

LETTERS TO THE EDITOR

Immediate allergy, drug-induced eruption, by entecavir

Editor

Case

A 30-year-old man had suffered hepatitis B virus infections. His doctor treated him with Entecavir 0.5 mg/day, orally, under hospitalization. Two days after this treatment, he had a hoarse voice and erythema with itching on his buttocks (Fig. 1). We treated him as drug allergy with steroid ointment and anti-histamine tablets. His doctor discontinued Entecavir on the 4th day and then started to treat him with Lamivudine 100 mg/day for 3 weeks,



Figure 1 Clinical findings of skin eruption. It shows erythema on the buttocks.

orally, on the 5th day. His laboratory results showed that the number of white blood cells increased on the second day of treatment, and then incidences of eosinophils increased from the 5th day (Fig. 2). Glutamate oxaloacetate transaminase (GOT) was 2058 (IU/l/37 °C) and glutamic pyruvic transaminase (GPT) was 3219 (IU/l/37 °C) on the day of his hospitalization, and after treatment, these levels decreased day by day (Table 1). The results of other laboratory examinations were as follows: HBs-Ag, 14.5 (negative); HBe-Ag, 27.1 (1>); HBs-Ab, 3+ (negative); HBe-Ab, 0 (1>); AFP, 6.7 ng/mL (0–16.5); HBV DNA (polymerase chain reaction), 7.7 log copy/mL < (2.6>); HBc-Ab (CLIA) S/CO, 2.91 (1>); (), normal range. We performed scratch tests and patch tests to investigate the drug allergy of this patient. The test materials were Entecavir 50% petrolatum and petrolatum as negative

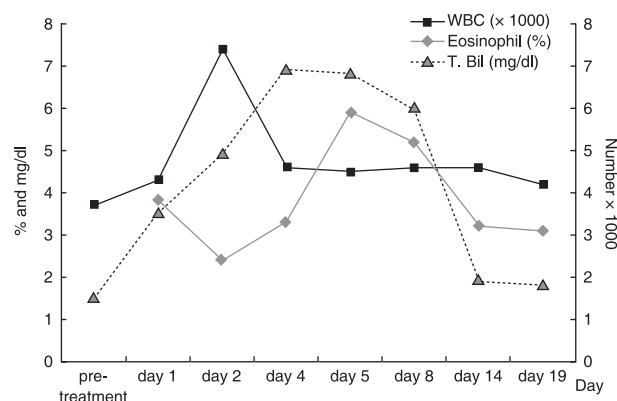


Figure 2 The results of laboratory findings (white blood cells, eosinophils and total bilirubin).

Table 1 The results of laboratory findings

Day	GOT (IU/l/37 °C)	GPT (IU/l/37 °C)	γ -GTP (IU/l/37 °C)	ALP (IU/l/37 °C)	LDH (IU/l/37 °C)
Pretreatment	2058	3219	98	312	1977
day 1	1063	2665	197	442	705
day 2	931	2447	223	531	626
day 4	921	1891	227	490	562
day 5	741	1560	225	453	397
day 8	653	1334	273	424	322
day 14	68	292	176	295	184
day 19	62	154	137	249	190

ALP, Alkaline phosphatase; LDH, lactate dehydrogenase.

control. The results of scratch tests using Entecavir showed positive reactions. The results of one volunteer with the same agents were all negative. His condition had improved day by day.

Discussion

About 400 million people suffer from chronic hepatitis B in the world. Previously, there were some treatments (interferon-alpha 2b or 2a, Lamivudine, Adefovir dipivoxil) given for this disease. Nucleoside analogs for hepatitis B are Lamivudine, Adefovir and Entecavir. These agents are well tolerated, orally administered, and have low adverse and antiviral effects over interferon.¹ Adefovir and Entecavir has a potent advantage over Lamivudine. This advantage is a low incidence of drug-resistant mutation.² Lamivudine is used as an anti-HIV agent world wide. Some side effects of anti-HIV drugs were reported,^{3,4} and there were some reports about cutaneous adverse effects induced by or associated with Lamivudine.^{4,5} Contact dermatitis due to Lamivudine, which was confirmed by patch testing, was reported in 2000.⁵ Entecavir has a higher antiviral effect than that of Adefovir and Lamivudine. Entecavir is a new nucleoside agent for hepatitis B, which was approved in the United States in 2005 and in the EU and Japan in 2006. Entecavir inhibits HBV DNA polymerase, which has less toxicity for mitochondria. The chemical structure of Entecavir is similar to the antiviral drugs Lobucavir, Acyclovir and Ganciclovir.⁶ Because our patient has never been treated with these antiviral agents (Lobucavir, Acyclovir and Ganciclovir) and Entecavir, it is a possibility that nucleotide analogs induce immunologic responses and our patient acquired allergy to Entecavir during this treatment. Possible adverse skin effects

due to Entecavir were present (personal communication, Bristol-Myers K.K.) in Japan. To our knowledge, there were no reports about cutaneous immediate allergy induced by Entecavir, which was confirmed by skin testing. If it is possible to get the ingredients of Entecavir, we might find what causes his allergy.

K Sugiura,††* M Sugiura,†† T Takashi,§ H Naoki,§ A Itoh§

†Department of Environmental Dermatology and Allergology, Daiichi Clinic,

‡Department of Dermatology and Allergy, Institute for Masuko Medical Research, §Department of Internal Medicine, Institute for Masuko Medical Research, Nagoya, Japan

*Correspondence: K Sugiura E-mail: ksugiura@daiichiclinic.jp

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