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Pityriasis rosea-like drug eruption due to nortriptyline in a patient with vulvodynia

Haider K. Bangash, MD. [Researcher],

The University of Chicago Pritzker School of Medicine, Department of Medicine, Section of Dermatology, 5841 S Maryland Ave, MC 5067, Chicago, IL 60637, haider.bangash@gmail.com

Tunisia Finch, MD [Co-Chief Resident, PGY-4],

The University of Chicago Pritzker School of Medicine, Department of Medicine, Section of Dermatology, 5841 S. Maryland Ave, MC 5067, Chicago, IL 60637, Tunisia.Finch@uchospitals.edu

Vesna Petronic-Rosic, MD, MSc [Associate Professor and Clinic Director],

The University of Chicago Pritzker School of Medicine, Department of Medicine, Section of Dermatology, 5841 S Maryland Ave, MC 5067, Chicago, IL 60637, vrosic@medicine.bsd.uchicago.edu

Aisha Sethi, MD [Assistant Professor of Medicine],

Associate Residency Program Director, The University of Chicago Pritzker School of Medicine, Department of Medicine, Section of Dermatology, 5841 S. Maryland MC 5067, Chicago, IL 60637, asethi@medicine.bsd.uchicago.edu

Emily Abramsohn, MPH* [Researcher], and

The University of Chicago Pritzker School of Medicine, Department of Obstetrics and Gynecology, Program in Integrative Sexual Medicine, Chicago, IL 60637, eabramsohn@babies.bsd.uchicago.edu

Stacy Tessler Lindau, MD, MAPP* [Associate Professor]

Director, Program in Integrative Sexual Medicine, The University of Chicago Pritzker School of Medicine, Department of Obstetrics and Gynecology, Medicine-Geriatrics, and the Comprehensive, Cancer Center, Chicago, IL 60637, slindau@babies.bsd.uchicago.edu

Abstract

Background—Nortriptyline and other tricyclic anti-depressants (TCAs) are widely used in the treatment of depression. They are also used in chronic pain syndromes such as vulvodynia. We report a case of pityriasis rosea (PR)-like eruption in a young woman who was treated with oral nortriptyline for vulvodynia.

Corresponding Author: Haider K. Bangash, MD., Researcher, The University of Chicago Pritzker School of Medicine, Department of Medicine, Section of Dermatology, 5841 S Maryland Ave, MC 5067, Chicago, IL 60637, haider.bangash@gmail.com.

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Case Report—The patient presented with photosensitivity and erythematous, well-defined, oval papules and patches, with fine collarettes of scale on the dorsal hands, upper arms and trunk. She showed a complete resolution of her rash with discontinuation of nortriptyline, thereby supporting the diagnosis of a drug-induced reaction.

Comment—PR-like drug eruptions have been associated with numerous medications, including angiotensin converting enzyme inhibitors, anti-rheumatic drugs, lithium, and, more recently, biologics such as imatinib, adalimumab and etanercept. A literature review did not reveal an association between PR-like drug eruptions and tricyclic antidepressants such as nortriptyline. We report a case of PR-like drug reaction to nortriptyline for clinical interest.

Keywords

Vulvodynia; pityriasis rosea; pityriasis rosea-like drug eruption; nortriptyline; tricyclic antidepressants

Report of a case

An otherwise healthy, sexually active 20-year-old white female presented in July 2010 to the gynecologist for treatment of lifelong primary dyspareunia and pain with tampon insertion. Her past medical history included anxiety, one episode of depression, and a childhood clavicle fracture. She was taking ibuprofen as needed and had a history of combined hormonal oral contraceptive use, discontinued 8 months prior. She had no known drug allergies. Tests for HIV, syphilis, hepatitis C, gonorrhea, Chlamydia, and Trichomonas were negative.

Implementation of dietary changes and avoidance of chemical irritants failed to control the patient's symptoms. She elected a trial of nortriptyline. A 10 mg daily oral dose was started, with a plan to increase by 10 mg every 5 days to as high as 100-150 mg daily if needed and tolerable. She returned to clinic two days into her 30 mg daily dose regimen with new onset of photosensitivity on the face, upper chest and arms, despite minimal sun exposure and autumn season in the midwest U.S. (~40° latitude). The patient was advised about the possibility of a drug reaction, to use sunblock and minimize direct sun exposure.

Two weeks later, the patient returned to the gynecologist while on day 3 of a 50 mg nortriptyline dose, complaining of a pruritic rash on her chest that started on day 5 of the 40 mg daily dose. Examination revealed red, scaly, blanching papules and plaques on the chest. The patient also complained of vulvovaginal itching and was found to have yeast vaginitis, for which she was treated with local antifungal therapy. She was instructed to decrease the dose to 20 mg daily and to discontinue entirely if the rash worsened. Over the next week, the lesions on her chest resolved, but the rash spread to her hands and arms. She recalled temporary improvement during a period of a few days when she missed her nortriptyline dose. During this time, the patient also reported using topical petrolatum to soothe the affected areas. Nortriptyline was discontinued due to a suspected drug reaction. The patient was seen in the dermatology clinic 2 days later. Multiple erythematous, well defined, circular- to oval-shaped papules and patches, with fine collarettes of scale were present on the dorsal hands, upper arms and trunk. Additionally, slight erythema of the palms was noted (Figures 1, 2). No mucosal involvement was noted. The remainder of the physical exam was unremarkable.

Histopathological findings and clinical course

Lesional punch biopsies showed spongiosis, focal parakeratosis with overlying normal, basket weave-patterned stratum corneum. A superficial perivascular infiltrate of

lymphocytes was intermixed with eosinophils. The findings were supportive of a PR-like drug eruption. (Figures 3, 4)

The patient was prescribed topical triamcinolone cream (0.1%), to control her symptoms, which she did not use. The eruption showed complete remission 3 weeks after discontinuation of the offending drug (Figure 4).

Discussion

PR is an acute, self-limited, papulo-squamous eruption that tends to occur in the fall and spring, mainly in the age range of 10-35 years, with a slight predilection for females (1.5:1). Recent evidence points towards a viral etiology; HHV-6 and HHV-7, in particular, have been implicated. Histopathological findings may include localized parakeratosis, lymphocyte exocytosis, spongiosis, acanthosis and hypogranulosis in the epidermis. Additionally, a perivascular lymphocytic, or occasionally eosinophilic and monocytic, infiltrate may be present in the dermis.¹

PR-like drug eruptions have been described with the use of various medications. Brazelli et al. recently reported a case series of 3 patients who developed biopsy-proven PR-like drug eruption while on the new tyrosine kinase inhibitor, imatinib mesylate.² The tumor necrosis factor-alpha (TNF- α) inhibitors adalimumab³ and etanercept⁴ have also been associated with PR-like drug eruptions. Other medications implicated include captopril, lisinopril, bismuth, ergotamine, terbinafine, benfluorex, lithium, gold salts, D-penicillamine or levamisole, omeprazole, isotretinoin, and metronidazole.⁵⁻⁷ Vaccines associated with the appearance of a PR-like eruption include pneumococcal, hepatitis B, Bacille Calmette-Guérin (BCG), and the now defunct small pox vaccine.^{8,9}

PR-like drug eruptions differ clinically from PR of Gilbert as they have a wide variety of morphological presentations.¹ Though not specific, histopathological findings in PR-like drug eruptions may commonly include an interface dermatitis and eosinophils.¹ The timing of the appearance of the rash and its subsequent resolution when the offending agent (nortriptyline) was withdrawn supports the diagnosis of a PR-like drug eruption.

This patient was taking nortriptyline for treatment of vulvodynia, an off-label use. The International Society for Study of Vulvovaginal Disease (ISSVD), defines vulvodynia as “vulvar discomfort, most often described as burning pain without relevant visible findings or a specific, clinically identifiable, neurologic disorder.”¹⁰ Patients may present with localized or generalized forms and often report a chronic (at least 3-6 months) history of pain, discomfort, burning, rawness, irritation or a combination of these symptoms.¹¹ Clinical examination of the vulva is often unremarkable. However, there may be erythema, especially in the vulvar vestibule, and point tenderness even with very light touch.¹¹

The evidence base for treatment of vulvodynia is limited. Patients are commonly first treated with non-specific measures such as education, counseling, avoidance of irritants, dietary changes, use of lubricants during sexual activity, and discontinuation of drugs like combined hormonal contraception.¹¹ Localized treatments include topical anesthetics such as lidocaine, topical or injected steroids, topical estrogen creams, physical therapy and, in extreme cases, surgical excision of the vulvar vestibule. Patients with generalized vulvodynia have been offered oral tricyclic anti-depressants (TCAs), gabapentin, and other centrally-acting agents. The mechanism of action of these medications for treating vulvar pain is thought to be through neuropathic modification,¹² although recent evidence offers little support for their efficacy beyond placebo.¹³

General skin rash has been described as a side effect of nortriptyline. However, a thorough review of literature using Pubmed/Medline since Jan 1962 - April 2012, with “pityriasis rosea” and “nortriptyline” or “tricyclic antidepressants” as keywords did not reveal any reports of PR-like eruptions associated with the use of nortriptyline.

We present this case of nortriptyline-induced PR-like drug eruption in a young woman, with her consent, for clinical interest.

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Figure 1.
Erythematous, scaly papules on the medial right arm

Figure 2.
Erythematous, scaly papules on the dorsal hands

Figure 3.
Spongiosis, overlying basket weave-patterned stratum corneum, and focal parakeratosis.
(Hematoxylin and eosin $\times 100$)

Figure 4. Superficial perivascular infiltrate composed of lymphocytes and eosinophils. (Hematoxylin and eosin $\times 200$)