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CIDP in a HIV endemic population: A prospective case series from Johannesburg, South Africa

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ABSTRACT

Objective: To describe patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) in Johannesburg, South Africa, a setting of high HIV prevalence, and to determine the influence, if any, of HIV on CIDP.
Methods: Patients were recruited prospectively. The study design was a hospital based case series of unselected consecutive CIDP patients. CIDP was diagnosed according to the European Federation of Neurological Societies/Peripheral Nerve Society criteria for the diagnosis of CIDP (First Revision). Demographic, clinical, laboratory and electrophysiological data were documented.
Results: Twenty three patients with CIDP were recruited over a two year period. Mean age was 38 years. The female to male ratio was 3.6:1. Less than half (43%) had a raised cerebrospinal fluid (CSF) protein. All patients had idiopathic CIDP, three had associated diabetes mellitus. Ten patients (43%) were HIV positive. Thirteen patients were HIV negative. Clinical and electrophysiological characteristics were identical in the two groups. In the HIV positive group all the patients were black females. The CD4 counts ranged from 87 to 747cells/mm^3. HIV positive status was associated with a progressive disease course and significantly with a CSF lymphocytic pleocytosis ($p = 0.007$). Albuminocytological dissociation was associated with HIV negative status.
Conclusions: Testing for HIV in patients with CIDP in a region of high HIV prevalence is recommended. CSF lymphocytic pleocytosis occurs in HIV associated CIDP.

1. Introduction

CIDP is an acquired autoimmune inflammatory peripheral nerve disorder. It is characterized by mononuclear cell infiltrates and macrophage-associated segmental demyelination with activation of both humoral and cellular components of the immune system [1–3]. CIDP occurs as an idiopathic disease or in the setting of other immune disorders namely, paraproteinemias, SLE, inflammatory bowel disease, sarcoidosis, and lymphoma.

Human Immunodeficiency Virus (HIV) infection is an immune dysregulation and deficiency state characterized by depletion of infected CD4 lymphocytes. The virus is also neurotropic and neurovirulent, and causes pathology of the brain, spinal cord and peripheral nerves. The spectrum of HIV associated peripheral nervous system disease has been extensively reviewed and encompasses distal sensory polyneuropathy, varying types of polyradiculitis, plexopathies, mononeuritis (including cranial), mononeuritis multiplex, and diffuse interstitial lymphocytosis syndrome (DILS) neuropathy [4]. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) can be a manifestation of seroconversion illness or may occur during later stage HIV disease [5]. CIDP has been documented during and throughout the course of HIV infection [5–9]. Clinically, the CIDP in HIV infected patients has been reported to be similar to that in patients without HIV. In the few small patient series and case reports describing CIDP in HIV the main difference is a cerebrospinal fluid lymphocytic pleocytosis, which is found in the HIV positive patients [5,7–9].

We prospectively studied 23 CIDP patients in a tertiary referral center in Johannesburg, South Africa, a region of high HIV prevalence. CIDP has not been studied in high HIV sero-prevalence regions, especially in sub-Saharan Africa, where the influence of HIV on CIDP can be determined.

2. Patients and methods

2.1. Study design

2.1.1. Prospective consecutive case series

We studied 23 consecutive patients with CIDP that presented to the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) over a two year period. CMJAH is one of two tertiary referral centers for the public health sector of Johannesburg, South Africa servicing approximately 7 million people. Patients presenting with peripheral neuropathy were assessed for CIDP using the European Federation of Neurological

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Societies/Peripheral Nerve Society criteria for the diagnosis of CIDP (First Revision) [10]. The patients were examined by at least two of the authors and entered into the study after informed consent was obtained. HIV testing was done on all patients with informed consent and pre/post-test counseling. The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand.

2.2. Assessment protocol

The following data were recorded:

Demographics: Age, sex and ethnicity.

Course of disease: Relapsing remitting, progressive, other.

Blood: Full blood count, urea, electrolytes, creatinine, liver function test, serum protein electrophoresis and immune fixation, antinuclear antigen, ganglioside antibodies (not available for all patients), thyroid function test, angiotensin converting enzyme, hepatitis studies, HbA1c and fasting glucose were done.

Cerebrospinal fluid (CSF): CSF was analyzed for biochemistry, cytology, microscopy and culture. Cryptococcal antigen was tested for.

Electrophysiology: Nerve conduction studies were obtained from the median and ulnar nerves in both upper limbs, and the tibial, peroneal and sural nerves in both lower limbs.

2.3. Data analysis

Data were described using means and standard deviations, or medians and ranges for normally distributed and skewed numerical data respectively and percentages for categorical data. Comparisons between groups were done using unpaired t-tests, Mann–Whitney and Fisher's exact tests as appropriate. Statistical analysis was performed using Stata (Stata Corp. 2013. Stata Statistical Software: Release 13. College Station, TX: Stata Corp LP.).

3. Results

3.1. Demographics

Twenty-three patients fulfilled the criteria for definite CIDP; 22 had typical CIDP, 1 had atypical CIDP (pure sensory ataxic variant). Five were male and 18 were female (female to male ratio = 3.6:1). Patient ages ranged from 12 to 68 years (mean 38 years; SD 17.4 years; median 42 years).

The ethnicity distribution of our cohort was 16 Black patients (70%), 4 patients of Indian descent (17%) and 3 White patients (13%).

3.2. Aetiologies/associated conditions

Three of the 23 patients had associated diabetes mellitus (all 3 were HIV negative). In the remainder no underlying immune or other disorder was identified. The patients were therefore all classified as having idiopathic CIDP.

3.3. HIV status

Of the 23 patients, 13 were HIV negative and 10 HIV positive (43%). All 10 HIV positive patients were black females aged 20 to 63 years (mean 38 years; SD 15.3 years; median 35 years) and all were of unknown HIV status and antiretroviral therapy naïve at the time of CIDP diagnosis. No statistically significant difference was found by the Student t-test or the Mann–Whitney test when comparing the ages of the HIV positive (mean 38 years) and negative groups (mean 39 years). CD4 cell counts of the HIV positive group ranged from 87 to 747 cells/mm^3 (mean 364 cells/mm^3; SD 217 cells/mm^3; median 341 cells/mm^3).

3.4. Disease course

Twelve patients followed a relapsing remitting course and the other 11 had a progressive course. The average age of the relapsing remitting group was 37 years (SD 19.0 years) and 39 years (SD 15.9 years) for the progressive group. No statistically significant difference could be found (by two-sample t-test and Mann–Whiney test) when comparing patients' ages and disease course.

The HIV positive group had 3 patients following a relapsing remitting course and 7 followed a progressive course, whereas in the HIV negative group 9 patients had a relapsing remitting pattern and 4 had a progressive course. By Fisher's exact test, HIV positive status is associated with a progressive course, albeit not statistically significant ($p = 0.099$).

3.5. CIDP subtypes

Twenty-two patients had typical CIDP with characteristic motor signs of proximal and distal weakness in the lower limbs and distal weakness in the upper limbs. Ten patients (43%) were unable to walk at presentation. The 1 patient with atypical CIDP had a GM2 antibody positive pure sensory ataxic variant; this was the only ganglioside antibody positive patient. All 10 HIV positive patients presented with typical CIDP.

3.6. Cerebrospinal fluid

CSF protein values ranged from 0.11 to 1.96 g/l with an average of 0.56 g/l (SD 0.49 g/l); 10 of the 23 patients (43%) had a CSF protein greater than the normal of 0.45 g/l. Average CSF protein was 0.55 g/l (SD 0.48 g/l) for the HIV negative and 0.57 g/l (SD 0.53 g/l) for the HIV positive subgroup respectively. The CSF proteins of the HIV-associated CIDP were raised in 40% (4 from 10) of patients and in 46% of the non-HIV patients (6 from 13). This difference is not statistically significant by Fisher's exact test ($p = 1.00$). Diabetes mellitus was associated with raised CSF protein in one of the three patients.

The HIV negative subgroup had a mean CSF lymphocyte count of 0.8 cells/μl (range 0 to 4 cells/μl), whereas the HIV positive group had a mean of 17 cells/μl (range 0 to 77 cells/μl; median 5.5 cells/μl). Five of the 10 HIV positive patients had raised CSF white cell counts above the normal value of 5 cells/ml. CSF pleocytosis was significantly associated with HIV positive status ($p = 0.007$).

Albuminocytological dissociation was present in 7 patients (30%) overall. Six of the 13 HIV negative patients (46%) and 1 of the 10 HIV positive patients (10%) had albuminocytological dissociation. Using Fisher's exact test, the absence of albuminocytological dissociation is associated with HIV positive status ($p = 0.089$).

No correlation was found amongst the HIV positive patients between their CD4 counts, CSF protein and CSF white cells (Table 1). Demographic data, clinical course and CSF parameters comparing the HIV positive and negative subgroups are summarized in Table 2.

4. Discussion

Our series of 23 consecutive unselected (in terms of HIV or other associated disease) patients represents the first prospectively collected CIDP cohort from South Africa, an HIV endemic region. We found 10 of the 23 patients (43%) to be HIV positive, allowing us to characterize and compare the HIV negative and positive subgroups and therefore determine the influence, if any, of HIV on CIDP. In doing so, our data set provides for useful discussion of the differences and similarities we found in comparison with the published literature.

Due to the overall small sample size, however we cannot infer any epidemiological conclusions about the apparent high frequency of this association that we found in our cohort.