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Facial Itching with Missed Doses of Vilazodone

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Authors' contributions

This work was carried out in collaboration between all authors. Author TLS provided the case, wrote the draft of the manuscript and designed the table. Author ACH assisted with the literature search and correction of the draft. Author EW contributed to the correction of the draft. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Aims: Our aim is to describe a case of moderate to severe facial itching associated with missed doses of vilazodone.
Presentation of Case: This report concerns a 53-year old woman with systemic lupus erythematosus and major depressive disorder who experienced sporadic episodes of moderate to severe facial itching around her eyes, cheeks, and forehead after she was prescribed vilazodone.
Discussion: Investigation into the potential causes of the reaction determined that it was not consistent with a SLE malar rash, photosensitivity, hydroxychloroquine-induced lichenoid eruption, or menopausal-related dry skin. The facial pruritus did not respond to antihistamine pharmacotherapy. Symptoms always recurred following missed doses and resolved immediately within 90 minutes after taking the vilazodone. Full compliance with vilazodone has eliminated any further facial itching symptoms.
Conclusion: The authors conclude that vilazodone is the most likely source of the intense pruritus. The reaction occurred consistently after missed doses of the medication and other potential causes were ruled out. This case provides important evidence for health care practitioners to utilize when monitoring and educating of their patients about vilazodone.

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Keywords: Vilazodone; facial itching; withdrawal symptom; nonadherence; treatment emergent adverse effect.

1. INTRODUCTION

It is estimated that 340 million people internationally, including 18 million US adults, suffer from major depressive disorder (MDD) [1]. MDD often recurs and may require lifelong therapy. MDD is most prevalent in those with chronic illness causing significant disability and health care expenditures [2-3]. The World Health Organization reports that unipolar depressive disorders are the third leading cause of global disease burden [4].

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder affecting women that targets several organs including the central nervous system. SLE often causes neuropsychiatric illness including depression and anxiety [5]. The prevalence of comorbid depression in SLE patients is high and ranges from 12 to 47% [6-8]. Therefore, antidepressant pharmacotherapy is a vital component for successful treatment of comorbid mental illness (e.g. depression, anxiety) experienced by SLE patients [9].

Many patients with MDD do not achieve an adequate response to pharmacotherapy even after several changes in their medication regimen. Additionally, treatment emergent adverse events (TEAEs) associated with antidepressants such as sexual dysfunction, weight gain, sleep disturbances, and fatigue are common causes for nonadherence and poor response [10]. In 2011, vilazodone was introduced in the United States for the treatment of MDD. It is considered a novel antidepressant and the first member of the serotonin partial agonist-reuptake inhibitor (SPARI) class that combines serotonin reuptake inhibition with 5-HT_{1A} partial agonism [11]. Vilazodone provides an alternative for those patients who do not respond or experience intolerable TEAEs to traditional first line pharmacotherapy such as selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs). Based on its mechanism of action, vilazodone may also be beneficial in those with comorbid anxiety disorders and has less frequent sexual side effects than those reported with SSRIs and SNRIs [11].

Vilazodone is generally well tolerated and the most common side effects are diarrhea, nausea, vomiting, headache, dizziness, dry mouth, and insomnia [12-15]. The manufacturer reports that abrupt discontinuation of vilazodone can lead to a myriad of symptoms including nausea, dysphoric mood, irritability, sweating, agitation, anxiety, tremor, headache, lethargy, hypomania, tinnitus, sensory disturbances (e.g. paresthesia, electric shock sensations), seizures, and confusion [15]. As a result, gradual dosage reduction is recommended by the manufacturer when discontinuing vilazodone and abrupt cessation should be avoided whenever possible [15].

2. CASE REPORT

A 53-year old woman with SLE, fibromyalgia, chronic neck and low back pain, MDD, and post-traumatic stress disorder was taking escitalopram 30 mg daily for several years. She experienced significant sexual side effects with the escitalopram and reported moderately severe morning fatigue. In late April, 2014, her psychiatrist tapered her off the escitalopram and prescribed vilazodone. The starting dose for vilazodone was 10 mg a day followed by gradual increases of 10 mg per week over a 30-day period to a final dose of 40 mg daily. Two months later, her rheumatologist prescribed hydroxychloroquine 400 mg at bedtime for joint pain and swelling. Previously reported TEAEs for this woman include a rash with amoxicillin, severe nausea and vomiting with meperidine, and exacerbated SLE symptoms from ibuprofen. Menopausal symptoms experienced by the patient include occasional hot flashes, fluid retention, weight gain, and vaginal dryness. The patient reports that she has no difficulties with dry skin or hair loss.

In addition to the vilazodone, she was taking bupropion XL 300 mg daily, loratadine 10mg daily and fluticasone nasal 1 spray each nostril daily. Her “as needed” (prn) medications included: alprazolam 0.5 to 1 mg (3 to 4 doses/month), hydrocodone and acetaminophen 10/325 (3 to 4 doses/month), zaleplon 5 mg (2 doses/month), acetaminophen 500 mg (2-4 doses/week), and naproxen sodium 220 mg (2-3 doses/month). Of important note is that she has been maintained on these medications for several years without any significant TEAEs.

In late September, 2014, the patient began having sporadic episodes of moderate to severe

facial itching around her eyes, cheeks, and forehead. The patient states that she experienced a SLE butterfly or "malar" rash when she was first diagnosed in 1981 but it has not recurred. She consistently wears sunscreen when spending time outdoors. She reports taking diphenhydramine 50mg as needed for the facial itching but did not receive any relief. Her rheumatologist determined that the reaction was not consistent with SLE-induced malar rash, photosensitivity, or a hydroxychloroquine-related lichenoid eruption.

Upon further investigation, the patient reported missing one or more doses of vilazodone on occasion and noticed that the symptoms always reappeared during these instances. When she forgot to take her morning dose, the reaction began to manifest later in the evening and grew in intensity over time. She discovered that after taking the missed vilazodone dose, all of her symptoms resolved within 90 minutes. This finding was confirmed with repeated challenges and observations.

The patient's SLE is currently in remission with normal findings on inflammatory and immunity markers (ESR 6 mm/HR; CRP < 0.20 mg/dl; C3 116 mg/dl, C4 20.4 gm/dl). She continues to have episodes of itching whenever she forgets to take her vilazodone.

3. DISCUSSION

There are several potential causes for the facial itching in this patient including SLE-related, medication-induced (vilazodone, hydroxychloroquine, hydrocodone), menopause, and photosensitivity. Her pain is well controlled, requires very little hydrocodone, and the itching does not coincide with hydrocodone dosing. The patient regularly wears sunscreen making a photosensitivity-like reaction highly unlikely. Additionally, it was determined that the dermatological characteristics associated with SLE, hydroxychloroquine, and menopause facial outbreaks are not consistent with the patient's presenting symptoms (see Table 1).

SLE causes several cutaneous manifestations including malar or "butterfly" rash, photosensitivity, calcinosis, cutaneous vasculitis, nonscaring hair loss, petechiae, livedo reticularis, palmar erythema, Raynaud's syndrome, and mucosal ulcerations [9]. Most SLE-related cutaneous reactions occur on the torso or extremities. The malar rash is the primary facial manifestation, has a distinctive appearance, and is characterized by an erythema over the cheeks and nasal bridge that forms the shape of a butterfly [9]. The SLE malar rash is persistent and may appear scaly but is not pruritic or involve the eyes and forehead region [9].

Hydroxychloroquine can cause lichenoid skin reactions which are described as scaly, annular eruptions that are centrally clear, very pruritic, persistent, and erythematous [15-17]. The lesions produced by hydroxychloroquine are found on both sun-protected and exposed areas involving the face, trunk, and extremities [16-18].

Menopause is commonly associated with several skin changes such as dryness and changes in texture and tone [19,20]. Dry skin can occur just about anywhere on the body (e.g. face, back, chest, elbows, genitals, fingernails) and is often associated with pruritus. Menopausal-induced pruritus is manifested by small bumps on the skin surface, red or irritated skin, rash, and abnormal touch sensations such as numbness, prickling, tingling, and crawling [20].

Table 1. Symptom characteristics of patient presentation compared to SLE malar rash, hydroxychloroquine lichenoid eruptions, and menopausal dry skin

Characteristic	Patient	SLE	Hydroxychloroquine	Menopause
Annular appearance	No	No	Yes	No
Centrally clear lesions	No	No	Yes	No
Dry skin	No	No	No	Yes
Eye area involvement	Yes	No	No	No
Persistent	No	Yes	Yes	Yes
Photosensitivity-related	No	Yes	No	No
Pruritic	Yes	No	Yes	Yes
Scaly	No	Yes	Yes	No
Torso and extremities involvement	No	No	Yes	Yes

Pruritus is not listed amongst vilazodone's adverse effects or withdrawal symptoms reported by the manufacturer [15]. There is however anecdotal evidence available on internet blogs and online forums discussing severe facial itching from vilazodone missed doses or during abrupt withdrawal of the medication. Unfortunately, no published cases or FDA Medwatch reports are currently available to inform the medical community of this significant TEAE.

Based on the evidence presented, vilazodone is the most likely source of the facial pruritus. The patient's MDD and PTSD are well controlled, she no longer experiences morning fatigue or sexual dysfunction and has decided to remain on vilazodone pharmacotherapy. She has not experienced any further facial itching as long as she is 100% compliant with her vilazodone.

4. CONCLUSION

Those suffering from chronic illnesses such as SLE frequently struggle with depression and anxiety. Antidepressant pharmacotherapy is associated with several TEAEs (e.g. fatigue, sexual dysfunction, sleep disturbance, weight gain, and gastrointestinal complaints) that often result in poor adherence and discontinuance of pharmacotherapy [10]. Recognition and management of TEAEs can be vital to successful treatment and improvement in health related quality-of-life. Many patients with MDD do not achieve an adequate response to pharmacotherapy even after several changes in their treatment regimen. The new SPARI class antidepressant vilazodone may offer a valuable alternative, be of great benefit in those with comorbid anxiety disorders, and have less frequent sexual side effects than those reported with other antidepressants [11].

This is the first case report documenting vilazodone-induced moderate to severe facial itching associated with missed or delayed doses. There is anecdotal evidence available online, but vilazodone-induced facial pruritus has yet to be reported to FDA Medwatch or by the manufacturer. Thus, the information presented here offers valuable evidence for health care providers to consider as part of educating and monitoring their patients taking vilazodone.

CONSENT

All authors declare that 'written informed consent' was obtained from the patient (or other approved parties) for publication of this case report.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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