Acute Generalized Exanthematous Pustulosis Induced by HIV Post-exposure Prophylaxis with Lopinavir-Ritonavir

Sir—Almost all available antiretroviral drugs can induce exanthema, but only a small number can cause life-threatening reactions [1, 2]. The drugs carrying the highest risk of causing severe cutaneous adverse reactions are nevirapine [3], efavirenz [4], and the nucleoside analogue abacavir [5]. To our knowledge, no cases of acute generalized exanthematous pustulosis (AGEP) have been reported in HIV-infected patients. We report a case of AGEP induced by lopinavir-ritonavir in a health care worker receiving postexposure prophylaxis.

A 39-year-old man was prescribed zidovudine, lamivudine, and lopinavir-ritonavir after occupational HIV exposure. He had no personal or familial history of psoriasis and was not receiving any other treatment at the time of the accidental exposure. The results of an HIV immunosorbent assay performed before treatment were negative, and his WBC count was normal. Twenty-four hours after the first dose of antiretroviral combination prophylaxis, he developed generalized pruritus and a pustular rash that spread rapidly over the dorsal surface of the trunk and neck. The pustules were tiny and nonfollicular, and arose on a diffuse erythematous background. His body temperature was 38.5°C. The findings of a physical examination were otherwise normal, with no mucosal involvement or palpable adenopathy. Lopinavir-ritonavir treatment was immediately discontinued, and prophylaxis with zidovudine and lamivudine was continued for a total of 28 days. His skin symptoms improved dramatically 48 h after withdrawal of lopinavir-ritonavir therapy, and there was marked desquamation. Samples of the pustules tested negative for bacterial and viral pathogens. Serologic tests retrospectively performed on samples obtained on the first day of prophylaxis suggested past exposure to Epstein-Barr virus and cytomegalovirus. The patient did not develop HIV infection during follow-up.

AGEP is a well-known severe skin disorder, most cases of which are drug-related [6, 7]. The main culpable drugs are antibiotics, some diuretics, azole antifungals, and chloroquine [8–11]. Viral infections can also trigger AGEP [12, 13]. Our patient had characteristic features of AGEP, including very rapid and acute onset after the first drug intake, a pustular eruption, and fever with a temperature of >38°C. The dramatic improvement and superficial desquamation observed when the lopinavir-ritonavir component of combination prophylaxis alone was withdrawn suggests that this component was responsible [6].

A similar case was reported in an HIV-seronegative subject receiving postexposure prophylaxis that included zidovudine, lamivudine, and indinavir after unprotected sexual intercourse with an HIV-seropositive partner [14]. AGEP occurred 3 days after treatment initiation. The same regimen was nonetheless continued for 25 days, and the lesions healed rapidly 2 days after withdrawal of all 3 drugs. It was, therefore, impossible to identify the culpable drug.

To the best of our knowledge, drug-related AGEP has never been reported in HIV-infected patients [1]. This may be because of HIV-related immune dysregulation with insufficient activation of drug-specific CD4+ and CD8+ T cells [15]. If so, then the quantitative and qualitative improvement in CD4+ T cell function that accompanies HAART [16, 17] might lead to an increase in the number of cases of AGEP in coming years. Physicians who treat patients with HIV/AIDS should, therefore, be aware that AGEP can be caused by protease inhibitors, such as lopinavir-ritonavir and indinavir. Protease inhibitors should be added to the list of drugs capable of triggering AGEP.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Jade Ghosn, Claudine Duvivier, Roland Tubiana, Christine Katlama, and Eric Caumes

Département des Maladies Infectieuses et Tropicales, Groupe Hospitalier Pitie-Salpetriere, Paris, France

References

Echovirus Type 11: Outbreak of Hand-Foot-and-Mouth Disease in a Thai Hospital Nursery

Str—Hand-foot-and-mouth disease (HFMD) is a mild exanthematous illness seen worldwide. The causative agents of HFMD include various serotypes of coxsackievirus, echovirus, and enterovirus [1, 2]. In recent decades, HFMD caused by enterovirus serotype 71 has undergone a transformation from a minor, self-limited illness to the cause of major epidemics with high associated morbidity and mortality. This has been particularly so in Asian-Pacific countries [3–7]. In Thailand, the annual incidence of HFMD was estimated to be 5.65 cases per 100,000 population, with no associated deaths, in 2003 [8]. We reported the first outbreak of HFMD caused by echovirus type 11 in a Thai hospital nursery.

On 16 March 2005, we were contacted by a staff member at the nursery unit of Thammasart University Hospital regarding a cluster of HFMD infections. The index case had been diagnosed on 10 March 2005. Over the next 6 days, 12 (20%) of 60 children subsequently developed painful vesicular lesions on the palms of their hands, the soles of their feet, and on their oral mucosa. The median age of the patients was 2.1 years (range, 1.1–2.9 years), and 6 (50%) were boys. All 12 children with HFMD had contact with the index case through shared toys and utensils.

HFMD was confirmed, and the epidemiologic curve was created (figure 1). No children infected with HFMD developed any complications, and all care providers were without evidence of infection.

Figure 1. Epidemiologic curve of a hand-foot-and-mouth disease outbreak in a Thai hospital nursery.

Stool samples for viral culture were obtained from 6 children infected with HFMD, 6 children not infected with HFMD, and all care providers. Cultures of environmental samples, including samples from activity and play room surfaces, tables, the computer, door handles, and the bathroom, were also performed. Multiple observations of pediatric care revealed modifiable breaches in infection control practices: towel-sharing, an irregular and unmonitored environmental cleaning schedule (for the nursery, toys, playroom, door handles, computer, and telephones), and poor compliance with hand hygiene. After extensive discussion with the hospital administration, the nursery was closed within 24 h after the infection control evaluation. During the 14-day unit closure, all soiled articles and clothing were cleaned, all surfaces were exposed to 1:10 sodium hypochlorite solution with 10-min dwell times, and a revised routine cleaning schedule for the nursery and an improved hand hygiene program were initiated. Stool cultures from 4 (66.6%) of 6 screened children infected with HFMD subsequently yielded echovirus type 11. No subsequent cases were identified in the 4 months after the nursery unit reopened.

Within the recognized limitations of retrospective study design, we report the first nosocomial outbreak of HFMD due to echovirus type 11. A definitive diagnosis of echovirus type 11 infection was made for the majority (66.6%) of symptomatic children with available stool for viral cultures. A presumptive diagnosis of echovirus type 11 infection was made for the other 6 symptomatic children who did not have stool culture performed. Our inves-