

CASE REPORT

Pityriasis rosea-like eruption associated with ondansetron use in pregnancy

Correspondence Malak Alame, School of Pharmacy, Lebanese International University, Beirut, Lebanon. Tel.: +961 170 6881; E-mail: malak.alame@liu.edu.lb

Received 19 November 2017; **Revised** 3 February 2018; **Accepted** 11 February 2018

Malak M. Alame¹, Dina J. Chamsy² and Hassan Zaraket³ 

¹School of Pharmacy, Lebanese International University, Beirut, Lebanon, ²Department of Obstetrics and Gynecology, Faculty of Medicine, American University of Beirut Medical Center, Beirut, Lebanon, and ³Department of Experimental Pathology, Immunology and Microbiology, Faculty of Medicine, American University of Beirut Medical Center, Beirut, Lebanon

Keywords adverse reaction, ondansetron, Pityriasis rosea, pregnancy

A 30-year-old pregnant female presented with a 2-week history of pityriasis rosea-like eruption. The rash started 2 days after the patient had started taking ondansetron 8 mg for alleviation of moderate-to-severe nausea and vomiting of pregnancy. Physical examination revealed erythematous papulosquamous lesions characterized by annular scaly margins and a dusky centre over the arms, chest, abdomen, lower back and legs. The rash did not involve the palms, sole or mucous membranes, and no lesions were observed on the lymph nodes. Ondansetron was discontinued. The rash ceased to spread and started to disappear within 2 weeks with full resolution noted after 1 month. Analysis of the case using the Naranjo adverse drug reaction probability scale indicated that ondansetron was the probable cause of the pityriasis rosea-like eruption. This is the first case report of pityriasis rosea related to ondansetron therapy.

Introduction

Pityriasis rosea is an acute, self-limited skin condition characterized initially by a single pink or red oval patch of scaly skin, known as the herald patch. The primary plaque is followed by the appearance of a secondary eruption consisting of numerous lesions arrayed along the Langer's lines [1, 2]. The generalized rash appears at intervals of a few days and reaches its maximum in about 2 weeks. This exanthem lasts between 2 weeks to a few months. Constitutional symptoms (e.g., malaise, nausea, anorexia, fever, joint pain, lymph node swelling and headache) may precede or accompany the skin eruption [3, 4]. The exact cause of pityriasis rosea is elusive [5]. A number of infectious and noninfectious etiologies have been proposed including viral agents, vaccines and drugs [6, 7]. Pityriasis rosea resolves spontaneously without any further complications. However, its occurrence in pregnancy should be carefully managed as it may be associated with higher rates of spontaneous abortions, premature delivery, or it may have worse fetal prognosis if eruption was seen before 20 weeks'

gestation [8]. In this report, we describe a case of pityriasis rosea-like drug reaction to ondansetron in a pregnant patient.

Ondansetron is an antiemetic medication that selectively inhibits the 5-hydroxytryptamine 3 receptor (5-HT₃ antagonist), blocking serotonin, both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone. It is widely used because of its efficacy and safety profile for management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy, and for prevention and treatment of postoperative nausea and vomiting. Severe or refractory nausea and vomiting of pregnancy (NVP) is also a common unlabelled indication for the use of ondansetron [9].

Case Report

A 30-year-old white female G1P0 presented at week 11 of pregnancy with a pruritic eruption on the upper and lower limbs, neck and trunk. The rash started 12 days prior to presentation as a single patch on the right arm and progressed

over the next 10 days to involve the trunk and lower extremities. The patient reported that the initial patch appeared 2 days after she started ondansetron 8 mg tablets for the control of moderate to severe NVP. The patient was not concurrently taking any other medications. She had neither fever nor symptoms of a viral infection within the previous weeks.

Physical examination revealed erythematous papulosquamous lesions characterized by annular scaly margins and a dusky centre over the arms, chest, abdomen, lower back and legs (Figure 1). The herald lesion was a 4-cm annular scaling plaque located on the right forearm. There were no lesions on the palms or soles, nor mucous membrane or lymph node involvement. Routine blood investigations were within normal limits (Table 1).

The clinical appearance was suggestive of pityriasis rosea. In the absence of viral prodromal symptoms, ondansetron was suspected to be the causative factor for the rash, and it was therefore discontinued. The patient was prescribed emollients and local corticosteroids to relieve pruritus.

The rash ceased to spread. Two weeks later, the skin lesions started to disappear, and the patient reported complete resolution of the rash after 1 month. The patient's oral consent was obtained for this case report.

The probability of adverse drug reaction (ADR) was assessed using the Naranjo algorithm [10]. It revealed a probable ADR for a score of +5. The adverse event appeared after ondansetron use (+2); the adverse event improved when the drug was discontinued (+1); there were no alternative drugs which could have caused this reaction (+2).

Discussion

Pityriasis rosea is a common exanthematous skin condition characterized by the appearance of slightly inflammatory, oval, papulosquamous lesions on the trunk and proximal



Figure 1

Erythematous annular scaling patch over arms, chest, abdomen, lower back and legs

Table 1

Summary of laboratory findings

CBC	Result	Reference Range
WBCs	7600	4000–11 000/cu.mm
RBCs	4.19	4.00–5.50 mil mm ⁻³
Haemoglobin	12.1	12.0–16.0 g dl ⁻¹
Haematocrit	36	37.0–46.0%
MCV	85.0	80.0–94.0 fl
MCH	29.0	27.0–31.0 pg
MCHC	34.0	30.0–35.0 g dl ⁻¹
RDW	13.0	11.6–14.6%
WBC Differential Count		
Polymorphonuclears	77	40–65%
Lymphocytes	15	25–40%
Monocytes	7	2–8%
Eosinophils	1	0–4%
Platelet count	213 000	150 000–400 000/cu.mm
Absolute neutrophil count	5852	1600–7200/cu.mm

areas of the extremities. A number of infectious and noninfectious etiologies have been proposed as causes of pityriasis rosea. Viral agents such as human herpesvirus-6 and human herpesvirus-7 infection have been reported as the possible etiologic agents [7, 11–13].

Pityriasis rosea-like eruptions have been reported as well after administration of *Bacillus Calmette-Guerin*, influenza, diphtheria, smallpox, hepatitis B and *Pneumococcus* vaccines. These eruptions have been also associated with drugs like

bismuth, captopril, barbiturates, clonidine, D-penicillamine, interferon, omeprazole, isotretinoin, metronidazole, sulfasalazine, terbinafine, lithium and imatinib mesylate. [6, 7]. Indeed, the extent of drug induced pityriasis rosea is possibly underreported.

NVP is a common condition that affects approximately 75% of pregnant women [14]. Ondansetron use in the management of NVP is in progressive increase although efficacy and safety data are still limited [15]. The recommended dose is 4 mg every 8 h for moderate NVP, and 4–8 mg every 8 h for severe NVP and hyperemesis gravidarum [16]. Known side effects of ondansetron include confusion, dizziness, constipation, dry mouth, headache, hyperventilation, tachycardia, insomnia, and rarely, hypersensitivity reactions, visual disturbances, chest pain and cardiac arrhythmias [16–18]. Although there are different cases reporting hypersensitivity reactions to oral and intravenous ondansetron, this side effect is rare and not common [19–21]. Fixed drug eruptions (FDE) were also reported in association with ondansetron use [22–24]. FDE has different manifestations from pityriasis rosea. FDE is a distinctive cutaneous drug reaction presents with a single or small number of dusky red or violaceous plaques that leave residual hyperpigmentation after resolution. These lesions typically appear within 30 min to 8 h of administration of the incriminated drug and resolve spontaneously in 7–10 days after discontinuation of the offending agent [25].

Our patient was suffering from moderate to severe NVP refractory to conservative measures. An initial treatment included dietary changes and over-the-counter remedies, such as vitamin B6 (pyridoxine) and ginger, but without any improvement. The patient was then started on antiemetic medication, metoclopramide, and was then switched to ondansetron after showing no improvement. The patient reported immediate alleviation of nausea and vomiting upon ondansetron use; however, it was stopped after she developed the rash. The patient was diagnosed with pityriasis rosea by history and physical examination. The patient's symptoms were typical regarding the presence of a herald patch, the characteristic morphology and distribution of the lesions, and the absence of symptoms other than pruritus. The patient's history and clinical presentation led to the diagnosis of ondansetron-associated pityriasis rosea. First, the onset of the lesions was associated with the initiation of the drug. Second, the patient was not taking any concurrent medication when the symptoms of pityriasis rosea developed. Third, patient's symptoms progressively improved directly after stopping ondansetron. Fourth, the lack of prodromal malaise eliminates the viral aetiology, although no laboratory testing was performed to fully exclude this possibility.

Conclusion

Although drug-induced pityriasis rosea has been reported for a variety of pharmacological agents, to our knowledge, this is the first reported case associating it with ondansetron. Using the Naranjo scale, ondansetron was considered the probable cause of the pityriasis rosea-like eruption. The clinical

diagnosis of a drug aetiology is confirmed by the recovery of the lesions upon withdrawal of the suspected agent.

Competing Interests

The authors have no competing interests to declare.

References

- 1 Blauvelt A. Chapter 42. Pityriasis Rosea. In: Fitzpatrick's Dermatology in General Medicine [Internet], 8th edn, eds Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K. New York, NY: The McGraw-Hill Companies, 2012. Available at: accessmedicine.mhmedical.com/content.aspx?aid=56033655 (last accessed 11 September 2017).
- 2 Stulberg DL, Wolfrey J. Pityriasis rosea-caring for common skin conditions. 2004; Available at: http://www.drplace.com/Pityriasis_rosea_-_Caring_For_Common_Skin_Conditions.16.18815.htm (last accessed 11 September 2017).
- 3 Drago F, Ciccarese G, Rebora A, Broccolo F, Parodi A. Pityriasis rosea: a comprehensive classification. *Dermatology* 2016; 232: 431–7.
- 4 Bianca S, Ingegnesi C, Ciancio B, Gullotta G, Randazzo L, Ettore G. Pityriasis rosea in pregnancy. *Reprod Toxicol* 2007 Nov 1; 24: 277–8.
- 5 Usatine RP, Smith MA, Chumley HS, Mayeaux EJ. Chapter 153. Pityriasis Rosea. In: The Color Atlas of Family Medicine [Internet]. 2nd ed. New York, NY: The McGraw-Hill Companies; 2013. Available from: accessmedicine.mhmedical.com/content.aspx?aid=57680273 (last accessed 11 September 2017).
- 6 Nair PA, Bhimji SS. Pityriasis, Rosea. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2017. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK448091/> (last accessed 10 September 2017).
- 7 VanRavenstein K, Edlund BJ. Diagnosis and management of pityriasis rosea. *Nurse Pract* 2017; 42 (1): 8–11.
- 8 Yang CS, Teeple M, Muglia J, Robinson-Bostom L. Inflammatory and glandular skin disease in pregnancy. *Clin Dermatol* 2016 May 1; 34: 335–43.
- 9 Ondansetron: drug information - UpToDate [Internet]. Available at: https://www.uptodate.com/contents/ondansetron-drug-information?source=search_result%26amp%3Bsearch%3Dondansetron%26amp%3BselectedTitle%3D1-132 (last accessed 12 September 2017).
- 10 Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30: 239–45.
- 11 Drago F, Ranieri E, Malaguti F, Losi E, Rebora A. Human herpesvirus 7 in pityriasis rosea. *The Lancet* 1997 May 10; 349: 1367–8.
- 12 Watanabe T, Kawamura T, Aquilino EA, Blauvelt A, Jacob SE, Orenstein JM, *et al.* Pityriasis rosea is associated with systemic active infection with both human herpesvirus-7 and human herpesvirus-6. *J Invest Dermatol* 2002 Oct 1; 119: 793–7.
- 13 Broccolo F, Drago F, Careddu AM, Foglieni C, Turbino L, Cocuzza CE, *et al.* Additional evidence that pityriasis rosea is associated

- with reactivation of human herpesvirus-6 and -7. *J Invest Dermatol* 2005; 124: 1234–40.
- 14** Kennedy D. Ondansetron and pregnancy: understanding the data. *Obstet Med Med Pregnancy* 2016; 9: 28–33.
- 15** Practice Bulletin No. 153: Nausea and Vomiting of Pregnancy. *Obstet Gynecol* 2015; 126: e12–24.
- 16** McParlin C, O'Donnell A, Robson SC, Beyer F, Moloney E, Bryant A, *et al.* Treatments for hyperemesis gravidarum and nausea and vomiting in pregnancy: a systematic review. *JAMA* 2016; 316: 1392–401.
- 17** Abramowitz A, Miller ES, Wisner KL. Treatment options for hyperemesis gravidarum. *Arch Womens Ment Health* 2017; 20: 363–72.
- 18** Treatment of hyperemesis gravidarum with the 5-HT₃ antagonist ondansetron (Zofran). | *Postgraduate Medical Journal* [Internet]. Available at: <http://pmj.bmj.com.ezproxy.aub.edu.lb/content/72/853/688.long> (last accessed 27 September 2017).
- 19** Leung J, Guyer A, Banerji A. IgE-mediated hypersensitivity to ondansetron and safe use of palonosetron. *J Allergy Clin Immunol Pract* 2013 Sep 1; 1: 526–7.
- 20** Mehra KK, Gogtay NJ, Ainchwar R, Bichile LS. Hypersensitivity to intravenous ondansetron: a case report. *J Med Case Reports* 2008 Aug 14; 2: 274.
- 21** Goyal P, Paramesh K, Puranik S, Proctor M, Sanghvi M. Delayed diagnosis of anaphylaxis secondary to ondansetron: a case report. *Eur J Anaesthesiol* 2016 Feb 1; 33: 146–7.
- 22** Bernand S, Scheidegger EP, Dummer R, Burg G. Multifocal fixed drug eruption to paracetamol, tropisetron and ondansetron induced by interleukin 2. *Dermatology* 2000; 201: 148–50.
- 23** Iglesias ME, España A, Redondo P, Quintanilla E. Fixed drug eruption secondary to ondansetron. *Dermatol Basel Switz* 1995; 191: 270–1.
- 24** Maitra A, Bhattacharyya S, Paik S, Pathak P, Tripathi SK. A rare case of fixed drug eruption due to ondansetron. *Iran J Med Sci* 2017; 42: 497–500.
- 25** Brahimi N, Routier E, Raison-Peyron N, Tronquoy A-F, Pouget-Jasson C, Amarger S, *et al.* A three-year-analysis of fixed drug eruptions in hospital settings in France. *Eur J Dermatol EJD* 2010; 20: 461–4.