25.014

Cellular Antigen Stimulation Test (CAST) as a Novel, Affordable Laboratory Technique to Assess Potential Hypersensitivity to All Available Antiretroviral Compounds

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Introduction: Recently,novel allergometric techniques allow to test inhalants,food,and also drugs by specific in vitro assays. A flow cytometry technique based on the search of sulphidoleukotrienes LCT4, LTD4 and LTE4 released by basophils stimulated in vitro by IL-3 in presence of the examined antigens (cellular antigen stimulation test,or CAST), has a 80—90% sensitivity-specificity rate,and becomes particularly useful when prick tests are not applicable, and allergic reactions are not mediated by allergen-specific IgE immunoglobulins.*Methods-Results:* During the past three years, 13 HIV-infected subjects (eight females and five males, aged 37—52 years),underwent a standardized, specific in vitro cellular antigen stimulation test (CAST),due to serious cutaneous (six cases),systemic (two patients), and combined cutaneous-systemic hypersensitivity reactions (five subjects),apparently not elicited by the introduction of abacavir and nevirapine (which are the antiretroviral agents burdened by the greatest frequency of expected early allergic reactions,mediated by already recognized pathogenetic mechanisms). Based on the results of CAST testing, an allergic intolerance to ritonavir (six cases), lopinavir,nelfinavir, and didanosine (three cases each), saquinavir and lamivudine (two cases), and fosamprenavir,zidovudine, zalcitabine, stavudine, and efavirenz (one case each), was documented: in 10 cases out of 13 (76.9.5%) multiple intolerances were detected. A perfect relationship was documented between the results of CAST testing and the panel of combined antiretroviral compounds recently experienced by each allergic patient,and a CAST-based elimination of in vitro allergenic molecules allowed a rapid introduction of another effective antiretroviral combination.

Conclusions: Adverse events to antiretroviral drugs are quite frequent among HIV-infected patients, compared with the general population. Further,controlled studies are needed to implement in vitro allergometric testing in patients treated for HIV infection,who are exposed to unpredictable drug intolerance reactions. In fact,HIV-infected subjects may suffer from frequent allergic drug reactions which may be difficult to be systematically recognized (due to the frequent,multiple concurrent pharmacotherapy, and the combined antiretroviral therapy itself).

doi:10.1016/j.ijid.2008.05.508

25.015

HIV Genotypes and Patterns of Drug Resistance in Patients Failing HAART in a University Hospital Clinic

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Background: HAART strategies yield excellent results in drug naïve patients starting first-line treatment. Yet, data from clinical cohorts indicate drug resistance emerging as a consequence of toxicity, drug interactions or adherence problems leading to sub-optimal serum drug concentrations.

The Aga Khan University Hospital, Nairobi, has comprehensive HIV care services since 2003 at the one stop clinic. About 500 patients are on current follow-up by standard international protocols.

Methods: Over one year, 38 patients failed ART and were referred to the laboratory for resistance testing performed by population sequencing technique using VIRASEQ (Abbott) by manufacturer's protocol. All clinical details were recorded during sample collection.

Results: All patients belonged to a high socioeconomic group with corporate health insurance cover and claimed excellent drug adherence.

Patient age ranged from 6 to 57 years with a median of 38 years. CD4 counts ranged from 12 to 450 with a median of 135. Viral loads ranged from 2100 to 13 million with a median of 140,000. 82% (31/38) of patients had multiple hospital admissions indicating 2 to 5 episodes of opportunistic infections of which TB (14 patients), PCP (11 patients), Cryptococcosis (10 patients) and Salmonellosis (8 patients) were most common. 4 patients had 3 simultaneous opportunistic infections. 6 patients had 2 simultaneous opportunistic infections. Only 8 patients were on second-line HAART which included boosted PI. 9 patients used ARVs for over 10 years. A, D and CRFO1 were predominant subtypes. Major NRTI/NNRTI mutations were seen in 80% of patients while major PI mutations were seen in 8% of patients. High-level resistance was seen to Tenofovir in 8% of patients, Nevirapine, Efaverenz, 3TC & FTC in 80% of patients and AZT in 29% of patients.

Conclusions: In the long run, high-level multiple resistance is inevitable in patients on HAART, with serious implications for national ARV programs and prophylactic regimens.

doi:10.1016/j.ijid.2008.05.509

25.016

Multi-Pronged Strategy Greatly Enhances Enrollment of HIV Positive Children Into HIV Care and Treatment: Experience from Uganda

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Background: Although Uganda had successfully rolled out Antiretroviral therapy (ART) in HIV-infected adults, enrollment of children aged less than 15 years onto ART had generally been very slow. However, the implementation of a multi-pronged strategy for scaling-up pediatric HIV care has