Int. J Med. Pharm. Res. (P-ISSN: 2958-3675 | E-ISSN: 2958-3683)
Available on: https://ijmpr.in/

International Journal
of Medical and Pharmaceutical Research

CASE REPORT **OPEN ACCESS**

Favipiravir-Induced Fluorescence of Nails and Hair in a Covid-19 Patient

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Received: 10-09-2024
Accepted: 06-11-2024
Available online: 11-11-2024

A B S T R A C T

Various dermatologic manifestations of COVID-19 and common side effects of drugs used in the treatment of COVID-19 have been identified previously. We report an observation of favipiravir-induced fluorescence of nails and hair in a 23-year-old woman who was treated for COVID-19. Further investigation is warranted to understand the exact pathophysiology behind the fluorescence and its clinical significance in patients treated with favipiravir.

Keywords: Favipiravir, COVID-19, nail discolouration, fluorescence.

INTRODUCTION

Favipiravir is a guanine analogue and antiviral drug approved in the treatment of COVID-19, influenza and Ebola virus infections [1, 2]. Favipiravir (6-fluoro-3-hydroxypyrazine-2-carboxamide) acts by selective inhibition of viral RNA-dependent RNA polymerase [3]. It gets phosphorylated inside the cells, leading on to chain termination, thereby halting the viral replication and causing lethal mutagenesis [4]. The recommended dose of favipiravir in COVID-19 is 1800mg twice daily and 800mg twice daily for the next six days.

COVID-19 commonly presents as a respiratory infection. However, various dermatologic manifestations of COVID-19 have been reported widely, including Mee's lines, Beau's line, splinter hemorrhages, leukonychia, red half-moon sign, and transverse orange nail lesions [5]. Here, we report a case of yellowish discolouration of nails in a COVID-19 patient who was treated with Favipiravir. Examination using Wood's lamp showed yellow-green fluorescence. Favipiravir has few well-described side effects, including pruritus, myalgia, skin rash, dyspepsia, diarrhea, tachycardia, neutropenia, hyperuricemia, elevation of liver enzymes and bilirubin and teratogenicity [6, 7]. Favipiravir-induced nail fluorescence is being demonstrated in our case report, which could be added to the side effect profile of the drug.

Case Report

A 23-year-old woman with no prior illness was diagnosed with COVID-19 category B during the initial wave of the COVID-19 pandemic. Her SARS-CoV-2 rapid antigen and RT-PCR were positive. She was treated with full dose of favipiravir for five days along with other supportive care. She became clinically better and her SARS-CoV-2 rapid antigen was negative at the end of one week of treatment. Two months later she noticed yellowish discoloration of her finger and toe nails. No history of exposure to other medications or chemicals that could cause the discoloration was noted.

Dermatologic and systemic examinations were normal except for yellowish discoloration of all finger and toe nails. Wood's lamp examination in a dark room showed yellow-green fluorescence of three-fourths of her fingernails and one-half of her toenails, predominantly in the lunula and nail plate portion near the proximal nail fold. Yellow-green fluorescence was also seen on the hair.

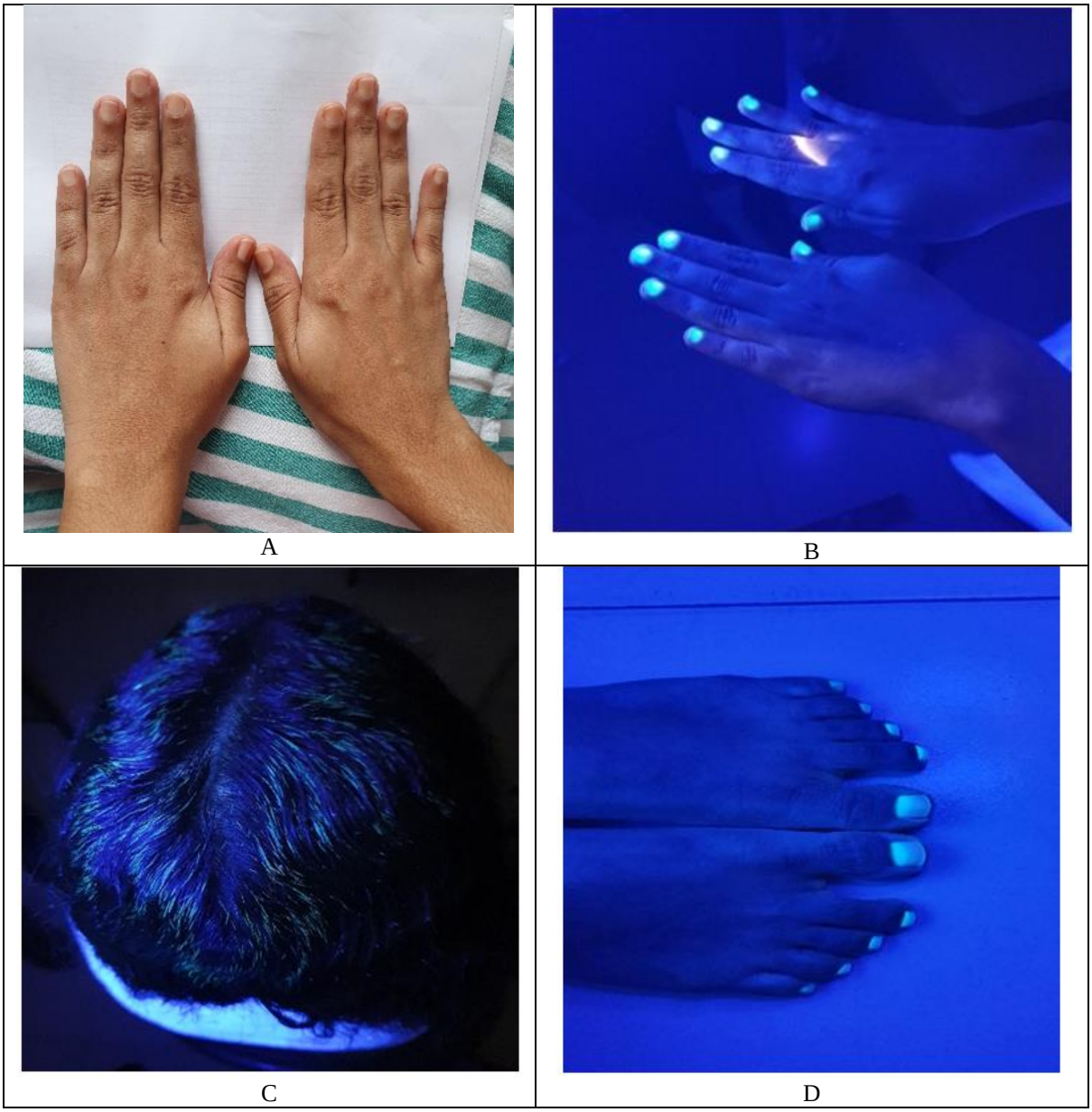

Figure 1: A) Yellowish discoloration of all fingernails; B) Wood's lamp examination showing yellow-green fluorescence of three-fourths of the nail plate beginning from the proximal nail fold; C) Yellow-green fluorescence of hair; D) Yellow-green fluorescence of one-half of the nail plate involving lunula

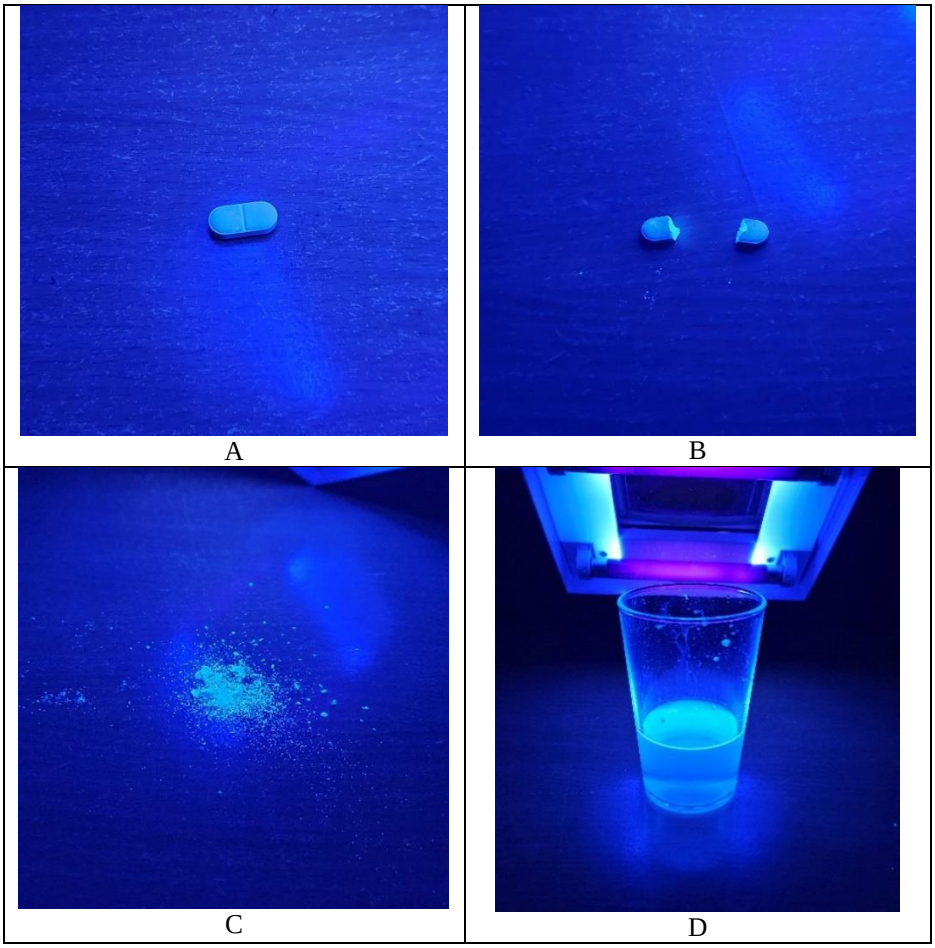

Figure 2: Demonstration of favipiravir fluorescence in-vitro: A) Whole tablet; B) Tablet broken into two halves; C) Tablet crushed into powder; D) Tablet dissolved in water

DISCUSSION

Nails and hairare structures that can indicate long-term exposure to a substance and can be used in the detection of abused drugs and poisoning [8, 9]. The nail plate extends distally over the nail bed and consists of layers of keratinized cells produced by the nail matrix. The average rate of elongation of fingernails is about 3.47mm/month and of toenails is about 1.62mm/month, whereas the average growth rate of hair is about 0.5 inches/month [10]. The growth rate may be influenced by age, gender, season, diseases, and drugs.

Drug-induced nail and hair fluorescence have previously been reported for drugs like quinacrine, hydroxychloroquine, tetracycline, tenofovir, and ribavirin, usually in a dose-dependent manner [11]. These drugs are known to also accumulate in the conjunctiva, teeth, and implants of patients using them.

Wood's lamp is a high-pressure mercury arc lamp that consists of a compound filter made of barium silicate and 9% nickel oxide. It emits ultraviolet light in the 320–400 nm spectrum with a peak at 365 nm [5]. When examining with a Wood's lamp in a dark room, fluorophore compounds absorb light energy and re-emit at a different wavelength which is observed as fluorescence [12]. Fluorescence occurs due to substances like elastin, collagen and melanin precursors found naturally in the skin or external factors like drug metabolites or excipients which accumulate in the skin [4].

The incidence of favipiravir-induced nail fluorescence was previously reported to be 81.9% [13]. However, the exact mechanism of fluorescence caused by the use of favipiravir is unknown. In one study, it was attributed to excipients such as titanium dioxide and yellow ferric oxide which are added to the favipiravir tablet for photo-stabilization of the formulation [14]. Pure favipiravir drug has also been shown to exhibit blue fluorescence under microscopic fluorescence examination [15]. However, fluorescence was not present in the nails of patients who were on other drugs that contained titanium dioxide and yellow ferric oxide as additives. Based on these reports, we postulate that favipiravir-induced nail fluorescence is caused by the drug itself rather than the additives. However, the doses of these once-per-day tablets could not be compared with the high dose of favipiravir.

In a study by Güder H *et al.*, nail fluorescence was observed in all patients who received the total dose of favipiravir. The density of the fluorescence was found to decrease in the second month and fully disappear in the third month. It was also noted that the patients who did not receive the loading dose of favipiravir showed no fluorescence [11]. These findings indicate that favipiravir-induced fluorescence is dose-dependent and decreases over time.

Apart from nail and hair fluorescence, bluish discoloration of cornea and whitish fluorescence of sclera and teeth have also been reported [2, 16].

CONCLUSION

This case report describes a novel potential side effect of favipiravir and underscores the importance of clinicians being aware of unusual drug-induced phenomena, prompting further research into the underlying mechanisms and long-term implications.

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