Menstruation-Related Recurrent Psychotic Disorder: a Case Report

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ABSTRACT
Menstruation-related recurrent psychotic disorder: a case report
Changes of mental status that are related to menstrual cycles cause significant mental problems. As an accepted disorder “premenstrual syndrome” do not cover all cases that are in literature. Menstruation-related psychotic episodes usually start 5-10 days before menstruation and end with the menstruation. In this article, we present a case of a 17 years old young single woman, who periodically represents brief psychotic episodes per month that are start before menstruation and end with menstruation, with comparing our findings with literature.

Key words: Menstruation, psychotic disorder, puberty

INTRODUCTION
Psychiatry is a more indefinite science than other medical sciences due to its field–specific characteristics (etiologic problems, popularity of phenomenological approaches rather than empirical data, paradigm shifts etc.) and also open to advancement due to reasons mentioned above. Diagnostic classification systems developed by American Psychiatric Association and World Health Organization (Diagnostic and Statistical Manual of Mental Disorders [DSM] and International Classification of Diseases [ICD]) takes phenomenological indicators (symptoms and signs) into consideration rather than changes in cognitive and biological processes for diagnostic validity (1). DSM-V which is expected to be issued in a short time is not expected to introduce a different classification system. However, this approach makes it difficult and even impossible to differentiate clinical conditions which are phenomenologically similar but having different processes. Examples of these conditions are clinical syndromes due to neurophysiologic interactions of sex hormones.

There are substantial data in the literature showing the role of sex hormones in the occurrence and severity of many psychiatric symptoms (2, 3). Premenstrual and menstrual phases of menstrual cycle which these hormones show their peaks are periods which are more sensitive to exacerbation of these psychiatric symptoms. It is already known that admission to psychiatry clinics increase in these periods (4).

Mental status changes due to menstrual cycle cause important health problems in women. “Premenstrual dysphoric disorder” defined as a disorder category by DSM cannot cover all clinical conditions related to menstrual pathophysiology reported in psychiatry literature (5). Also, current understanding of psychiatry and psychopathology do not generally consider menstrual physiology in the pathogenesis and etiology of psychotic disorders (6). In this context, “recurrent
psychotic disorder" and related syndromes with abnormal behavior which have strong relations with menstruation were not included in a separate category.

**Historical View**

Relationship between psychosis and menstruation was first described in 1896 by Kraft-Ebvang (7). Attention was paid to a clinical condition with psychotic features in some women during or just before menstruation which serum estrogen levels are very low and this concept lead to the diagnostic category named as “menstrual psychosis” (2). Frank whom first used the term “premenstrual tension” (8) reported some cases which showed the relationship of this condition with psychosis. Williams and Weeks (9) reported “menstrual psychosis” cases characterized by mania and catatonic schizophrenia. Significant differences were demonstrated in psychotic behaviors in the last 10 days of menstrual cycle by Ota et al. in 1952 (10) and by Gregory in 1957 (11). In Japan, Wakoh et al. (12) reported cases with acute onset psychotic features in the luteal phase of menstrual cycle. “Menstrual psychosis” without accompanying premenstrual syndrome symptoms was first described by Lingjaerde and Bredland (13).

**Clinical Manifestations**

Cases reported were generally under 20 years old and around 16 years old, unmarried young women. The syndrome may occur concomitantly with puberty or just after puberty (14). In the psychotic state there are delusions, hallucinations, confusion, depersonalization, insomnia, hyperactivity, emotional instability, unexpected behaviors and autonomic nervous system signs such as flushing, anorexia and vomiting (15,16). Main characteristics of “Periodical Psychosis of Puberty” named by Altschule and Brem (17) were delusions, auditory and visual hallucinations, agitation and insomnia. Emotional instability, bizarre posture, absence seizures and disorientation may also be observed. Symptoms typically occur in the luteal phase of menstrual cycle, a few days before menstrual bleeding and resolves within a few days with the menstruation and recurs in the following menstrual period. Initial symptoms are generally seen in the first years after menarche and continue for a few years if untreated (18). No family history of psychiatric disorder is evident in most of the cases (19,20). Symptoms may vary in every episode (14).

Monthly periods of attacks were also reported in men but Berlin et al. (18) reported that case reports condensed in women, episodes repeat in luteal phase and progesterone may play a role in the etiology.

**Pathogenesis**

The most striking example strongly suggesting the relationship between hormonal changes and psychiatric conditions are premenstrual relapses of psychotic symptoms in women with postpartum psychotic disorder and long-term continuation of these symptom recurrences after the birth (21).

Psychiatric conditions such as schizophrenia and mood disorders may exacerbate correlated with hormone levels during menstrual cycle, together with the relationship between fluctuations in postpartum estrogen levels and psychiatric disturbance risk. (4). While sex hormones may play a role in these symptom fluctuations, possible mechanisms were not identified yet. Estrogen, progesterone and levels of their metabolites decrease in premenstrual (late luteal) phase and remain low in menstrual (follicular) phase. It is already known that these gonadal steroids regulate the functions of central neurotransmitters such as serotonin, dopamine, norepinephrine and GABA (22). During menstrual cycle, gonadal steroid levels change and this may lead to changes in psychiatric symptoms (23).

Increased prolactin and luteinizing hormone (LH) levels and high estradiol/progesterone ratio may play a role in the pathogenesis of this syndrome. In this context, bromocriptine is suggested for high prolactin level and progesterone or clomifene citrate which is an estrogen antagonist is suggested for high LH levels. (18). Inefficacy of antipsychotic agents used in either low or high doses in nearly all of the literature directed the investigators to these hormonal therapies.
 Suppressing menstrual bleeding to prevent the syndrome which starts a few days before the bleeding was also thought and oral contraceptive agents were used for treatment (6). Presence of concomitant premenstrual dysphoric disorder in a substantial amount of cases supports oral contraceptive use for treatment and there are cases treated this way in the literature (14,15). It was proposed that while treating with contraceptives containing higher estrogen, estrogen decreases monoamine oxidase activity, alters norepinephrine levels in synapses and subsequently controls the total clinical picture (20). Danazole and steroid derivatives which suppress ovulation and menstruation were agents successfully used for treatment (15). Antidepressant agents and electroconvulsive therapy were also among other treatment options used (15,18). It was reported that recurrence of psychotic symptoms under adequate antipsychotic treatment and relief of symptoms after antipsychotic withdrawal may indicate spontaneous remission of the syndrome and positive results were seen in long-term follow-up without medication (6,14,19).

CASE

The patient whom was hospitalized in the adolescent clinic of our hospital was informed about the current study and her consent was obtained about sharing her condition as a case report in scientific media (congresses, meetings, journals etc.).

The female patient whom was 17 years old, single, high school graduate, eldest of three siblings and preparing for university exams admitted to the hospital accompanied with her sister due to decrease in speech, dullness, introversion, refusing eating, fears and cannot stay alone.

Her sister said that four days ago patient’s facial expression changed rapidly, started not speaking to anyone, lost interest in her lessons, stopped going to university exam preparation courses, started sitting in the house without doing anything, being influenced from television, continuously blaming herself, got afraid of her ex-colleagues doing harm to herself and her family, not sleeping and eating.

She said “While I am talking, another person tells me something else”. The patient reported female and male voices saying “Do this, do that, don’t behave like this, behave like a human being” and also said that these voices sometimes talk with each other and she could not understand them.

The patient was admitted to the hospital with the preliminary diagnosis of “brief psychotic disorder” and her psychomotor activity was retarded, affect was blunted and looked confused. Response time to verbal stimuli was increased; she was replying questions and cooperating with difficulty. She could not remember some of the recent events. In her thought content, there were reference delusions like “being told about her and given messages to her in the television” and persecution delusions like her ex-colleagues will rape her and her mother. She also reported ordering and criticizing auditory hallucinations.

According to the history taken from her family, her symptoms first started four months ago when she began working as a secretary in a company after failing to pass university entrance exams. Her first complaints were depressed mood, social withdrawal, lack of appetite and insomnia. She tries not to go outside due to discomfort from others’ gazes. She thinks that ÖSYM (Student Selection and Placement Center) follows her, her colleagues think of harming her and her family and she and her mother will be raped. When she first applied to our outpatient clinic, 0.5 mg/day risperidone and 50 mg/day chlorpromazine were started. Both she and her relatives told in the control appointment that her symptoms were fully resolved at the first day of treatment but they continued the treatment according to physicians’ advices. In the interview, it was learned that her symptoms start 1-2 days before menstruation and resolves a few days after it stops and drug treatment was not changed.

About a month after patient’s symptoms resolved and while she was using the recommended treatment, she applied to the outpatient clinic again with anhedonia, low self-esteem, thoughts of self-blame, insomnia and lack of appetite. Due to recurrence of reference and persecutory delusions, drug doses increased two-fold.
Her first episode lasted 12 days and second lasted one week and she returned her premorbid health and functionality. At this stage she did not have menstrual bleeding but symptoms start at the expected menstruation. At the first two episodes, patient had regressive attitudes and started going to bed with her mother.

At the following appointment, she described similar symptoms after her first improvement and thought that it resolves in any case so there is no need to go to doctor and did not use her drugs regularly. At that time her symptoms continued for a week and resolved spontaneously.

One month later, as the family particularly noticed, a few days before the expected menstrual bleeding date fourth episode occurred with similar symptoms and same treatment started. Her symptoms resolved in one week like in the previous episodes. One month later, at the fifth episode patient was brought to our emergency department by her family and hospitalized.

Her family said that symptoms recurred although she took her drugs, first episode started a few days before menstrual bleeding, symptoms resolve after bleeding starts and other episodes possibly in concordance with the menstrual bleeding periods. Her menarche was at 14 years old and her menstrual periods were reported to be quite regular by her family. Amenorrhea occurred in the first three months of pharmacotherapy but her family said that they know when her bleeding will start due to her regular periods and episodes occurred in one month intervals when menstrual bleeding is expected.

Full improvement is reported by both she and her family between episodes and did not describe any depressive or hypomanic episodes except psychotic attacks. She went to university exam preparation courses between the episodes.

Her blood chemistry test was normal except minimal total cholesterol elevation (285 mg/dL). No abnormality was detected in complete blood counting and thyroid function tests as well. Her electroencephalogram and cranial computerized tomography were also normal. LH, FSH, progesterone, estradiol, prolactin and testosterone levels repeated in different phases of menstrual cycle were normal for those periods. Quetiapine 300 mg/day was started and at the third day her psychomotor activity returned to normal, her affect was euthymic and her associations were normal as well. Delusional and perceptional pathologies of the patient resolved dramatically and drug treatment stopped.

After her discharge from the hospital she was regularly followed-up in the first 6 months and no affective or psychotic symptom was observed and no therapeutic intervention was needed for 3 years.

**DISCUSSION**

The aforementioned syndrome which we described as “premenstrual psychotic disorder”, points out a psychotic disorder which does not exist in current psychiatric classification systems. Our case, with cases reported in the literature, indicates various manifestations of this disorder:

1. Abruptly starting psychotic symptoms a few days before menstruation (with, during or in the middle of menstrual bleeding in some cases). Symptoms resolve a few days after the menstruation and repeats indicating a disruption in mid or late luteal phase and in close relation with one of the cycles (not necessarily in every cycle) (24).

2. Most of the patients are asymptomatic between psychotic episodes (24).

3. Relationship between typical functional psychoses and perimenstrual psychotic disorders is not clear. Most cases do not have a family history of psychiatric disorder (25).

4. Clinical manifestations may vary at every menstrual cycle, are non-specific and usually do not fit the definitions of functional psychoses (25).

5. In most of the case reports, no serious psychosocial stressor was mentioned before the unexpected psychotic episode. However, in two cases reported by Brockington (24), there was a separation from parents before the psychotic episode started and exaggerated dependency attitude was mentioned during episodes. Our case resembles these previously reported cases with the occurrence of first episode after the failure at examination and regressive
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...attitude to the mother during psychotic episodes.

6. No evidence on organic etiology and relationship with alcohol and substance abuse was found in the literature (26).

7. In most of the case reports, first psychotic episode occurs in early adolescence. However, there are many case series which first episode or exacerbation of the previous perimenstrual psychosis occur in perinatal period which accompanies affective disorder (often) or schizophreniform disorder (less often) (27).

8. Prognosis was not monotypic in cases reported in the literature and followed-up for 12-14 years. Some cases were characterized with full remission and others with partial remission (25,28).

9. In most cases, prognosis of perimenstrual psychotic episode was not found to be related to treatment with antipsychotic, antidepressant or mood stabilizer agents. Only a few cases fully improved with lithium and one severe case fully improved with electroconvulsive therapy (ECT) (19,25).

CONCLUSION

Current psychiatric disorder classification systems were constructed with a phenomenological point of view rather than pathogenetically-based approach due to some inadequacies. Current biochemical, genetic and imaging-based scientific studies advanced in accordance with pathogenetically-based classification. Our case report which mentioned the relationship of cyclic psychotic episodes seen in adolescence with the menstrual cycle may contribute to the understanding of the pathogenesis of this kind of psychotic disorders. There is a strong need to enlighten the etiology and phenomenology of this disorder by future case reports and interdisciplinary prospective studies.

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