

The HIV-RNA level had been undetectable (below 200 copies/ml) under the first line, whereas the CD4 cell count slowly dropped to 176 cells/ μ l. After the first line was stopped, Cotrimoxazole prophylaxis was started in June 2005, but no antiretroviral treatment was given during the 8 months after HAART ended. A new line of treatment was started in March 2006 with lopinavir, tenofovir and emtricitabine. Under this treatment, the HIV-RNA level is presently below 40 copies/ml and the CD4 cell count is 220 cells/ μ l.

A retrospective diagnosis of NRH was made based on criteria defined by Mallet *et al.* [1]: (i) cryptogenic liver disease with abnormal liver function for more than 6 months, signs of portal hypertension and ultrasonographic liver dysmorphism; (ii) micronodulation with an alteration of thickened and compressed liver cells or suspected with the association of sinusoidal dilatation and clinical signs of portal hypertension. Finally, NRH is a classic evolution of peliosis.

Our case is very similar to those reported by Mallet *et al.* [1] and emphasizes the seriousness of this complication: the risk of variceal haemorrhage, indication for some patients of transplantation (three out of eight of the cases reported by Mallet *et al.* [1]). Only HIV infection and HAART have been identified as potential co-factors. Nevirapine toxicity is well known, has not been

specifically incriminated in NRH pathogenesis, but was also taken by our patient as well as by eight patients reported by Mallet *et al.* [1]. We agree with the authors that special attention should be paid to any hepatic dysfunction, however minor, under HAART that cannot be related to an identifiable cause.

Pierre-Francois Sandrine^a, Abel Sylvie^a, Edouard Andre^b, Diedhiou Abdoulaye^c, Liautaud Bernard^a and Cabie Andre^a, ^aService des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Fort de France, BP 632, 97261 Fort de France Cedex, France; ^bService de Gastro-entérologie, Centre Hospitalier Universitaire de Fort de France, BP 632, 97261 Fort de France Cedex, France; and ^cService d'Anatomopathologie, Centre Hospitalier Universitaire de Fort de France, BP 632, 97261 Fort de France Cedex, France.

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Reference

1. Mallet V, Blanchard P, Verkarre V, Vallet-Pichard A, Fontaine H, Lascoux-Combe C, Pol S. **Nodular regenerative hyperplasia is a new cause of chronic liver disease in HIV-infected patients.** *AIDS* 2007; **21**:187–192.

Severe bruising in an HIV-positive patient with haemophilia after using a needle-free gas-powered injection device

The Biojector 2000 is a needle-free carbon-dioxide-powered injection system currently undergoing evaluation for delivering subcutaneous enfuvirtide (Fuzeon) [1–4]. As needle-related injection site reactions (ISR) associated with enfuvirtide are postulated to occur as a result of the delivery of a bolus of drug into the subcutaneous tissue, gas-powered injection systems, which rapidly force medication through the skin and disperse the drug into the subcutaneous area, may be better tolerated. Preliminary results indicated that compared with the standard needle-syringe system, jet injection reduced the severity of ISR and improved quality of life without compromising enfuvirtide plasma levels [1–4]. The maker of the Biojector 2000 has cautioned that 'patients receiving anticoagulants or persons with hemophilia or other coagulation disorders may present greater incident of postinjection bleeding [and should] take the same precautions as when using a needle and syringe' [5]. We report the case of an HIV-positive patient with haemophilia who experienced significant ecchymosis and a haematoma with enfuvirtide using the Biojector device, but not with needles.

A 43-year-old caucasian man with haemophilia A, HIV and hepatitis C had used enfuvirtide in 2003, but discontinued it as a result of severe ISR consisting of painful nodules and some intermittent mild bruising; he had no intramuscular bleeding. In July 2005, he re-initiated enfuvirtide using the Biojector 2000 as part of a clinical trial. Concomitant antiretroviral agents included lopinavir/ritonavir, atazanavir and tenofovir. He was not taking any anticoagulants, antiplatelet or chemotherapeutic agents. Clinic staff instructed the patient on the standard use of the Biojector and he self-administered the first dose using the device under nursing supervision on 29 July 2005. Within 8 h, he noticed a significant ecchymosis at the site of injection. By 12 h, the ecchymosis had worsened and significantly increased in diameter. He continued administering enfuvirtide, varying the injection sites and paying close attention to the technique. Before one injection, he administered a standard dose of factor VIII, but noticed no difference in the extent of bruising. He also reported intramuscular bleeding after an injection into the left thigh region. No bleeding or bruising was noted at non-injection sites. He discontinued all antiretroviral



Fig. 1. Photo of patient showing marked ecchymosis after using a gas powered device.

medications on 1 August 2005 and returned to the clinic on 5 August 2005, when the marked ecchymosis was photographed (Fig. 1). Two weeks later, the bruises were still evident, although resolving. The patient recovered completely without further intervention and has not resumed any antiretroviral therapy.

The use of the gas-powered system coupled with our patient's underlying blood disorder probably led to his severe ecchymosis. With no previous self-reports of significant bruising at injection sites, it is likely that the Biojector device was the main contributor to this adverse event. Although no injections using no. 2 needle-free syringes penetrated the muscle in a subset of 18 healthy patients [5], our patient had advanced HIV disease and may have had more subcutaneous fat wasting increasing his risk of an intramuscular event. Also potentially increasing his risk may have been the use of two protease inhibitors in his antiretroviral regimen, a class of drugs that has been documented to increase bleeding in patients with haemophilia [6,7]; although he had previously used protease inhibitors without significant increases in bleeding episodes, including his previous needle-administered enfuvirtide-containing regimen, which included amprenavir and lopinavir/ritonavir.

We enrolled three other patients with haemophilia into the Biojector study (total $N=272$), two of whom developed ecchymoses (grade 0–1 and grade 3), and discontinued the Biojector but were able to persist with enfuvirtide using the needle-syringe system, and one who had no difficulties and continued with the Biojector System [3]. Harris *et al.* [1] reported one patient with local bruising at the site of injection that led to discontinuation, and the WAND study [8] reported one needle-free injection device-related haematoma that resulted in hospitalization occurring in a 68-year-old

patient with no bleeding risk factors. Subsequently, a Dear Investigator letter was issued by Trimeris and Roche on 10 March 2006 advising patients not to inject in or near bumps, not directly over a blood vessel or into moles, on or near scars/old surgery locations, bruises, or areas that could be irritated by a belt or waistband [9]. While we await the results of the BOSS study [10], we suggest that gas-powered devices should be used with extreme caution and close monitoring in patients with underlying bleeding disorders.

Deborah Yoong^a, Mona Loufty^{b,c,d}, Tom Chin^{e,f} and Ahmed M. Bayoumi^{c,d,g}, ^aPositive Care Clinic, St. Michael's Hospital, Toronto, Canada; ^bMaple Leaf Medical Clinic, Toronto, Canada; ^cDepartment of Medicine, University of Toronto, Toronto, Canada; ^dDepartment of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Canada; ^ePharmacy Department, St. Michael's Hospital, Toronto, Canada; ^fFaculty of Pharmacy, University of Toronto, Toronto, Canada; and ^gDivision of General Internal Medicine, St. Michael's Hospital, Toronto, Canada.

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