HIV antibody profiles in serum and CSF of patients with neurological disease can serve as predictors of outcome

Anita Desai, V Ravi, P Satishchandra, N Khanna, Shivaji Rao, M Gourie-Devii, A Chandramuki

Abstract
The serum and CSF antibody profiles were investigated in 100 patients with HIV in relation to the type and severity of neurological disease. Among them, 87 were positive for anti-HIV antibodies in the CSF. In 30 of 87 patients detailed analysis by western blot could be performed. In 20 of 30 the profiles were dissimilar, with more of bands being found in the serum than in the CSF. The correlation of western blot profiles to the clinical outcome indicated that the number of anti-HIV antibody bands as well as the index in the CSF of fatal cases were significantly less compared with non-fatal cases (p=0.019 and p=0.039 respectively).

Keywords: HIV/AIDS; western blot; neurological manifestations; predictors

HIV antibody profiles

Human immunodeficiency virus (HIV) infection was first detected in India during 1985–6. Since then the seropositivity rate has been steadily on the increase and at present it is 22/1000 samples tested. There are very few studies on the neuropsychiatric aspects of HIV infection in India. In a study conducted 5 years ago at our centre, Desai et al. reported a seropositivity rate of 1.2% (3/247) among patients with neurological disorders. However, since then there has been a dramatic increase in the number of HIV positive patients presenting with neurological and psychiatric manifestations and in the year 1998 the seropositivity rate was 14% (80/573). Although some reports pertaining to the various types of neurological manifestations seen in HIV/AIDS are available, there are very few studies which have attempted to search for prognosticators of neurological morbidity in AIDS. The frequent presence of HIV or its genome in the CSF, increased concentrations of IgG, and the presence of oligoclonal bands in the CSF and detection of HIV p24 antigen in the CSF have been described in both symptomatic and asymptomatic subjects infected with HIV. As it would be of considerable clinical value to evolve laboratory predictors for the outcome of patients with and without neurological involvement, so that antiretroviral therapy and other interventions can be initiated early, we evaluated the role of serum and CSF antibody profiles as predictors of outcome in patients infected with HIV. In this paper we present our results in relation to the type and severity of neurological disease and outcome in HIV positive patients.

Materials and methods

PATIENTS
A total of 3230 patients seen between 1989 and 1997 at the NIMHANS hospital with neurological signs and symptoms underwent HIV testing and 189 (5.9%) were found to be HIV positive. Among them 100 patients with neurological manifestations in whom a CSF sample was available for HIV testing constituted the study group. All these patients had voluntarily consented for HIV testing and were counselled pretest and post-test.

HIV ANTIBODY PROFILES

Coded serum and CSF samples were initially tested for the presence of HIV antibodies using either an enzyme linked immunosorbent assay (ELISA) (Innogenetics Inc, USA, UBI Magiwell, USA and Detect Biochem, Canada) or rapid immunoassay (Immunocomb, Israel, HIV spot, USA) kits supplied under the National AIDS control programme. Reactive samples were retested twice using different kits before considering them as positive. Among those positive, 30 pairs of serum and CSF samples (where sufficient amount of sample was available) were taken up for detailed analysis by western blot using a commercial HIV 1 rapid immunoassay kit (GeneLabs, USA). Briefly, 2.5 ml of 1: 50 diluted serum or CSF sample was added onto nitrocellulose strips (containing the electrophoresed and transferred viral proteins) and incubated on a rocking platform for 2 hours at room temperature on a rocking platform. Subsequently the strips were washed thrice and bands visualised by adding the substrate. The results were recorded by two independent...
investigators (AD and VR) blind to the code of the sample. The results were also expressed as an index using a graded scoring system provided by the manufacturer of the kit. In this system the presence of each HIV-1 viral protein band was given the following score: gp 160 or gp 41=1; gp 120=1, p66, or p51, or p24=0.5; p31 or p17=0.25. Thus the maximum index that could be assigned to any HIV-1 positive sample would be 3.25.

Results

Clinical Findings

Among the 100 HIV positive patients most of them were men (93%) in the age group of 18–60 years (mean=32.2 years) and heterosexual contact was the major risk factor for acquiring HIV infection reported in 80%. Only 30 patients underwent detailed analysis by western blot and in the remaining 70 it could not be carried out because the CSF sample was not adequate. The clinical presentation in all but one of the 30 patients was opportunistic infections of the CNS. These were cryptococcal meningitis (n=9), neurotuberculosis (n=6), toxoplasmosis (n=3), cryptococcal meningitis with neurotuberculosis (n=3), cryptococcal meningitis with toxoplasmosis (n=2), neurotuberculosis with toxoplasmosis (n=1), and herpes encephalitis (n=2). Among these 30 patients 16 succumbed and the remaining 14 recovered from opportunistic infections.

HIV Antibody Profiles

Among the 100 patients whose serum samples were positive for HIV antibodies by ELISA or rapid immunosays in 87 patients anti-HIV antibodies were detected in the CSF. In 29 of 30 patients in whom western blot analysis was carried out antibodies to HIV-1 proteins were detected whereas in one reactivity to both HIV 1 and 2 antigens was noted. Antibody profiles obtained in the 20/30 patients were dissimilar in serum and CSF, with more bands being found in the serum than in the CSF (figure). However, in one of these 20 patients a p51 band was seen in the CSF but not in the serum. Antibodies to the HIV-1 glycoproteins (gp160, gp120, and gp 41) and p66 were seen in almost all the 30 serum and CSF samples. However, antibodies to three other HIV-1 proteins—p55, p39, and p17—were seen significantly less often in the CSF than in the serum. In the lone patient who was positive for both HIV-1 and HIV-2 antibodies the band to HIV gp 36 was detectable in the serum but not in the CSF. Correlation of the mean levels of HIV antibody bands obtained in the western blot with the clinical outcome is presented in the table. The number of HIV-1 bands as well as...
the index value in the CSF of fatal cases were significantly less compared with the non-fatal cases. However this was not true for antibody profiles obtained in the serum between the two groups.

Discussion

Patients with HIV infection may manifest neurological symptoms during the initial stages of infection. Abnormalities in the CSF such as increased white blood cell count, increased total protein concentrations, presence of HIV p24 antigen, and isolation of HIV have been reported in patients with and without neuropsychiatric findings. Some earlier studies have suggested that HIV antibody patterns can be used to prognosticate the evolution of HIV related CNS disease, although not for predicting the outcome of patients with neurology.

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