

Exuberant Positive Patch Test to Abacavir in a Patient with the HLA-B*5701 Haplotype

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We report the case of a 28-year-old man diagnosed with HIV since 2005, referred to our allergy department for an episode of Steven-Johnson syndrome (SJS), consisting of a maculopapular exanthem with oral mucosal involvement during an episode of secondary syphilis. He was treated with penicillin benzathine 2,400.00 UI intramuscularly in only 1 dose, with good response. In addition to this, he received emtricitabine, tenofovir, atazanavir, and ritonavir for HIV infection (started 15 days before the exanthema), and a symptomatic treatment with metamizole and fluconazole for an oropharyngeal mycosis, started 7 days and 1 day before the exanthema, respectively. At the time of allergy study for the current SJS, the patient reported that, in 2005, when he was diagnosed HIV, he developed an extended maculopapular exanthema, with malaise and fever, 7 days after beginning treatment with abacavir. He was attended in the emergency department, abacavir was withdrawn, and he was treated with antihistamines and corticosteroids intramuscularly, with a complete resolution of symptoms within only a few days. Since that episode, he has not received any more abacavir.

In 2005, the screening for HLA-B*5701 was not a routine test and so it was not performed, although the correlation between this haplotype and the risk of severe hypersensitivity reactions was known.

Thus, we performed an allergy study of the current episode of SJS and, in addition, a study of the suspected abacavir hypersensitivity reaction (AHR) of 2005.

At the time of the allergy study, we did not know the result of the blood test that confirmed haplotype HLA-B*5701. However, considering the needs of antiretroviral treatment of our patient in the future and assessing risk and/or benefits, we decided to perform the patch test (PT) with abacavir to know cross-reactivity with tenofovir and atazanavir. The patient's haplotype was positive for HLA-B*5701, and the PT with abacavir (10% in dimethyl sulfoxide) was positive on day 2 reading, which showed erythema and micropapules (Figure 1). The cutaneous lesion progressed with increased edema, erythema, papules, and the appearance of pustules on days 3 and 4 (Figure 2), and an area of dermal necrosis on day 7 (Figure 3). Control tests with abacavir (10% in dimethyl sulfoxide) in 5 healthy subjects were negative.

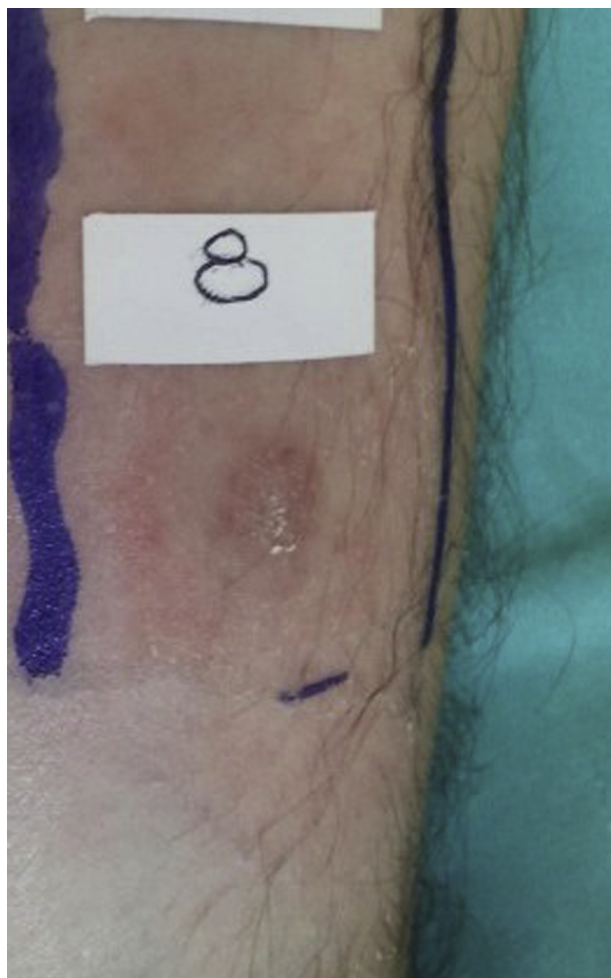


FIGURE 1. Patch test reading on day 2.

Skin biopsy¹ (Figure 4) showed necrosis, perivascular lymphocytes and eosinophils, and a central area of folliculitis. These findings are compatible with a type IV reaction.

The microbiological culture of the lesion was negative for bacteria and fungi. The patient was treated with topical 0.1% hydrocortisone acetate for 3 weeks, with improvement of the skin lesion produced by the PT in several days.

The PTs with all the drugs involved in the SJS were read as negative on days 2, 4, and 7 (Table 1) using the International Contact Dermatitis Research Group guidelines. We performed an oral single blind challenge test (OCT) with fluconazole because this class of medication is likely to be required in a patient with HIV; this OCT was negative. We did not perform an OCT with the antiretroviral drugs or metamizole because a new antiretroviral treatment regimen with raltegravir, darunavir, and

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FIGURE 2. Patch test reading on day 4.



FIGURE 3. Patch reading on day 7.

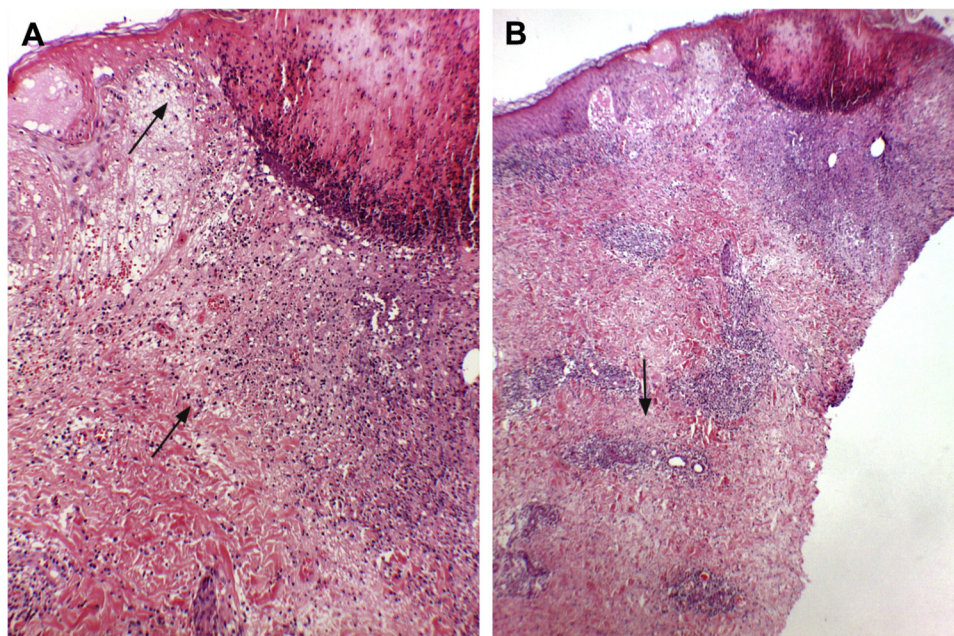


FIGURE 4. The pictures show necrosis of dermal and epidermal tissue (up arrow in **A**), with a central acute folliculitis area and an inflammatory infiltrate (lower arrow in **A**), perivascular lymphocytes and some eosinophils (arrow in **B**) without vasculitis characteristics. The rest of epidermis does not show any type of alteration.

TABLE I. Patch test's drug concentrations

Drug	Percent	Day 2	Day 4	Day 7
Fluconazole	10% in DMSO	—	—	—
Metamizole	1% in PET	—	—	—
Emtricitabine	10% in DMSO	—	—	—
Tenofovir	10% in DMSO	—	—	—
Atazanavir	10% in DMSO	—	—	—
Omeprazole	1% in PET	—	—	—
Abacavir	10% in DMSO	+	++	+++

DMSO, Dimethyl sulfoxide; PET, petrolatum.

ritonavir was started and well tolerated, and the metamizole was not an essential drug. Tenofovir and atazanavir were not restarted.

An AHR is a combination of symptoms such as fever, malaise, gastrointestinal and respiratory disturbances, and in some cases, skin rash.²

The strong association of AHR with HLA-B*5701 is now well known; the PT has a sensitivity of 79% and a specificity of 100%

in patients with AHR, remaining positive after several years,³ as in our patient. Although the PT is a valuable means for diagnosis of type IV immune-mediated reactions, it is not helpful for predicting risk of AHR in unexposed patients.⁴

Regarding our patient, we confirmed the likely immune-mediated AHR through the positive PT, with an unusually exuberant reaction,⁵ although the last exposure to the drug dated back to 9 years previously.

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