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Getting to the Diagnosis: A Case Study on a 51-Year-Old Female with Anxiety, Depression, and Suicidal Ideations

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Abstract

This case study explores the diagnosis and treatment of a 51-year-old female with exacerbated anxiety and depressive symptoms, which worsened prior to menstruation. Initial concerns involved the maximum dosage of psychiatric medications with persistent major depressive disorder and suicidal ideations. This led to a referral for a comprehensive evaluation to assess potential underlying medical conditions. The evaluation revealed multiple contributing factors, including hormonal imbalances, hypothyroidism, and vitamin deficiencies. This case highlights the importance of a thorough diagnostic approach to identify and address underlying conditions that may exacerbate mental health issues.

Keywords

Premenstrual Dysphoric Disorder, Hypothyroidism, Anxiety, Depression, Vitamin Deficiency, Hormonal Imbalance

1. Introduction

This paper presents a clinical case study focusing on the diagnosis and management of a 51-year-old female patient with persistent major depressive disorder and associated comorbidities. The patient endured years of depression and social withdrawal without relief from psychiatric medications. Her inadequate response to treatment led her therapist to refer her for further evaluation. This case involves ongoing major depression, anxiety, and suicidal ideation, which persisted despite numerous psychiatric interventions.

The depressive episodes typically start about a week before her menstrual cycle and last for 3 - 4 days. This pattern suggests the patient may be experiencing

premenstrual dysphoric disorder, a severe form of premenstrual syndrome characterized by a range of physical, emotional, and behavioral symptoms that arise during the luteal phase of the menstrual cycle and resolve with the onset of menstruation, align with research on PMDD [1].

Research suggests a connection between hormonal imbalances, such as those observed during perimenopause, and mental health disorders, with studies indicating that perimenopausal women may experience an increased risk of depression and anxiety [2]. Additionally, conditions like hypothyroidism and vitamin D deficiency have been increasingly recognized as exacerbating factors for mood disorders, including depression and anxiety. Hypothyroidism, for instance, can lead to mood disturbances due to disruptions in thyroid hormone regulation. At the same time, vitamin D deficiency has been linked to an increased risk of depression and mood fluctuations [3].

This case underscores the importance of a comprehensive evaluation, considering both psychiatric and medical factors in treatment-resistant depression, particularly in women experiencing perimenopausal and premenstrual symptoms. By integrating hormonal, thyroid, and nutritional assessments, the case highlights the complex relationship between endocrine health and mental health disorders. Informed consent was obtained from the patient for the publication of this case study, ensuring that her privacy and confidentiality were maintained in accordance with ethical standards.

2. Case Presentation

2.1. History of Present Illness (HPI)

This is a 51-year-old female patient who reported experiencing anxiety and depressive symptoms intensifying one week before menstruation, lasting 3 - 4 days. Symptoms included extremely low energy, depression, shortness of breath, difficulty focusing, and suicidal thoughts without plans for ten years. The patient also described repetitive thoughts, social withdrawal, and a feeling of being out of control. The patient was initially presented to a mental health clinic about three years ago for a telemedicine visit, exhibiting signs and symptoms of Major Depressive Disorder, including suicidal thoughts. These symptoms worsened prior to menses. Psychiatric treatments focused on managing depression, generalized anxiety, sleep disturbances, and suicidal thoughts. Medications such as Quetiapine and Bupropion were continued to manage depression, anxiety, and sleep disturbances. The patient was referred from the psychiatry clinic for further evaluation because maximum doses of psychiatric medications yielded no therapeutic effects. The patient was diagnosed with Major Depressive Disorder with suicidal ideation and plans.

2.2. Psychiatric Management and Intervention

The patient, a 51-year-old female with Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD), initially showed moderate improvement in

anxiety with Sertraline 50 mg daily, but depressive symptoms and premenstrual exacerbations persisted. Increasing Sertraline to 100 mg and adding Quetiapine 25 mg for sleep provided some relief, though daytime sedation required reducing Quetiapine to 12.5 mg. Six months later, Bupropion 100 mg daily was introduced for persistent fatigue and depression, leading to notable improvement in mood, energy, and motivation. After a year, due to concerns about weight gain, the patient transitioned to Bupropion monotherapy, maintaining 100 mg daily with sustained benefits. Temporary dose increases of Bupropion to 150 mg and later 300 mg during premenstrual exacerbations were tried. However, side effects like insomnia and anxiety led to a reduction back to 100 mg, which proved effective long-term.

Throughout treatment, the patient engaged in CBT, group therapy, and self-help techniques such as journaling and mindfulness, which improved her coping skills. Counseling was also provided via BetterHelp, an online platform, and self-help resources like Mind Over Mood were recommended. Regular follow-ups monitored sleep quality and suicidal thoughts, and the patient was encouraged to use the suicide hotline if needed. Psychotherapy, including CBT and motivational interviewing, helped address maladaptive behaviors, though the patient struggled to fully connect her actions with their impact on mental health. Given the partial response, particularly with premenstrual symptoms, she was referred for endocrinological evaluation while continuing Bupropion 100 mg as the most effective dose.

2.3. Patient profile

Menstrual History

- **Cycle**: Every 28 days, lasting seven days.
- **Menarche**: At seven years old.

Contraception

- None.

Sexual History

- Married, male partner.

Current Medications

- Quetiapine 25 mg, 1/2 tablet PO QHS for sleep.
- Bupropion 100 mg QD.

Past Medical and Surgical History

- The patient denied any past medical or surgical history.

Family History

- Mother had breast cancer at 48 years old and colon cancer at 63 years old.

Social History

The patient lives with her son and his family, including her husband and two children. She is independent in activities of daily living, cooks for the whole family, and walks in a park for 30 to 40 minutes 3 times a week. She quit smoking 30 years ago and denies drinking alcohol or using recreational drugs.

Review of Systems

The review of symptoms was positive for depressive signs and symptoms. All other systems were reviewed and negative.

Physical Examination

- **Weight**: 125 lbs.
- **Height**: 5'3".

2.4. Initial Assessment and Plan

Premenstrual Dysphoric Disorder (PMDD)/Major Depression:

The patient's symptoms are indicative of PMDD, which involves significant mood and anxiety exacerbations linked to her menstrual cycle. Notably, her anxiety and depressive symptoms intensified during the luteal phase, prompting a focus on PMDD management alongside her other psychiatric conditions. According to the DSM-5-TR, PMDD is diagnosed when a patient exhibits at least five symptoms—such as affective lability, irritability, depressed mood, anxiety, loss of interest, fatigue, feeling emotionally overwhelmed, or physical symptoms—during most menstrual cycles over the past year, with at least one of these symptoms involving mood-related issues. In this case, the patient's recurrent depressive episodes, anxiety, fatigue, and mood swings, particularly during the luteal phase, align with these diagnostic criteria. Her symptoms consistently disrupted daily functioning, especially in work and social settings, further supporting the diagnosis of PMDD.

- Continue Bupropion 100 mg QD.
- Start Vitamin B complex (timed release) daily.
- Start Vitamin B6 for 14 days before menstruation (luteal phase).
- Start Vitamin D 5000 IU with Vitamin K2 daily.
- Start Omega-3 fatty acids daily.
- Start Magnesium glycinate 300 mg in the morning and evening.

Since the patient's laboratory results were unavailable at the initial visit, immediate treatment was initiated, focusing on cellular-level supplementation to address potential deficiencies. The following labs were ordered to assess her overall health: hormonal levels (FSH, LH, Progesterone, SHBG, Testosterone, Estradiol, Estrone, DHEA, Prolactin), metabolic and inflammatory markers (CMP, CBC, CRP, TSH, Free T4, Free T3, Vitamin D, HbA1c, ESR), urinalysis, and genetic testing (MTHFR, TPO-Ab). These tests aimed to identify conditions like hypothyroidism or vitamin deficiencies that could be contributing to her PMDD symptoms. The patient was instructed to follow up in 1 - 2 weeks for test results and further management.

2.5. Follow-Up Visit Diagnostic Tests and Results

- TSH: 4.72 H (indicative of hypothyroidism) TPO < 1.
- Vitamin D: 23 L (indicative of deficiency).
- Testosterone total 12 (indicative of deficiency).

- MTHFR Positive for one copy of C677T variant and one copy of A1298C.
- FSH: 21.8/LH 8.4 (Perimenopause).
- Progesterone < 0.5 (indicative of deficiency).
- Estradiol 30.
- Estrone 32.
- Cholesterol 194/HDL 83/LDL 87/Triglycerides 144.
- FBS 93.
- GFR106/AST 17/AST 11.
- HgbA1 c 5.4.
- CBC hgb 14.5/hct 43.2.
- UA WNL.
- Vitamin B 12 370.
- CRP < 3.0.
- Prolactin 4.8.
- Sex Hormone Binding Globulin 58.

2.6. Follow-Up Assessment and Plan

1) Premenstrual Dysphoric Disorder (PMDD)/Major Depression:

2) Hypothyroidism:

- Start NP Thyroid 15 mg, one tablet PO QAM.
- Repeat TSH in 6 weeks.

3) Vitamin D Deficiency:

- Start ergocalciferol 1.25 mg (50,000 IU) oral capsule weekly.

4) Perimenopause/Hormonal Imbalance:

- Start Low progesterone: Topical 200 mg/1 gram, 1 click daily (luteal phase).
- Start Low testosterone: Topical 2.5 mg/1 gram, one-click daily.

5) MTHFR Gene Mutation (Gene A and Gene C):

- Avoid all folic acid (fortified cereals, anything fortified).

3. Discussion

Plan of Care—from the initial visit—while waiting for lab results.

3.1. Diagnosis and Treatment Plan

The patient was diagnosed with PMDD and started on a treatment regimen that included the following supplements:

- Vitamin B complex (timed release) daily.
- Vitamin B6 for 14 days before menstruation (luteal phase).
- Vitamin D 5000 IU with Vitamin K2 daily.
- Omega-3 fatty acids daily.

These supplements were introduced based on their documented benefits in managing PMDD symptoms and improving overall mental health in women. Given that the patient's labs had not yet been performed, initiating treatment at the cellular level was essential to address potential deficiencies that could exacerbate

her symptoms.

3.2. Vitamin B Complex and Vitamin B6

Research suggests that Vitamin B6 plays a crucial role in serotonin production, which can help alleviate depressive symptoms in women with PMDD. Studies have shown that Vitamin B6 supplementation can reduce irritability, depression, and anxiety during the luteal phase of the menstrual cycle [4]. Adding a Vitamin B complex ensures that other B vitamins, such as B12 and folate, are available to support overall brain function and energy levels, further helping to stabilize mood in women with PMDD [5].

3.3. Vitamin D with Vitamin K2

Vitamin D deficiency has been associated with mood disorders, including depression, and research indicates that maintaining adequate Vitamin D levels may help reduce the severity of PMDD symptoms [6]. Vitamin D, combined with Vitamin K2, plays an essential role in calcium metabolism, supporting bone health and promoting hormonal balance. This is particularly important for women in perimenopause, whose fluctuating hormones can exacerbate mood disorders [7]. Vitamin D supplementation has been linked to improved mood and reduced depressive symptoms, making it a critical component of the treatment plan for PMDD.

3.4. Omega-3 Fatty Acids

Omega-3 fatty acids, particularly EPA and DHA, have anti-inflammatory properties that benefit both physical and mental health. In women with PMDD, Omega-3 supplementation has been shown to reduce depressive symptoms and improve overall emotional well-being [8]. Omega-3s help regulate neurotransmitter function and reduce inflammation, which can play a role in mood stabilization and anxiety reduction.

3.5. Magnesium Glycinate

Magnesium glycinate is beneficial for managing PMDD due to its role in regulating neurotransmitters and reducing symptoms of mood instability. Magnesium helps alleviate anxiety, irritability, and depression by supporting serotonin production, a key neurotransmitter that influences mood [9]. Additionally, magnesium glycinate has been shown to reduce physical symptoms of PMDD, such as menstrual cramps, by relaxing smooth muscles [5]. It also improves sleep quality, often disrupted in PMDD, promoting better overall emotional well-being [10]. Unlike other forms of magnesium, glycinate is easily absorbed and less likely to cause gastrointestinal side effects, making it a preferable long-term treatment option for women with PMDD [11].

4. Discussion: Follow-Up Visit with Lab Results

The follow-up lab results revealed that the patient is transitioning from Premenstrual

Dysphoric Disorder (PMDD) to perimenopause. She was also diagnosed with vitamin D deficiency, hypothyroidism, low testosterone, and a positive result for the MTHFR gene variants. With these results, we now have clearer information to guide her treatment, which was previously limited to weekly therapy sessions and psychiatric medication adjustments. Ideally, a collaborative effort with her therapist in a shared clinical setting would enhance the management of this case, but this is rarely feasible. However, thorough diagnostic tests now provide us with valuable insights.

This case highlights the complexity of diagnosing and managing mental health symptoms that are significantly influenced by underlying medical conditions. The patient's exacerbated anxiety and depression, particularly before menstruation, required a comprehensive diagnostic approach to uncover the root causes of her symptoms. This discussion will explore the pertinent diagnostic testing, differential diagnoses, pathophysiology, evidence-based management, and follow-up for the patient.

The patient is transitioning from PMDD to perimenopause, a phase that precedes menopause and is marked by significant hormonal fluctuations, including a decline in progesterone and testosterone levels. These hormonal deficiencies are commonly associated with symptoms such as mood swings, fatigue, and decreased libido [8]. We aim to optimize her health and alleviate her symptoms by addressing these imbalances at the cellular level.

At 51 years old, the patient also tested positive for MTHFR gene variants A1298C and C677T. The MTHFR gene plays a critical role in the methylation process, essential for DNA repair, detoxification, and neurotransmitter production. Variants in this gene can result in reduced enzyme activity, leading to impaired folate metabolism and increasing the risk of mental health disorders, cardiovascular issues, and inflammatory responses [12]. These gene variants may contribute to symptoms such as brain fog and a sensation of "brain inflammation", potentially exacerbating the challenges she faces during perimenopause [13].

Additionally, it is essential to note that folic acid is often added to food products in the United States. This can pose a challenge for individuals with MTHFR gene variants, as their bodies may struggle to metabolize synthetic folic acid efficiently, which could complicate their treatment plan [13].

In summary, this case underscores the importance of integrating comprehensive diagnostic testing with personalized treatment strategies to address the patient's mental and physical health needs. A collaborative, multidisciplinary approach remains essential in managing the complex interplay between hormonal imbalances and mental health conditions in perimenopausal women.

4.1. Differential Diagnoses

Beyond PMDD and major depression, several differential diagnoses were considered:

1) Polycystic Ovary Syndrome (PCOS): Characterized by menstrual irregularities,

hyperandrogenism, and metabolic issues, PCOS can exacerbate mood disorders [14].

2) Adrenal Dysfunction: Conditions like Addison's disease or Cushing's syndrome can present with mood disturbances due to cortisol imbalances [15].

3) Perimenopausal Transition: Hormonal fluctuations during perimenopause can lead to significant mood changes, including anxiety and depression [16].

4) Subclinical Thyroid Disorders: Both hyperthyroidism and hypothyroidism can influence mood, and autoimmune thyroiditis was considered [17].

5) Iron Deficiency Anemia: Iron deficiency, particularly in women with heavy menstrual cycles, can contribute to fatigue and mood disturbances [18].

4.2. Pathophysiology

The patient's transition from Premenstrual Dysphoric Disorder (PMDD) to perimenopause introduces significant changes in hormone regulation, particularly declining levels of progesterone and testosterone, both of which play a critical role in mood stabilization, energy levels, and overall well-being [2]. PMDD is already characterized by mood disturbances linked to the luteal phase of the menstrual cycle when progesterone levels fluctuate. As perimenopause progresses, these hormonal fluctuations become more pronounced, contributing to emotional and physical symptoms such as mood swings, fatigue, irritability, and sleep disturbances [1].

In addition to these hormonal changes, the patient's MTHFR gene mutation adds a layer of complexity. The MTHFR (methylenetetrahydrofolate reductase) gene is essential for converting folate into its active form, methylfolate, which is critical for neurotransmitter synthesis, detoxification, and DNA repair. Variants of the MTHFR gene, such as the ones found in this patient, are associated with reduced enzymatic activity, which can impair methylation processes and increase the risk of mental health disorders, including anxiety and depression [13]. Research suggests that individuals with MTHFR mutations may have difficulty metabolizing synthetic folic acid, commonly fortified in food, leading to a potential buildup of unmetabolized folic acid and an increased risk of neuropsychiatric symptoms [13].

The hypothyroidism diagnosis further complicates the picture, as thyroid hormones play a significant role in regulating metabolism, mood, and cognitive function. Elevated TSH levels in hypothyroidism lead to sluggish metabolism and neurotransmitter imbalances, contributing to symptoms such as depression, fatigue, and cognitive decline [17]. Vitamin D deficiency also plays a pivotal role in brain health and has been linked to depression and impaired cognitive function. Low vitamin D levels reduce the brain's ability to regulate neurotransmitters like serotonin, further exacerbating the patient's mood instability [7].

Additionally, the presence of low testosterone levels—common during perimenopause—can contribute to fatigue, decreased libido, and mood disturbances. Testosterone has been linked to feelings of vitality and well-being, and its decline

during the perimenopausal period can worsen the mental health symptoms the patient experiences [19].

In summary, the patient's mental health issues are being driven by a combination of hormonal imbalances, genetic predispositions (MTHFR mutation), and deficiencies in essential nutrients like vitamin D. Addressing these root causes at the cellular level is crucial for effective treatment. By understanding the interaction between these factors, we can approach her treatment with a holistic, evidence-based strategy that not only targets her mental health symptoms but also corrects underlying physiological dysfunctions.

4.3. Evidence-Based Management

The management of this patient involved a multidisciplinary approach that incorporated both pharmacological and non-pharmacological strategies:

Hormone Therapy: The patient was started on bioidentical hormone replacement therapy (BHRT) with topical progesterone (200 mg/1 gram, one-click daily, stopped during menses and restarted after menses) and topical testosterone (5 mg/1 gram, one-click daily) to address hormonal imbalances. Evidence suggests that BHRT may offer a more favorable side-effect profile compared to synthetic hormones, particularly in managing hormonal fluctuations in perimenopausal women [16].

Thyroid Hormone Replacement: The patient was prescribed NP Thyroid (15 mg, one tablet daily in the morning on an empty stomach) with a plan to recheck TSH levels in six weeks. This treatment is in line with guidelines that recommend maintaining a lower TSH range for optimal symptom control in patients with hypothyroidism [17].

Vitamin D Supplementation: High-dose vitamin D supplementation was initiated to correct severe deficiency and improve mood symptoms associated with low vitamin D levels. Vitamin D plays a critical role in mental health, and its supplementation is supported by evidence showing improvement in depressive symptoms in deficient individuals [7].

Psychiatric Medications: The patient continued her current psychiatric medications, quetiapine and bupropion. Additionally, the use of an SSRI, such as fluoxetine, was considered for intermittent dosing during the luteal phase to manage PMDD symptoms. This approach aligns with evidence supporting the efficacy of SSRIs for PMDD when used during the luteal phase [20].

Lifestyle Modifications: Recommendations were made for regular physical activity, a balanced diet, and stress reduction techniques. These lifestyle changes are essential adjuncts to pharmacotherapy in managing mood disorders and promoting overall well-being.

Patient Outcome: Follow-Up at 6 Weeks

At the six-week follow-up, the patient reported significant improvements in her mood and energy levels. The initiation of thyroid hormone replacement and vitamin D supplementation led to noticeable improvements in her overall well-

being. The addition of bioidentical hormone therapy stabilized her mood during the luteal phase of her menstrual cycle, reducing the severity of her premenstrual symptoms. She was able to resume her daily activities with greater ease and experienced fewer depressive episodes. Continued follow-up and potential adjustments to her treatment plan were scheduled to ensure sustained symptom management and overall health improvement.

5. Conclusion

In patients with complex mental health issues, identifying and addressing underlying medical conditions such as thyroid dysfunction, vitamin deficiencies, and hormonal imbalances is vital. In this case, reaching the correct diagnosis was crucial, as the patient's mental health was severely affected, with her describing her brain as feeling "on fire". A multidisciplinary approach that integrates hormone therapy, supplementation, and continuous mental health support is essential in managing such cases effectively. It is also important to recognize that in the U.S., folic acid is often added to food, which can complicate treatment for individuals with MTHFR gene variants, as they may have difficulty metabolizing synthetic folic acid. Ongoing follow-up and tailored treatment adjustments are vital to ensuring long-term positive outcomes. I want to extend my gratitude to my patient, who encouraged me to write this case in her honor, in hopes that it will inspire other providers to look beyond mental health diagnoses and explore underlying medical conditions that may exacerbate their patients' mental health.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Yang, Y., Valdimarsdóttir, U.A., Manson, J.E., Sievert, L.L., Harlow, B.L., Eliassen, A.H., *et al.* (2023) Premenstrual Disorders, Timing of Menopause, and Severity of Vasomotor Symptoms. *JAMA Network Open*, **6**, e2334545. https://doi.org/10.1001/jamanetworkopen.2023.34545

[2] Khan, M.M., Naila, F., Muneeb, P., Afridi, A. and Zaman, S. (2021) Effectiveness of Cognitive Behavioral Therapy for Premenstrual Dysphoric Disorder (PMDD)—A Randomized Controlled Trial. *Journal of Pharmaceutical Negative Results*, **12**, 204-210.

[3] Parker, G.B., Brotchie, H. and Graham, R.K. (2017) Vitamin D and Depression. *Journal of Affective Disorders*, **208**, 56-61. https://doi.org/10.1016/j.jad.2016.08.082

[4] Wyatt, K.M., Dimmock, P.W., Jones, P.W. and Shaughn O'Brien, P.M. (1999) Efficacy of Vitamin B-6 in the Treatment of Premenstrual Syndrome: Systematic Review. *British Medical Journal*, **318**, 1375-1381. https://doi.org/10.1136/bmj.318.7195.1375

[5] Siminiuc, R. and Țurcanu, D. (2023) Impact of Nutritional Diet Therapy on Premenstrual Syndrome. *Frontiers in Nutrition*, **10**, Article 1079417. https://doi.org/10.3389/fnut.2023.1079417

[6] Głąbska, D., Kołota, A., Lachowicz, K., Skolmowska, D., Stachoń, M. and Guzek, D. (2021) Vitamin D Supplementation and Mental Health in Inflammatory Bowel

Diseases and Irritable Bowel Syndrome Patients: A Systematic Review. *Nutrients*, **13**, Article 3662. https://doi.org/10.3390/nu13103662

[7] Holick, M.F. (2010) Vitamin D and Health: Evolution, Biologic Functions, and Recommended Dietary Intakes for Vitamin D. In: Holick, M.F., Ed., *Vitamin D*, Humana Press, 3-33. https://doi.org/10.1007/978-1-60327-303-9_1

[8] Freeman, E.W. (2010) Associations of Depression with the Transition to Menopause. *Menopause*, **17**, 823-827. https://doi.org/10.1097/gme.0b013e3181db9f8b

[9] Eby, G.A. and Eby, K.L. (2010) Magnesium for Treatment-Resistant Depression: A Review and Hypothesis. *Medical Hypotheses*, **74**, 649-660. https://doi.org/10.1016/j.mehy.2009.10.051

[10] Mah, J. and Pitre, T. (2021) Oral Magnesium Supplementation for Insomnia in Older Adults: A Systematic Review & Meta-Analysis. *BMC Complementary Medicine and Therapies*, **21**, Article No. 125. https://doi.org/10.1186/s12906-021-03297-z

[11] Rosanoff, A., Weaver, C.M. and Rude, R.K. (2012) Suboptimal Magnesium Status in the United States: Are the Health Consequences Underestimated? *Nutrition Reviews*, **70**, 153-164. https://doi.org/10.1111/j.1753-4887.2011.00465.x

[12] Friso, S., Choi, S., Girelli, D., Mason, J.B., Dolnikowski, G.G., Bagley, P.J., *et al.* (2002) A Common Mutation in the 5,10-Methylenetetrahydrofolate Reductase Gene Affects Genomic DNA Methylation through an Interaction with Folate Status. *Proceedings of the National Academy of Sciences*, **99**, 5606-5611. https://doi.org/10.1073/pnas.062066299

[13] Zhang, Y., Yang, L., Gai, C., Cheng, C., Guo, Z., Sun, H., *et al.* (2022) Association between Variants of MTHFR Genes and Psychiatric Disorders: A Meta-Analysis. *Frontiers in Psychiatry*, **13**, Article 976428. https://doi.org/10.3389/fpsyt.2022.976428

[14] Shahid, M. and Wajid, M. (2024) Polycystic Ovary Syndrome in North America. In: Rehman, R. and Sheikh, A., Eds., *Polycystic Ovary Syndrome*, Elsevier, 229-236. https://doi.org/10.1016/b978-0-323-87932-3.00039-6

[15] Nieman, L.K. (2018) Recent Updates on the Diagnosis and Management of Cushing's Syndrome. *Endocrinology and Metabolism*, **33**, 139-146. https://doi.org/10.3803/enm.2018.33.2.139

[16] (2021) Management of Osteoporosis in Postmenopausal Women: The 2021 Position Statement of the North American Menopause Society. *Menopause*, **28**, 973-997. https://doi.org/10.1097/GME.0000000000001831

[17] Garber, J.R., Cobin, R.H., Gharib, H., Hennessey, J.V., Klein, I., Mechanick, J.I., *et al.* (2012) Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocrine Practice*, **18**, 988-1028. https://doi.org/10.4158/ep12280.gl

[18] Kassir, A. (2017) Carence en fer: Une perspective diagnostique et thérapeutique en psychiatrie. *L'Encéphale*, **43**, 85-89. https://doi.org/10.1016/j.encep.2016.08.002

[19] Schmidt, P.J. and Rubinow, D.R. (2009) Sex Hormones and Mood in the Perimenopause. *Annals of the New York Academy of Sciences*, **1179**, 70-85. https://doi.org/10.1111/j.1749-6632.2009.04982.x

[20] Carlini, S.V. and Deligiannidis, K.M. (2020) Evidence-based Treatment of Premenstrual Dysphoric Disorder. *The Journal of Clinical Psychiatry*, **81**, Article 6789. https://doi.org/10.4088/jcp.19ac13071