Jpn. J. Infect. Dis., 54, 2001

Laboratory and Epidemiology Communications

Skin Eruption 8 Days after a Single Dose of Efavirenz-Containing Combination Therapy

Hirohisa Yazaki, Yoshimi Kikuchi and Shinichi Oka*

AIDS Clinical Center, International Medical Center of Japan, Toyama 1-21-1, Shinjuku-ku, Tokyo 162-8655

Communicated by Hiroshi Yoshikura

(Accepted January 15, 2002)

A 24-year-old woman visited our clinic on 14 August 2001 because of a generalized skin eruption and fever of 37.1°C. The eruption had appeared on the preceding night on her lower extremities and had extended to her whole body within 1 day. A photograph of her forearms is shown in Fig. 1. Examination showed erythematous discrete papules surrounded by white skin, causing severe itching. These features resembled those of eruptions induced by efavirenz (EFV). Written informed consent was obtained from this subject to report this unusual eruption and to include her photograph.

The husband, a 31-year-old hemophilia A patient, was infected with HIV-1 following infusion of a contaminated blood product before 1985. He had been treated with 40 mg bid stavudine (d4T), 150 mg bid lamivudine (3TC), and 600 mg q.d. EFV since February 2000. The couple got married in December 2000. At the time of presentation, a blood sample taken from the husband showed a CD4 count of >400 cells/μL and viral load <50 copies/mL. After sexual intercourse without using a condom on the night of 4 August 2001, the wife decided to take 40 mg d4T, 150 mg 3TC, and 600 mg EFV only once the next morning as postexposure prophylaxis. She reported not taking any other or repeat dose of the above prophylaxis thereafter. She had been well until the eruption appeared on 13 August and had never previously taken anti-HIV-1 drugs. An antihistamine was used for 2 days for the treatment of eruptions, which resulted in a gradual disappearance of eruptions within 1 week without scarring. No other clinical symptoms, including fever, were noted during the clinical course. Blood tests on 14 August revealed no abnormalities, including a WBC of 4,200/μL with normal differential count, hemoglobin 12.5 g/dL, platelets 18.6/μL, aspartate aminotransferase 13 U/L, lactate dehydrogenase 133 U/L, and C-reactive protein 0.20 mg/dL. Immunoglobulin G (IgG) antibodies to measles, rubella, and cytomegalovirus were already positive, and IgM antibodies to these viruses were negative at presentation. All of the anti-HIV-1 antibody tests performed on 14 August, 5 October, and 8 November were negative. HIV-1 RNA in plasma was also negative on 8 November. The patient had no histories of food or drug allergies and denied eating exceptional food or taking any medications for at least 1 week before the eruption.

The skin eruption in our patient was very similar to the skin rash occasionally observed in patients treated with EFV, which has a very unique appearance and can easily be distinguished from other eruptions caused by drugs commonly used with EFV. The EFV-induced eruption often appears around 10 days after commencement of therapy and sometimes improves spontaneously without medication within 1 week, even when the same therapy is continued at the same dose. The skin eruptions seen in our patient also appeared 8 days after taking d4T, 3TC, and EFV and improved within 1 week. Thus, the clinical presentation and course were very similar. However, the striking difference between this case and other HIV-1 cases of EFV-induced eruption was that our patient took the drugs only once, while a full course of treatment is usually taken by HIV-1 patients. Eruption induced by EFV is usually considered to be an allergic reaction to the drug, in which hypersensitivity is evoked during therapy. However, the usual resolution of eruptions without discontinuation of the same therapeutic dose argues against drug-induced hypersensitivity. For example, trimethoprim/sulfamethoxazole (T/S)-induced hypersensitivity is successfully desensitized by restarting a very low dose of T/S (1). In some cases, most if not all of the causative drugs or their metabolites can have toxic effects, which could manifest as skin eruptions. However, in our case, drugs or their metabolites had already been

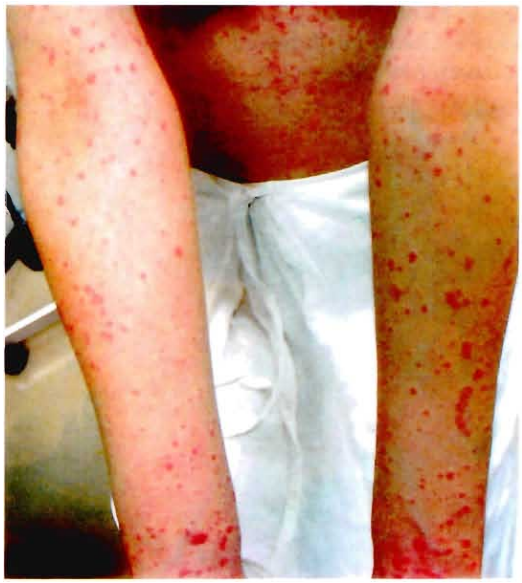

Fig. 1. A photograph of the forearms of the affected patient taken on 14 August 2001. Eruptions were itchy, erythematous discrete papules surrounded by white skin, and measured 1-5 mm in diameter. The appearance of the skin lesion and the clinical course was quite similar to that of EFV-induced lesions.

*Corresponding author: Tel/Fax: +81-3-5273-5193, E-mail: oka@imcj.hosp.go.jp

excreted at the onset. We first thought that the eruption was a clinical manifestation of acute viral infection. However, we were able to exclude various acute viral infections often associated with generalized erythematous papules, including HIV-1 infection, by clinical, biochemical, and serological examinations, although very rare viral infections could not be ruled out. If the skin eruption in our patient was actually caused by EFV, the mechanism of EFV-induced eruption must be considered to be more heterogeneous than previously thought.

EFV is likely to be used widely in the future as a post-exposure prophylaxis, including after needle injury, as it has proved itself useful in the expanded therapeutic regimen (2). While its continued use is impossible for those who develop severe complications of the central nervous system after the first few doses (3), a possible occurrence of skin eruptions should also be monitored from the start of therapy, and such individuals should be followed for at least 2 weeks after discontinuation of therapy.

REFERENCES

1. Yoshizawa, S., Yasuoka, A., Kikuchi, Y., Honda, M., Gatanaga, H., Tachikawa, N., Hirabayashi, Y. and Oka, S. (2000): A 5-day course of oral desensitization to trimethoprim/sulfamethoxazole (T/S) in patients with human immunodeficiency virus type-1 infection who were previously intolerant to T/S. Ann. Allergy Asthma Immunol., 85, 241-244.
2. Centers for Disease Control and Prevention (2001): Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. Morbid. Mortal. Wkly. Rep., 50, RR-11.
3. Marzolini, C., Telenti, A., Decosterd, L.A., Greub, G., Biollaz, J. and Buclin, T. (2001): Efavirenz plasma levels can predict treatment failure and central nervous system side effects in HIV-1-infected patients. AIDS, 15, 71-75.