

Four Episodes of Classic Scabies Associated with Ocrelizumab Therapy

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Abstract

Introduction: Scabies is a skin infection caused by the *Sarcoptes scabiei* (variety hominis) mite. The classic variant produces pruritic lesions with intense, persistent itching. Immunosuppressed patients develop a more aggressive form of the infection known as crusted (Norwegian) scabies.

Clinical cases: We present four episodes of ocrelizumab-treated multiple sclerosis patients with B-cell lymphopenia who developed the classic variant of scabies.

Conclusion: To our knowledge, no cases have been published in the literature, which relate ocrelizumab with the development of scabies. The maintenance of cellular immune response protects of development of crusted scabies.

Keywords: B-cells • Lymphopenia • Multiple sclerosis • Ocrelizumab • Scabies

Abbreviations: CD: Cluster of Differentiation • EDSS: Expanded Disability Status Scale • HIV: Human Immunodeficiency Virus • IFN β : Interferon Beta • MS: Multiple Sclerosis • PPMS: Primary Progressive Multiple Sclerosis • RRMS: Relapsing-Remitting Multiple Sclerosis • Th1: Type 1 Helper T Cells • Th2: Type 2 Helper T Cells

Introduction

Ocrelizumab is a licensed drug for the treatment of relapsing-remitting (RRMS) and primary-progressive multiple sclerosis (PPMS). It is a monoclonal antibody against the CD20 antigen that produces a selective depletion of B cells [1], increasing the risk of opportunistic infections.

Scabies is a skin infection caused by the *Sarcoptes scabiei* (var. hominis) mite. It's principally transmitted by close contact between people. The classic variant produces pruritic lesions with intense itching of the skin especially at night. In immunosuppressed patients, a more aggressive form of the infection known as crusted or Norwegian scabies commonly develops with scale-crust psoriasiform lesions. The diagnosis of scabies is confirmed through visualization of the mite, its eggs or faeces [2].

We describe 4 episodes of classic scabies in patients with MS and B-cell lymphopenia under ocrelizumab treatment. To our knowledge, no cases have been published in the literature, which relate ocrelizumab with the development of scabies.

Clinical Case Series

A 33 year-old female, smoker, with RRMS since 2007. Patient presented suboptimal response to IFN-beta-1b (2008-2013) and fingolimod (2013-September 2016) and started ocrelizumab in December 2016 with an

Expanded Disability Status Scale (EDSS) 2.0 at those moment. Received 2 cycles of 300 mg of ocrelizumab in December 2016. Confirmed diagnosis of classic scabies was performed in January 2017. Blood test (January 2017) showed normal total lymphocyte count but subset analysis showed B-cell lymphopenia. Patient received a new cycle of 600 mg of ocrelizumab in June 2017. She was diagnosed of confirmed classic scabies 1 week after ocrelizumab treatment. The blood test result in June 2017 showed B-cell lymphopenia (Table 1).

A 34 year-old male with untreated psoriasis diagnosed of RRMS since 2014. Patient presented suboptimal response to IFN-beta-1b (2014-2016) and started ocrelizumab in February 2017 with an EDSS 0. Received 300 mg of ocrelizumab, but treatment was suspended due to hepatotoxicity. Patient initiated with dimethyl fumarate in October 2017 with an EDSS 0. He was diagnosed of confirmed classic scabies in November 2018. The blood test in November 2018 showed normal total lymphocyte count, but B-cell lymphopenia.

A 47 year-old male with PPMS since October 2018. Patient started ocrelizumab treatment in December 2018 with an EDSS 3.0. He received 2 cycles of 300mg of ocrelizumab in December 2018 and January 2019. Confirmed diagnosis of classic scabies was performed in February 2019. The blood test showed normal total lymphocyte count, but B-cell lymphopenia.

All cases were diagnosed by dermatological examination, presenting complete resolution after treatment with permethrin, without suspension of ocrelizumab. The diagnosis of classic scabies was confirmed by dermoscopic examination, with mite burrows and mites observed in the dermoscopic image of the 'delta wing jet' sign. In the last case, mites and eggs were identified through optical microscopy (Figures 1-3).

Prior to each dose of ocrelizumab, 100mg of intravenous methylprednisolone were administered. Except for the immunomodulatory treatment, there were no other causes of immunosuppression. The medical department of Roche Farma S.A. was informed of all 4 episodes for drug safety monitoring. In our centre other 40 patients were under ocrelizumab treatment and they did not develop scabies.

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Received 04 May, 2019; **Accepted** 11 May, 2020; **Published** 18 May, 2020

Table 1. Clinical characteristics.

Patient number	Sex/Age	Diagnosis Time of Diagnosis	EDSS	Treatments	Scabies diagnosis	Lymphocytes count* (cells/ μ l)
1	F/33	RRMS/2007	2.0	IFN-beta-1b (2008-2013)	January 2017	B lymphocytes: 38 Normal (90-660)
				FYT (2013-September 2016). OCZ December 2016-Current date (2 doses)		
1	F/33	RRMS/2007	2.0	IFN-beta-1b (2008-2013)	June 2017	B lymphocytes: 52 Normal (90-660)
				FYT (2013-September 2016). OCZ December 2016-Current date (3 doses)		
2	M/34	RRMS/2014	0.0	IFN-beta-1b (2014-2016)	November 2018	B lymphocytes: 88 Normal (90-660)
				OCZ February 2017 (1 dose)		
3	M/47	PPMS/2018	3.0	DMF October 2017-Current date	February 2019	B lymphocytes: 38 Normal (90-660)
				OCZ December 2017-Current date (2 doses)		



Figure 1. Eczematous lesions and skin abrasions.



Figure 2. Mite burrow.



Figure 3. Dermoscopic image in which the mite burrow can be seen and the mite at one end, resulting in the pathognomonic 'delta wing jet' sign of scabies.

The main risk factor for scabies is close contact with infected persons, which is facilitated by overcrowded living conditions, sexual relations, towel/clothes sharing, etc. It can also occur in the context of a hospital outbreak [3]. However, after an epidemiological study of contacts, which included care staff, and of sites where the patients might have coincided (outpatient care facilities, MR unit, external consulting...), direct infection by contact was discarded. Scabies can produce epidemic outbreaks; however, we also discarded community outbreaks of scabies in our zone at the moment of the infection of our patients.

Immunosuppression is another risk factor for the development of scabies. As a result of the Th1/Th2 imbalance in patients with scabies, it manifests in the form of classic or aggressive scabies: the Th2 (humoral) response failure is associated to the classic variant, and the Th1 (cell) response failure to the aggressive variant [4]. Despite the immunosuppression, these patients did not develop crusted scabies. One possible reason for this is that ocrelizumab maintains the Th1 response and protecting the development of the crusted variant of scabies. Furthermore, in HIV-infected patients, crusted scabies has also been related to the low CD4 count (normal in our cases).

Scabies has a tendency to recur, and its treatment does not prevent its relapse [5]. Our first patient presented 2 episodes of scabies in a 6-month period, with both occurring after treatment with ocrelizumab. Though this could be a reinfection, the short period of time that elapsed between the episodes

Discussion

We present 4 episodes of confirmed classic scabies in MS patients who received treatment with ocrelizumab. B cells are responsible for the attack to extracellular parasites. However, in our knowledge, the depletion of B cells by ocrelizumab is not associated with opportunistic infections.

does not allow us to discard a recurrence due to relapse. The second patient developed scabies after more than one year without taking ocrelizumab and when under treatment with dimethyl fumarate. Although we cannot discard the possibility of the dimethyl fumarate contributing to the development of the infection, we believe that, as the biological effect of ocrelizumab lasts a long time and as our patient still presented its effect (B-cell lymphopenia), ocrelizumab contributed to the development of the infection.

Conclusion

In conclusion, we present 4 episodes of classic scabies in MS patients associated to ocrelizumab. Other than ocrelizumab-induced B-cell lymphopenia, no risk factor for scabies was found in our patients. The maintenance of cellular immune response protects the development of crusted scabies. Ocrelizumab-treated patients who present with pruritic skin lesions, after discarding the possibility of infusion reactions, should be tested for scabies - even when a considerable period of time has elapsed since the suspension of the ocrelizumab treatment if B-cell lymphopenia persists. These patients should be carefully monitored, as there is a possibility of scabies relapse. Further studies are required to improve the treatment and follow-up of scabies in patients treated with ocrelizumab.

Declaration of Interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

We acknowledge to Malcolm for writing assistance.

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How to cite this article: José Vicente Hervás García, Anna Gil-Sánchez, González-Mingot C, Yhovany Gallego, et al. "Four Episodes of Classic Scabies Associated with Ocrelizumab Therapy." *J Neurol Disord* 8 (2020): 420 doi: 10.37421/jnd.2020.8.420