CASE REPORT

Atypical molluscum contagiosum on multiple sclerosis patients treated with fingolimod: A case report

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Abstract

Molluscum contagiosum (MC) is a skin infection caused by a virus of the DNA poxvirus family that has already been reported by Fingolimod. We report two cases. MC can resist standard therapy and discontinuation of the fingolimod may be the only way to treat it.

KEYWORDS

fingolimod, molluscum contagiosum, multiple sclerosis

1 **INTRODUCTION**

Fingolimod as a sphingosine-1 phosphatase modulator causes lymphocytes to get trapped in the lymph nodes, thus preventing the autoreactive lymphocytes from invading the brain.¹ Fingolimod was the first oral drug approved for the treatment of relapsing-remitting multiple sclerosis (MS).² Clinical and post-marketing studies have suggested an increased risk of infection with the herpes family viruses due to this immunosuppressive drug.³ Molluscum contagiosum (MC) is a skin infection caused by a virus of the DNA poxvirus family. It has already been reported by Fingolimod.⁴ Due to the rarity of MC reported with fingolimod, we have given an account of two cases, among our patients, with this skin infection.

2 CASE REPORT

2.1 Case 1

A 26-year-old woman with MS has been on treatment with fingolimod for about a year. Her MS began 4 years ago, and she was treated with interferonβ1a (INF b-1a) subcutaneously for the first 3 years. Due to a new relapse, her treatment has been escalated to fingolimod. Her disease has been stable during treatment with fingolimod. She came to the clinic because of skin lesions on the anterior and middle part of her thigh. A skin examination revealed more than 20 waxy 3-5 mm umbilicated flesh-colored papular lesions without itching and swelling (Figure 1A). In the laboratory test, white blood cells (WBC) = $3800 \text{ cells}/\mu$ l

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with World Health Organization (WHO) grade II lymphopenia (700 cells/ μ l) were reported. The human immunodeficiency virus (HIV) test was negative. The remainder of the laboratory test was normal. Skin biopsy was done, and



FIGURE 1 More than 20 waxy 3–5 mm umbilicated fleshcolored papular lesions on the anterior and middle part of the thigh and posterior of the foreleg 153×213 mm (96 × 96 DPI)



FIGURE 2 Skin lesions reveal a vertucous proliferation of keratinocytes containing molluscum bodies. H&E stain 165 ×94 mm (96 × 96 DPI)

pathology was in favor of MC (Figure 2A). Cryotherapy was performed three times within 3 months without any obvious efficacy, but the lesions did not increase in size and number. Fingolimod therapy was discontinued, and glatiramer acetate was prescribed after 5 months the lesion had completely subsided.

2.2 | Case 2

A 24-year-old woman was first diagnosed with MS 6 years ago. During the first 2 years of her illness, she was prescribed INF b-1a IM per week in her treatment. Her medication was changed to fingolimod 4 years ago due to new attacks and her condition stabilized on treatment with fingolimod. She was referred to our neurology clinic for bilateral medial thighs skin lesions. Examination of the skin lesions showed a lot of waxy umbilicated papular lesions, 3-4mm in diameter without itching and swelling on the bilateral medial thighs (Figure 1B). Tests were carried out and WBC = $3900 \text{ cells}/\mu l$ with grade-II WHO lymphopenia (800 cells/µl) was reported. The HIV test was negative. The remainder of the test was normal. Pathology of the skin confirmed MC (Figure 2B). Cryotherapy was performed two times, a month apart without any obvious efficacy and the lesions progressed continuously. Fingolimod therapy was discontinued, and rituximab was initiated after 6 months the lesions had completely subsided.

3 | DISCUSSION

Molluscum contagiosum is a common viral infection of the keratinocytes, which is self-limited in cellular immunocompetent immunity. MC virus belongs to the Poxvirus family and could infect the genitalia, inner surface of the thigh, and lower abdomen by direct or sexual contact in adults. With a reduction in the number of and in the function of T-lymphocytes in conditions like HIV infection, cancer, and immunosuppressive therapy, MC might present atypical symptoms with worsening signs and be difficult to treat.⁶ A reduction in CD4+ T-cells <200 is associated with an increased risk of MC⁷ and based on the mechanism of action, fingolimod brings about similar cellular immunity immunosuppressive changes. Fingolimod reduces circulating lymphocytes by trapping lymphocytes in the lymph nodes.¹ Although the number of effector memory T cells remains unchanged, their proliferation changes when faced with viral antigens like varicella zoster.^{8,9} Finally, fingolimod will show extensive immunosuppressive effects. Atypical MC, for example, in HIV patients has not responded to one

TABLE 1 Case reports of MC in MS patients on treatment with fingolimod

Age (years)			
Sex	Source	Location of MC	Treatment
18 M	Bahle et al. ⁴	The Genito-anal region, the inner thighs, and on the lower abdomen	Removed with a sharp curette, disinfectant cream fingolimod continues
41 F	Wetzel et al. ¹¹	Head, trunk, and groin	Liquid nitrogen, curettage, and topical imiquimod 5% cream Fingolimod discontinued
29 M	Bennani et al ¹²	Everywhere on the body such at the trunk, neck, back, 4 limbs, and at the genital area	Removed mechanically potassium hydroxide solution 5%
39 F	Monnier et al. ⁵	Anterior and posterior part of genitalia	Laser CO ₂ fingolimod discontinued

ing fingolimod treatment were reported (Table 1). A case series reported 8 MC patients among 1003 MS patients on treatment with fingolimod. This case series defined that although the incidence of MC was not so high during treatment with fingolimod, its treatment could be difficult and many of these patients might be candidates for switching of treatments¹⁰ We pursue two important goals in defining these two cases of MC in MS patients. Firstly, neurologists who are involved in treating MS patients should consider this rare complication caused by fingolimod and secondly, but more important than the first point is that MC can resist standard therapy and discontinuation of the fingolimod may be the only way to treat the disease in some MS patients.

treatment modality. So far, few case reports of MC dur-

4 | CONCLUSION

Molluscum contagiosum has been reported in MS on treatment with fingolimod. Although the probability is not high, it can be annoying for the patient. However, molluscum during treatment with fingolimod may not respond to its usual treatments and it is necessary to change the medication of fingolimod.

AUTHOR CONTRIBUTIONS

H.C. contributed to the conceptualization, roles/writing, supervision, and investigation. S.M.B. served as the corresponding author and contributed to the methodology, project administration, writing—original draft, writing—review and editing, and data curation. M.G. contributed to the validation, formal analysis, and resources.

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ETHICAL APPROVAL

The Regional Ethics and Hospital Management Committee of Mazandaran University School of Medicine approved the study (IR. MAZUMS.REC.1399.8188).

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

- Chun J, Hartung H-P. Mechanism of action of oral fingolimod (FTY720) in multiple sclerosis. *Clin Neuropharmacol.* 2010;33(2):91-101.
- Chun J, Brinkmann VA. Mechanistically novel first oral therapy for multiple sclerosis: the development of fingolimod (FTY720, Gilenya). *Discov Med.* 2011;12(64):213.
- Pfender N, Jelcic I, Linnebank M, Schwarz U, Martin R. Reactivation of herpesvirus under fingolimod: a case of severe herpes simplex encephalitis. *Neurology*. 2015;84:2377-2378.
- Behle V, Wobser M, Goebeler M, Stoevesandt J. Extensive molluscum contagiosum virus infection in a young adult receiving fingolimod. *Mult Scler*. 2016;22(7):969-971.
- Monnier J, Collet-Villette A-M, Olmi X, et al. Prise en charge par laser de molluscum contagiosum génitaux profus apparus sous fingolimod. *Ann Dermatol Venereol*. 2017;144(12):S340.
- 6. Chen X, Anstey AV, Bugert JJ. Molluscum contagiosum virus infection. *Lancet Infect Dis.* 2013;13:877-888.
- Czelusta A, Yen-Moore A, Van der Straten M, Carrasco D, Tyring SK. An overview of sexually transmitted diseases. Part III. Sexually transmitted diseases in HIV-infected patients. J Am Acad Dermatol. 2000;43(3):409-436.

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- Grebenciucova E, Pruitt A. Infections in patients receiving multiple sclerosis disease-modifying therapies. *Curr Neurol Neurosci Rep.* 2017;17(11):88.
- 9. Ricklin ME, Lorscheider J, Waschbisch A, et al. T-cell response against varicella-zoster virus in fingolimod-treated MS patients. *Neurology*. 2013;81(2):174-181.
- 10. Schneider S, Do D, Fuller R, Berger JR. Molluscum contagiosum in the setting of fingolimod: the experience at one institution. *Mult Scler Relat Disord*. 2022;58:103419.
- 11. Wetzel M, Tidwell WJ, Callen JP. Disseminated molluscum contagiosum associated with immunomodulatory therapy. *JAAD Case Rep.* 2020;6:708-709.
- 12. Bennani M, Benkirane S, Ziani J, et al. Disseminated molluscum contagiosum in a patient on fingolimod for multiple sclerosis. *Biomed J Sci Tech Res.* 2020;27(3):20720-20722.

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