

DR. KAMAL KANT SAHU (Orcid ID : 0000-0002-0382-6882)

Article type : Brief Report

Article title:

Disseminated herpes zoster following treatment with benralizumab.

Ajay Kumar Mishra¹, Kamal Kant Sahu¹, Atem James¹

Corresponding author,

Dr Ajay Kumar Mishra
Department of Internal Medicine
Saint Vincent Hospital
Worcester, Massachusetts
USA, 01608

Ajay.Mishra@stvincenthospital.com

Phone: 5087626692

Key words: Disseminated, Zoster, Immunotherapy

Conflict of interest: the authors declare that they do not have any conflict of interest

Previous submission: None

Patient consent: Taken

Presentation in conference: None

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/crj.12998

This article is protected by copyright. All rights reserved.

Affiliations

1 Department of Internal Medicine, Saint Vincent Hospital, Worcester, Massachusetts, USA.

ABSTRACT

Background:

Disseminated herpes zoster infection occurs mostly in immunocompromised hosts. There have been recent reports of disseminated zoster with chemotherapeutic regimens and newer monoclonal antibodies.

Case report:

The present case describes a 61-year-old patient presenting with disseminated herpes zoster after initiation of benralizumab, an anti-IL-5 monoclonal antibody for severe persistent asthma. His initial vesicular lesions limited to left lumbar dermatomes progressed extensively resulting in dissemination on his body. The diagnosis was confirmed with PCR and he had remarkable clinical improvement with acyclovir and supportive medical management.

Conclusion:

Clinical trials have reported an association of mepolizumab, another anti-IL-5 monoclonal antibody with herpes zoster. This report of herpes zoster following initiation of benralizumab might suggest a possibility of a class effect of anti-IL-5 monoclonal antibody.

Introduction

In herpes zoster, involvement of two or more adjacent dermatomes is defined as multi-dermatomal herpes zoster. Involvement of two non-adjacent dermatomes is called as herpes zoster multiplex. In disseminated herpes zoster, twenty or more vesicles are present beyond the primary and adjacent dermatome of involvement.¹ We report an uncommon presentation of disseminated herpes zoster within one week of taking benralizumab.

Case description

A 63-year-old male patient with past medical history of hypertension, hyperlipidemia, chronic eosinophilic pneumonia was receiving treatment with prednisolone, cyclophosphamide, and inhalers (albuterol, steroids and ipratropium) for severe persistent asthma. Due to persistence of symptoms, he was started on anti-IL-5 monoclonal antibody, benralizumab. On 5th-day post injection, he noticed localized erythema on the skin overlying his loin. In next three days, he started developing extremely painful skin lesions over the same location. On examination, we noted erythematous, vesicular lesions on left L1- L3 dermatome (Figure 1a). In the following two days, he also developed extensive vesicular lesions over his chest and upper back (Figure 1b, c). Herpes zoster PCR was positive confirming the diagnosis of herpes zoster. He was initiated on intravenous acyclovir with which he had significant clinical improvement (Figure 1d). At the time of discharge, his therapy was changed to oral valacyclovir.

Discussion

Multi-dermatomal zoster is reported mostly in elderly and immunocompromised.^{2,3} Recently there have been reports of viral infections with the use of monoclonal antibodies and chemotherapeutic agents.^{4,5} Reports of herpes zoster is common in patients receiving TNF alpha inhibitors like infliximab and adalimumab.⁴ To our best of knowledge, there are no reports of herpes zoster with the use of humanized monoclonal antibodies against IgE or related cytokines precipitating inflammation in asthma alike omalizumab or benralizumab. Currently, three anti-IL-5 monoclonal antibodies approved for asthma treatment in adults are benralizumab, mepolizumab and reslizumab. While benralizumab works against the alpha chain of IL-5 receptor, the latter two antibodies recognize and block IL-5. A Cochrane metanalysis including 13 studies and 6000 patients showed that, together these three drugs decrease the asthma exacerbation by 50%.⁶ Herpes zoster has been reported with mepolizumab as early as 2009. An initial clinical trial with 29 patients using mepolizumab reported only one patient developing shingles as compared to none in the control arm.⁷ Subsequently, there are rare cases of shingles reported in association with mepolizumab. Hence, the risk of developing herpes zoster is included in the product monograph of mepolizumab, with the recommendation of varicella vaccination prior to initiation. However, the same is not present in the drug information brochure for benralizumab and reslizumab. This report of herpes zoster following benralizumab could suggest that this may be a class effect of anti-IL-5 monoclonal antibodies. The appearance of disseminated herpes zoster in our patient following initiation of benralizumab might just be incidental, as patients with severe asthma are also prone to develop herpes zoster.⁸ But at the same time, it is hard to ignore such incidents due to fact of temporal correlation of drug usage (benralizumab in this case) and subsequent development of herpes infection.

Recently, many new immunotherapeutic drugs and antibodies are being used for various malignant and benign conditions.⁹ With such reports of drug related immune adversities and infections on rising trend, it would be apt to undertake randomised trials addressing drug induced side effect profile.^{10,11}

References.

1. Okuma, H. S., Kobayashi, Y., Makita, S., Kitahara, H., Fukuhara, S., Munakata, W., Suzuki, T., Maruyama, D., Tobinai, K. "Disseminated herpes zoster infection initially presenting with abdominal pain in patients with lymphoma undergoing conventional chemotherapy: A report of three cases". *Oncology Letters* 12.2 (2016): 809-814.
2. Gnann JW Jr, Whitley RJ. Herpes zoster. *N Engl J Med* 2002; 347:340-346.
3. Mishra A.K, Kuriakose C.K, George A.A, Chandiraseharan V.K, John A, O, Hasndak S, G. Herpes Zoster and Cryptococcal meningitis Co-infection. *International Journal of Contemporary Microbiology*. Jan-Jun. 2016 Vol 2, No 1:pg 78-81.
4. Gentile G, Foa` R. Viral infections associated with the clinical use of monoclonal antibodies. *Clin Microbiol Infect* 2011; 17: 1769–1775.
5. Sahu KK, Varma SC. Herpes zoster complicating bortezomib therapy. *Indian J Med Res*. 2015 Feb;141(2):247-8.
6. Farne HA, Wilson A, Powell C, Bax L, Milan SJ. Anti-IL5 therapies for asthma. *Cochrane Database Syst Rev*. 2017 Sep 21;9:CD010834. PMID: 28933516.
7. Halder P, Brightling CE, Hargadon B, Gupta S, Monteiro W, Sousa A, Marshall RP, Bradding P, Green RH, Wardlaw AJ, Pavord ID. Mepolizumab and exacerbations of refractory eosinophilic asthma. *N Engl J Med*. 2009 Mar 5;360(10):973-84.
8. Kwon HJ, Bang DW, Kim EN, Wi CI, Yawn BP, Wollan PC, et al. Asthma as a risk factor for zoster in adults: a population-based case-control study. *J Allergy Clin Immunol* 2016; 137:1406–1412.
9. Sahu KK, Varma SC. Lenalidomide in Nonmalignant Disorders: A New Ray of Hope for Refractory Sarcoidosis. *Chest*. 2015 Dec;148(6): e188-e189.
10. Sahu KK, Badhala P, Malhotra P, Aggarwal AN. A rare case of rituximab induced interstitial lung disease. *Lung India*. 2016 Jul-Aug;33(4):472-3.
11. Sahu KK, Mishra A, Chastain I. Novel anticancers and dermatological adversities: old rivals but new challenges. *BMJ Case Rep*. 2018 Dec 14;11(1)

Figure: 1

1a: Clusters of clear vesicular lesions in the back ground of erythematous skin rash extending from L1 to L3 dermatome

1b, 1c: Widespread vesicular lesions over the back and chest

1d: Post healing necrosis involving the affected dermatome

Acknowledgement: Dr. Sundar Vadivel, Dr. Srinivas Nadadur, Dr. Anu Anna George

