoms emerged. This was partly due to the unreliable nature of the menstrual history provided by a patient in an actively psychotic state. In addition, we were not able to obtain blood investigations to document serum hormonal levels during the acute episode, such as those of oestrogen and prolactin, to further evaluate the underlying pathogenesis. Although our patient's acute psychotic exacerbation resolved with uptitration of olanzapine, there may be a need to consider alternative treatment in the form of hormonal therapy to prevent her cyclical relapses, while simultaneously bearing in mind potential adverse effects in a young female of childbearing age.

This case illustrates the complexity of mental illness in women's health. It is important for clinicians to elicit psychotic symptoms in relation to the menstrual cycle in female patients. Patients can also be encouraged to monitor their symptoms via menstrual diaries. More emphasis should be placed on perimenstrual psychoses and we hope to encourage further research into the possible underlying hormonal aetiology, which can in turn provide evidence for treatment strategies other than conventional psychotropics. Considering the potential role of anovulatory cycles and oestrogen in perimenstrual psychoses, psychiatrists should also be aware of the use of antipsychotics that may exacerbate anovulation via hyperprolactinaemia.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the participants for publication of their cases and any accompanying tables/images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

TP performed a literature review and wrote the paper. YSL performed a literature review and advised on the concept of the case report. CTT conceived of and designed the case report. All authors read and approved the final manuscript.

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