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Prospective Cerebral MR Study of HIV Seropositive and Seronegative Men: Correlation of MR Findings with Neurologic, Neuropsychologic, and Cerebrospinal Fluid Analysis

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Purpose: As part of a longitudinal study of human immunodeficiency virus type 1 (HIV) infection, we attempted to identify early cerebral MR findings that might correlate to clinical evidence of central nervous system involvement. **Methods:** We studied 65 seropositive and 40 seronegative homosexual males using cranial MR, neurologic, immunologic, and neuropsychologic examinations. **Results:** The incidence of mildly enlarged ventricles, sulci, and punctate areas of abnormal signal in both groups was similar in both groups. Diffuse, poorly defined areas of abnormal white matter signal were difficult to consistently identify in seropositives. Enlarged adenoidal lymphoid tissue was found in 30 (46%) of seropositives and 2 (5%) of seronegatives ($P = .0001$). The incidence of sinus inflammatory change was similar in the two groups. **Conclusion:** MR of intracranial contents is substantially normal in a non-AIDS HIV(+) population.

Index terms: Acquired immunodeficiency syndrome (AIDS); Brain, magnetic resonance

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Up to 75% of patients with human immunodeficiency virus type 1 (HIV) infection will have central nervous system (CNS) involvement sometime during the course of their illness. A progressive dementia, characterized by decreased concentration, poor memory, psychomotor slowing, motor weakness, loss of fine motor control, apathy, and occasionally frank psychosis, is a frequent and debilitating manifestation of advanced HIV disease (1-4). Despite numerous attempts, correlation of imaging abnormalities to the clinical manifestations of AIDS dementia has been difficult. Post et al compared postmortem histologic

changes to antemortem computed tomography (CT) and magnetic resonance (MR) examinations in 22 patients, all of whom had pathologic proof of HIV infection of the CNS and 17 of whom had neurologic symptoms (5). Imaging studies showed enlargement of ventricular and sulcal structures. Parenchymal abnormalities found with MR or CT had good pathologic correlation; however, many histologically apparent microglial nodules were not demonstrated with either imaging modality. Direct clinical correlation was not possible with this study because several weeks to months separated the imaging studies and the histologic examinations.

Recent cohort studies have evaluated subjects seropositive for HIV who have less advanced disease (6-9). Although these studies have yielded conflicting results, there have been suggestions that patients with early HIV infection have few measurable neurologic or neuropsychologic abnormalities. Limitations in many of these studies occurred because extensive neurologic, neuropsychologic, and laboratory evaluations were usually performed on subgroups of subjects, such as those who had abnormal response on a screening test battery.

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We also evaluated cranial MR for changes that might correlate with comprehensive neurologic, neuropsychologic, and immunologic findings in subjects who are seropositive for HIV with minimal or no neurologic symptoms. We are reporting the results of our initial evaluation performed as part of an ongoing longitudinal study comparing homosexual men seropositive for HIV infection to demographically similar seronegative controls. We are attempting to identify and determine the prevalence of early imaging findings that are indicative of neurologic or neuropsychologic dysfunction.

Methods

HIV(+) and HIV(-) homosexual or bisexual men were recruited from the community and from a cohort established to characterize the clinical course of HIV infection (10). Subjects were excluded if they had AIDS, known active neurologic disease, neurologic complaints elicited on a screening interview, or were unavailable for follow-up for at least 1 year.

Baseline examination consisted of history, physical examination, neurologic evaluation, neuropsychologic test battery, immunologic studies, and MR, as described previously (11). MR was obtained on HIV(+) subjects who underwent lumbar puncture and a random subset of HIV(-) subjects. Tests included in the neuropsychologic battery and the functions evaluated by each are listed in Table 1. All neurologic and neuropsychologic examinations were performed by examiners blinded to the HIV serostatus of the subject. Blood tests, obtained from all subjects, consisted of routine complete blood count, lymphocyte subset analysis, and evaluation for antibody to HIV by enzyme-linked immunoassay (ELISA) and Western blot assay. Cerebrospinal fluid (CSF), requested from all seropositive subjects, was examined for cells, glucose, protein, VDRL, and HIV antibody (ELISA), and was cultured for HIV. In the first 38 subjects who had CSF studies, the presence of HIV p24 antigen in serum and in CSF was evaluated and total daily intrathecal IgG synthesis was calculated. Serum to CSF ratios of p24 antibody were calculated. Total intrathecal IgG synthesis >3 mg/day and serum/CSF p24 antibody ratios ≤ 5.5 were felt to indicate CSF infection with HIV, as was isolation of HIV from CSF by culture (11). Using the Wilcoxon rank sum test (two-tailed), neuropsychologic test scores were compared between subsets of patients based on the MR findings. Neuropsychologic test differences with $P < 0.05$ are reported.

MR examinations were performed on a 1.5-T system (GE Signa, General Electric, Milwaukee, WI) using sagittal and axial T1-weighted sequences (600/20-TR/TE) and axial and coronal spin density and T2-weighted sequences (2500-2700/20, 80). Slices were 5-mm thick with a 2.5-mm interslice gap. MR studies were interpreted independently by two neuroradiologists (W.C., K.R.M.) who remained blinded to the HIV status of the participants and to

TABLE 1: Neuropsychologic test battery

Language
Vocabulary scale (WAIS-R)
Boston Word Naming
Controlled Oral Word Association Test
Verbal aphasia
Verbal memory
Selective Reminding test
Recall 10 trials
30-minute recall
Wechsler Memory Scale
Logical Paragraphs
30-minute delay
Attention/speed of information processing
Digit Span (WAIS-R)
Paced Auditory Serial Addition Test
Halsted Rhythm Test
Executive Functions
Halsted Category Test
Wisconsin Card Sort Test
Trail Making B
Motor
Finger-tapping-dominant
Finger-tapping-nondominant
Digit Symbol (WAIS-R)
Visuomotor processes
Perceptual speed
Trails A
Visual aphasia
Benton Visual Retention Test
Sensorimotor Perception
Auditory
Tactile
Graphesthesia
Finger agnosia

their laboratory, neurologic, and neuropsychologic test results throughout the period of scan evaluation. Initial scan interpretation was performed independently. Interpretative disagreements were reviewed by both neuroradiologists together and a consensus decision reached. Ventricular and sulcal size were evaluated by a subjective general assessment (normal, mild, moderate, or markedly increased in size for age) and by computer-generated linear measurements using the following protocol. Ventricular, brain, and calvarial boundaries were identified on T2-weighted images by a single observer (R.G.) and marked with a cursor. The distance between cursor-marked points was calculated using standard distance-measuring software supplied by the manufacturer. Measurements of the ventricular system were made at three levels: 1) Minimum width of the third ventricle measured through the trigonum habenulae. 2) Maximum width of the frontal horns of the lateral ventricles. 3) Minimum width of the lateral ventricles at the level of the caudate-putamen impingement. Width of the brain and

width of the calvarium (inner table) were measured at the same anterior to posterior position within the skull as the ventricular measurements. Ratios of ventricular width to brain width and to calvarial width, used to standardize for head size, were used for the purpose of data analysis (Fig. 1).

Regions of abnormal MR signal were defined as areas of signal different from the surrounding uninvolved tissue, whether white or gray matter. The presence of mass effect, appearance of the margins of the abnormal signal (sharp margins implying focal lesions, ill-defined margins suggesting diffuse lesions), size of a lesion, location of the lesion, and the relative signal intensity of the lesion were identified and characterized on all imaging sequences. Specifically, a diffuse white matter lesion (DWM lesion) was characterized as an ill-defined pattern of increased signal in the white matter without mass effect present on spin-density and T2-weighted images. Punctate lesions were defined as 2- to 6-mm sharply marginated foci of abnormal signal. A lesion that caused visible displacement of parenchymal structures was defined as a mass lesion.

After our initial evaluation and data analysis, it became apparent that detection of subtle DWM lesions was difficult. To evaluate this further, a reliability study was performed in 14 patients selected to include HIV(+) and HIV(-) subjects with and without DWM lesions. The neuroradiologists remained blinded both to the original MR interpretation, to the results of laboratory assessments, and to the HIV serostatus of the patients. Within this group of 14 subjects, 10 were HIV(+) and four were HIV(-). Of these 14 subjects, seven had been interpreted as having DWM lesions on the first analysis, while the remaining seven were randomly selected from the patients who were initially interpreted as being without DWM lesions. The presence of abnormal signal in the white matter was again assessed on all three imaging sequences: T1, spin density, and T2. Particular attention was paid to areas of increased spin density and T2 signal in the forceps major, the periventricular white matter, and the centrum semiovale. The results of this second analysis were later correlated with HIV status and the original interpretation of the presence or absence of DWM lesions.

Extracranial changes, such as adenoidal enlargement, abnormal signal within the nasopharyngeal soft tissues, and the presence, extent, and location of sinus inflammatory disease were also evaluated on the MR images and correlated to immunologic status, clinical history, and physical examination.

Results

Demographics

At the time of these analyses, total enrollment in the study consisted of 160 HIV(+) and 76 (HIV-) males. Of these, 65 (41%) of seropositive and 40 (53%) of seronegative subjects underwent cranial MR examinations. In the HIV(+) group with MR, 24 subjects were Centers for Disease

Control (CDC) group II (asymptomatic), 28 were group III (persistent generalized lymphadenopathy), and 13 were group IV non-AIDS (constitutional symptoms, oral candidiasis, or hairy leukoplakia).

Comparison of the subgroup of HIV(+) subjects who underwent MR with the subgroup who did not revealed similar demographic and clinical characteristics, including illicit drug use, number of lifetime sexual partners, and subjective symptoms (Table 2). Immunologic measures in the peripheral blood, including means of the absolute and percentage T4 lymphocyte count (T4, %T4) were also comparable. The groups differed

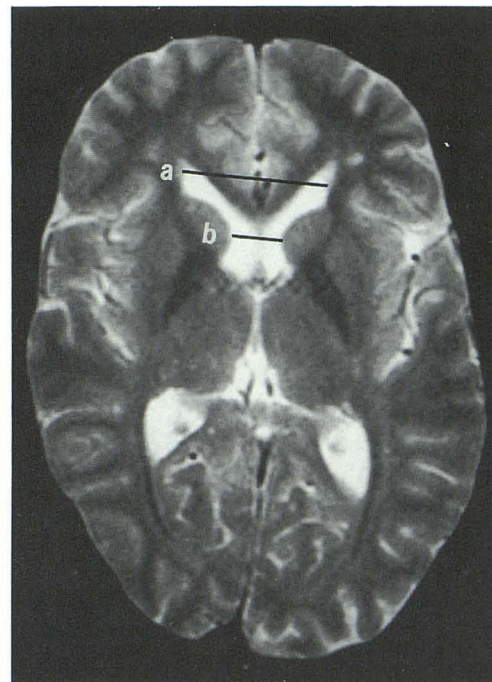


Fig. 1. Measurements of the width of the lateral ventricles were made at two points, shown on these T2-weighted images. Line (a) is through the frontal horns at the widest point and line (b) is through the frontal horns at the level of the caudate-putamen impingement. Calvarial width and brain width measurements were made at each level. Measurements were also made of the width of the third ventricle at the trigonum habenuale.

TABLE 2: Demographics of HIV(+) and HIV(-) subjects

	HIV(+) (N = 65)	HIV(-) MR (N = 40)
Age (yrs)	36.8 ± 6.4	37.1 ± 8.4
Years education	15.6 ± 2.2 ^b	16.1 ± 2.4
T4 cells ^a (per mm ³)	506 ± 247	926 ± 291
T4 cells ^a (%)	26.8 ± 10.3	45.6 ± 6.7

Note.—All values mean ± standard deviations.

^a Immunologic measures were significantly lower in HIV(+) than HIV(-) subjects ($P = .0001$).

^b $P = .04$.

slightly in the number of years of education: those without MR studies had a mean of 14.9 years versus 15.6 years in those with cranial imaging ($P = .04$). Similar comparability was present in HIV(-) subgroups without and with MR examinations. As expected, mean T4 and %T4 values were lower in HIV(+) compared to HIV(-) subjects.

Imaging Findings

Ventricular and Sulcal Enlargement-Subjective Assessment. Mild diffuse enlargement of the ventricles (Fig. 2), as evaluated by subjective visual assessment without knowledge of HIV status was present in six (9%) of 65 HIV(+) and three (8%) of 40 HIV(-) subjects (Table 3). No subject had moderate or marked ventricular enlargement. Ten (15%) of 65 HIV(+) and 9 (23%) of 40 HIV(-) individuals demonstrated enlargement of sulci. These findings were not associated with a history of drug or alcohol use, either current or past, or with T4 count. Within the group of HIV(+) subjects, CSF culture for HIV, neurologic examination abnormalities, such as cranial nerve dysfunction, or neuropsychologic test results did not differ in subjects with large ventricles and sulci compared to those without them (Table 4). Similarly, the results of neurologic and neuropsychologic evaluations of HIV(-) subjects were comparable in patients with enlarged ventricles and sulci compared to those without these findings. Ventricular enlargement without

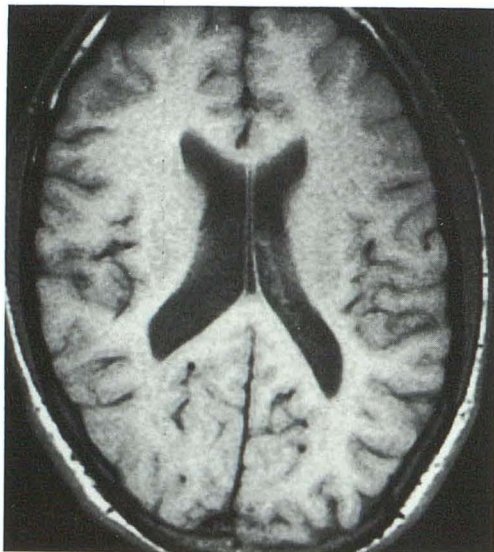


Fig. 2. Ventricular enlargement was mild, as seen in this 29-year-old HIV(+) man. No men had marked ventriculomegaly in our study population.

sulcal enlargement did not demonstrate correlations with any clinical or laboratory characteristic. **Ventricular Enlargement-Linear Measurements.** Measurements were performed in 53 (82%) of 65 HIV(+) and 27 (68%) of 40 HIV(-) subjects. In 12 HIV(+) and 13 HIV(-) subjects, scans could not be retrieved from tape to perform linear measurements. There were no significant differences in the ventricular measurements between the two groups (Table 5). Mean ratios of ventricular to cranial widths of the anterior third ventricle, of the frontal horns at the level of the caudate, and of the frontal horns at their widest point were similar in HIV(+) subjects compared to HIVs(-). The five HIV(+) subjects whose ventricles appeared larger by subjective assessment showed a trend toward significantly larger ventricles using linear measurements when compared to HIVs(+) with normal ventricles; (third ventricle, $P = .06$; frontal horns at caudate, $P = .03$; frontal horns at widest point, $P = .06$).

DMW lesions. Ill-defined hazy areas of signal intensity greater than surrounding white matter on the long TR images were judged to represent DWM lesions (Fig. 3). These changes were visible in eight (12%) of 65 HIV(+) and four (10%) of 40 HIV(-) men at the initial evaluation. The areas of abnormal signal were found primarily around the occipital horns in the forceps major and around the posterior bodies of the lateral ventricles at the level of the centrum semiovale. In cases where this process was slightly more extensive, the regions of abnormal signal extended forward toward the posterior frontal region. In general, the hazy, increased periventricular signal, when subtle, was difficult to distinguish from variations in appearance of normal white matter on a high-field imaging system. To improve reliability of interpretation, attempts were made to determine if these signal changes localized to specific anatomical structures, such as the splenium. However, no consistent location nor diagnostic characteristic could be observed.

To determine the degree of reliability of our subjective interpretation of DWM, a reliability study of a subgroup of 14 patients was performed as described. We were able to confirm the initial diagnosis of DWM lesions in only 4/7 HIV(+) patients. Two of the seven HIV(+) patients in this subgroup, who were originally thought to be without DWM abnormal signal, were diagnosed as positive for DWM lesions on this second, blinded reading, while 3/7 were now thought to be without DWM lesions. No HIV(-) patients were

TABLE 3: MR findings/immunologic status

	HIV(+) (N = 65)			HIV(-) (N = 40)		
	Number of patients (%)	Absolute T4 ^a (per mm ³)	%T4 ^a	Number of patients (%)	Absolute T4 ^a (per mm ³)	%T4 ^a
Ventricles						
Enlarged ^b	6 (9)	486 ± 252	22.8 ± 7.7	3 (8)	800 ± 206	50.3 ± 10.3
Normal	59 (91)	508 ± 248	27.2 ± 10.5	37 (92)	937 ± 297	45.2 ± 6.3
Sulci						
Enlarged ^b	10 (15)	599 ± 309	24.4 ± 9.3	9 (23)	840 ± 204	49.2 ± 7.2
Normal	55 (85)	489 ± 233	27.3 ± 10.5	31 (77)	952 ± 310	44.5 ± 6.2
Ventricles or sulci						
Enlarged ^b	12 (18)	537 ± 319	23.1 ± 9.1	10 (25)	858 ± 201	49.6 ± 6.9
Normal	53 (82)	498 ± 231	27.7 ± 10.5	30 (75)	949 ± 315	44.2 ± 6.1
Punctate lesion outside basal ganglia						
Present	28 (43)	497 ± 214	28.2 ± 9.9	13 (33)	952 ± 426	43.9 ± 8.0
Absent	37 (57)	512 ± 272	25.8 ± 10.6	27 (67)	914 ± 207	46.3 ± 5.9

Note.—Comparison of HIV(+) subgroups without and with MR and between HIV(-) subgroups without and with MR showed no significant statistical differences.

^a Mean ± standard deviations.

^b Assessment based on visual inspection.

TABLE 4: MR findings/CSF results^a

	Isolation of HIV from CSF ^b (N = 56)	Intrathecal IgG > 3 ^c (N = 34)	ELISA Serum/CSF ≤ 5.5 ^c (N = 34)
Ventricles enlarged ^d	2/5 (40%)	1/3 (33%)	3/3 (100%)
Ventricles normal	29/51 (57%)	14/31 (45%)	28/31 (90%)
Sulci enlarged ^d	3/9 (33%)	2/7 (29%)	6/7 (86%)
Sulci normal	28/47 (60%)	13/27 (48%)	25/27 (93%)
Punctate lesions outside basal ganglia			
Present	13/24 (54%)	6/13 (46%)	12/13 (92%)
Absent	18/32 (56%)	9/21 (43%)	19/21 (90%)
Ventricles/sulci enlarged	3/10 (30%)	2/7 (29%)	6/7 (86%)
Ventricles/sulci normal	28/46 (61%)	13/27 (48%)	25/27 (93%)

^a Number of patients HIV(+) only.

^b Among patients who had both CSF culture and MR.

^c Among patients who had MR scans and analysis of intrathecal IgG synthesis and serum/CSF antibody ratios.

^d Assessment based on ventricular inspection.

reinterpreted as having DWM abnormalities. These data confirmed our impression that the MR diagnosis of early DWM lesions was unreliable and difficult to characterize. Because of this we did not attempt to correlate the presence of DWM lesions with immunologic, CSF, neurologic, or neuropsychologic test results.

Punctate Lesions. Scans were evaluated for the presence of punctate, or focal lesions, in regions other than basal ganglia (Fig. 4). Lesions within

the basal ganglia were difficult to distinguish from normal perivascular spaces; therefore, they were excluded from the analysis. Punctate lesions outside of the basal ganglia were found in 28 (43%) of 65 HIV(+) and 13 (33%) of 40 HIV(-) subjects (Table 3). There were no differences in size, signal intensity, or configuration of these small areas of signal change between the two study groups. Additionally, the presence or absence of non-basal ganglion punctate lesions did not correlate

TABLE 5: Ventricular measurements

	HIV(+) ^a (N = 53)	HIV(-) ^a (N = 27)	P Value
Third ventricle (mm)	4.84 ± 1.91	4.50 ± 1.54	.49
Third ventricle/cranium	0.04 ± 0.01	0.03 ± 0.01	.25
Third ventricle/brain	0.04 ± 0.01	0.04 ± 0.01	.36
Frontal horns-widest (mm)	32.75 ± 2.40	32.25 ± 2.69	.45
Frontal horns-widest/cranium	0.29 ± 0.02	0.28 ± 0.02	.17
Frontal horns-widest/brain	0.11 ± 0.03	0.10 ± 0.02	.13
Lateral ventricle-caudate (mm)	13.39 ± 3.27	12.31 ± 2.26	.29
Lateral ventricle/cranium	0.11 ± 0.02	0.10 ± 0.02	.27
Lateral ventricle/brain	0.11 ± 0.03	0.10 ± 0.02	.13

Note.—See text for details.

^a Mean ± standard deviation.

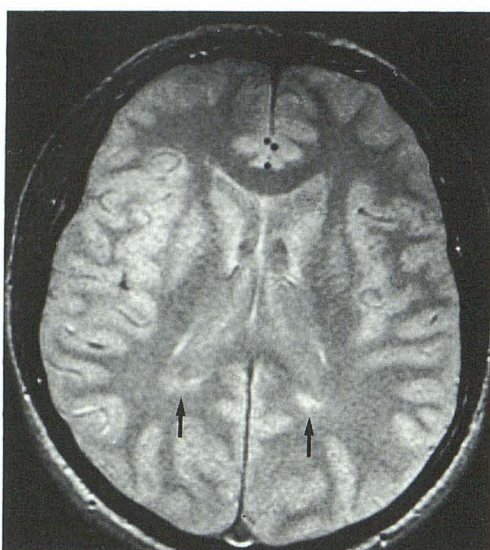


Fig. 3. Subtle, periventricular areas of increased T2 signal were quite difficult to diagnose and were commonly appreciated as small areas of increased signal with ill-defined borders. For example, in this subject they were noted posterior to the atria on the proton-density image (arrows).

to subjective assessment of ventricular size. However, within the group of HIV(+), those with non-basal ganglion punctate lesions were more likely to have mild enlargement of the lateral ventricle at the level of the caudate nucleus by linear measures ($P = .04$). Within the group of HIV(+) subjects, immunologic findings in CSF and blood were similar in those without and with non-basal ganglion punctate lesions (Table 5).

Mass Lesions. No subject had a noncongenital mass lesion. Two HIV(+) subjects had incidental arachnoid cysts.

Extracranial Changes. Adenoidal tissue within the nasopharynx was considered abnormal if it measured 10 mm or greater in thickness on a sagittal MR image, if patchy, increased signal was present on T2-weighted images, or if both crite-

ria were present (Fig. 5). Adenoidal tissue 10 mm or thicker was observed in 30 (46%) of 65 HIV(+) and two (5%) of 40 HIV(-) subjects ($P = .0001$). In HIV(+) subjects, adenoidal tissue 10 mm or thicker tended to be present in individuals with a history of generalized lymphadenopathy ($P = .13$). At the time of initial physical examination, HIV(+) patients with enlarged adenoids on MR were more likely to have palpable adenopathy in axillary, cervical, or occipital nodes than HIV(+) without enlarged adenoids (62% vs 49%), although this was not statistically significant. No other areas of adenopathy were noted on MR; however, the neck inferior to hyoid bone was not scanned. Absolute T4 and %T4 were lower in HIV(+) subjects with enlarged adenoids than in the remainder of HIVs(+) (Table 6); however, this did not reach statistical significance. Two HIV(-) subjects had enlarged adenoidal tissue without clear immunologic factors to explain this finding. One had acute pharyngitis at the time of the MR examination; the cause in the other remains unknown. In contradistinction to the adenoidal changes, the prevalence of inflammatory changes within the sinuses was similar in HIV(+) and HIV(-) subjects. Forty-nine (75%) of 65 HIV(+) and 27 (68%) of 40 HIV(-) individuals had mild mucosal thickening, increased fluid in the sinuses, or both findings visible on the MR examination. These findings were compatible with inflammatory sinus disease and could not be related to any other factors, such as a history of drug use, T4 count, or CDC group. No subject had either masses or areas of abnormal signal within the parotid glands.

Immunologic Studies/CSF Studies

Immunologic findings were compared in subjects with and without MR abnormalities, such as large ventricles, large sulci, or punctate lesions outside the basal ganglia. Findings on MR could not be related to differences in peripheral blood values of absolute T4 or %T4 either within either the group of HIV(+) or the group of HIV(-) subjects (Table 3). Similarly, in the HIV(+) subjects, the prevalence of positive cultures for HIV from CSF was unrelated to findings seen on the MR studies (Table 4). In the subgroup of patients who had measurement of daily intrathecal IgG synthesis and HIV p24 antibody, neither IgG synthesis >3 mg per day, nor ELISA serum/CSF p24 antibody ratio ≤ 5.5 , both taken to indicate

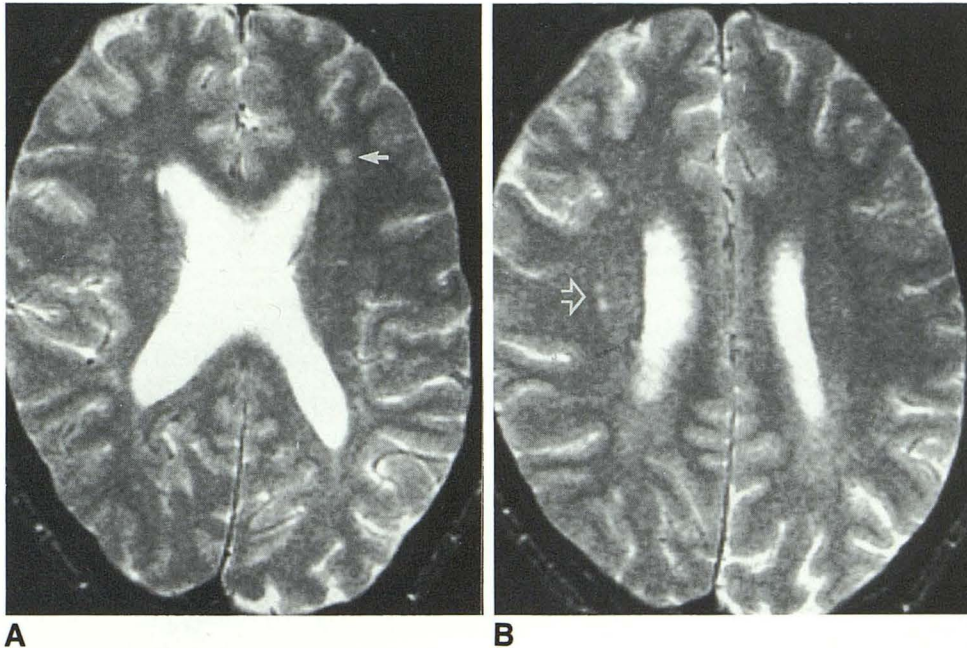


Fig. 4. A, Punctate focus of increased T2 signal (arrow) is visualized in the left frontal white matter in this 29-year-old HIV(+) subject. These findings, present in 43% of HIV(+) and 33% of HIV(-) subjects, were isointense on T1-weighted images and hyperintense on T2-weighted images.

B, These punctate foci were occasionally difficult to distinguish from perivascular spaces, seen in the right corona radiata (open arrow).

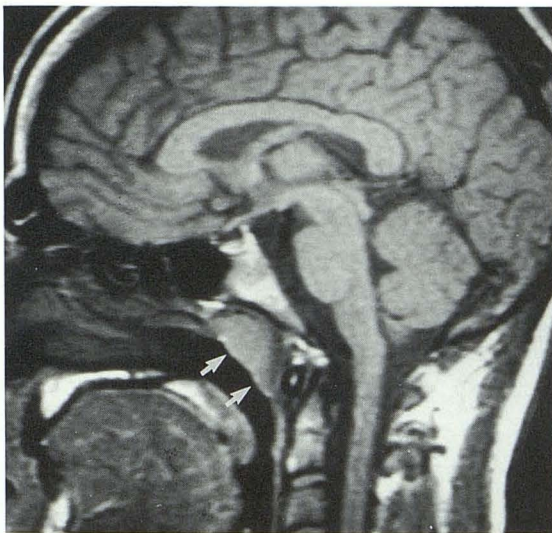


Fig. 5. Midline, sagittal T1-weighted MR image showing typical thickening of nasopharyngeal tissues (arrows). This tended to correlate to the presence of other palpable lymph node groups.

involvement of the CSF by HIV, could be correlated to the presence or type of MR abnormality.

Neurologic/Neuropsychologic Correlations

Patients were initially excluded if they had neurologic complaints elicited at the initial interview or known neurologic disease. Despite this, careful questioning by board-certified neurologist detected subjective complaints in 34 (52%) of 65 HIV(+)'s and nine (23%) of 40 HIVs(-). Minor neurologic signs were found in 25 (38%) of 65

HIV(+) subjects with MR and 24 (67%) of 36 HIV(-) subjects with MR. None of these findings causes clinically important impairment.

Neuropsychologic test scores in HIV(+) subjects with normal MR were compared with scores of HIV(+) subjects with specific MR abnormalities. There were no significant trends. The 11 HIV(+) subjects with mildly enlarged ventricles or sulci displayed delayed verbal memory (Selective Reminding Test-30-minute recall) compared to the 51 HIV(+) subjects with normal ventricles and sulci ($P = .03$). Nine HIV(-) subjects who had enlarged ventricles or sulci compared to the 26 HIV(-) subjects with normal MR examinations had decreased visuomotor scanning (Perceptual Speed Test, $P = .003$) and decreased cognitive flexibility (Trails-B seconds, $P = .05$) without other significant differences in neuropsychologic test scores. Mean neuropsychologic test scores demonstrated no correlations to ventricular size in either HIV(+) or HIV(-) subjects. The 26 HIV(+) subjects with punctate lesions outside the basal ganglia had fewer errors on the Wisconsin Card Sort test ($P = .02$) compared to the 36 HIV(-) without this finding. In the HIV(-) s, 10 subjects with punctate lesions outside the basal ganglia had reduced verbal fluency and initiative (Controlled Oral Word Association Test, $P = .02$) than the 25 subjects without this finding. There were no other mean neuropsychologic test results that showed statistically significant differences.

TABLE 6: Extracranial changes

	HIV(+) (N = 65)			HIV(-) (N = 40)		
	Number	Absolute T4 ^a (per mm ³)	%T4 ^a	Number	Absolute T4 ^a (per mm ³)	%T4 ^a
Normal adenoids (≤9 mm)	35 (54%)	544 ± 263	28.8 ± 10.9	38 (95%)	936 ± 296	45.7 ± 6.7
Enlarged adenoids (≥10 mm)	30 (46%)	461 ± 222	24.5 ± 9.2	2 (5%)	751 ± 57	42.0 ± 7.1
Sinus inflammatory changes	49 (75%)	525 ± 270	26.5 ± 11.0	27 (68%)	911 ± 327	45.2 ± 7.1
Normal sinuses	16 (25%)	446 ± 150	27.7 ± 8.1	13 (32%)	957 ± 205	46.2 ± 5.8

^a Mean ± standard deviation.

Discussion

CNS abnormalities in HIV(+) subjects have been evaluated in several recent cohort studies using cranial MR as well as clinical evaluation methods. Results of these studies have differed. Grant et al, using MR, found atrophy and abnormal areas of increased white matter signal on T2-weighted images in 14 of 29 HIV(+) patients with AIDS (12). Levin et al compared 25 patients in CDC groups II, III, and IV to demographically similar seronegative subjects (13). Cerebral atrophy, based on measures of CSF volume obtained from MR studies, correlated with CDC stage and with a measurable slowing in the rate of information processing on neuropsychologic testing. There were no correlations between the presence of focal lesions and CDC stage or neuropsychologic findings. McArthur et al limited MR examinations to 25 seronegative and 35 seropositive subjects who had abnormal results on a neurologic/neuropsychologic screening battery (6). Focal areas of increased T2 signal present in four seropositive and 1 seronegative patient and increased sulcal prominence in one seronegative subject were the only abnormalities reported. Only two of the subjects who underwent MR also had evaluation of the CSF. Koralnick et al reported the results of electrophysiologic, neurologic, and MR (0.35 T) studies of two groups of homosexual men, 29 who were seropositive and 33 seronegative for HIV infection (7). Minimal neurologic or MR abnormalities were found in either group. Post et al, in a prospective study of 24 neurologically symptomatic and 95 asymptomatic HIV(+) subjects, found that cranial MR studies showed few abnormalities in asymptomatic HIV(+) subjects (14). No HIV(-) subjects were imaged in this study.

We performed a comprehensive neurologic, neuropsychologic, and immunologic evaluation in a group of HIV(+) subjects irrespective of functional status. Due to cost considerations, MR was performed in a subset of HIV(+) subjects.

We correlated MR findings to neurologic and neuropsychologic function and were able to compare these findings to similar results in a demographically similar HIV(-) group.

A small proportion of our population had abnormal MR examinations. Abnormalities included mildly enlarged ventricles, mildly enlarged sulci, or prominent punctate foci of increased T2 signal. None of the subjects had mass lesions. Neither neurologic, neuropsychologic, nor immunologic status could be related to any imaging finding. Enlarged ventricles, sulci, or both were present in 18% of our HIV(+) subjects and 25% of our HIVs(-). Punctate regions of increased T2 signal, presumed to be prominent perivascular spaces, were present in 43% of HIV(+) and 33% of HIV(-) subjects. Our rate of detection of MR abnormalities was lower than the 69% reported by Grant et al (12). This probably reflects our examination of a group of patients at an earlier stage of HIV infection. In Grant's study, MR was performed in patients whose mean T4 values were less than 200/mm³, while patients with higher T4 counts and no symptoms did not undergo MR (12). Similar to our results, McArthur et al found no significant MR differences between his groups of seropositive and seronegative subjects (6) and Post et al demonstrated a low rate of MR abnormalities in their HIV(+) subjects (14). Additionally, our study design permitted us to correlate immunologic measurements in both blood and CSF to MR findings. In HIVs(+), neither the presence of HIV by culture nor the presence of detectable antibody to HIV within the CSF could be related to changes on cranial MR.

The presence of regions of increased T2 signal in the periventricular white matter has been mentioned by others. Correlating premortem MR with autopsy specimens led Post et al to suspect that the DWM lesions represented demyelination (5). Balakrishnan et al found astrocytosis associated with myelin pallor in early HIV disease, while gliosis, macrophage infiltration, and multinuclea-

ted giant cells correlated to more extensive regions of increased T2 white matter signal without mass effect (15). Olson et al noted either a diffuse or a patchy pattern of increased white matter signal on T2-weighted images in 82 of 365 patients. This was attributed to HIV infection in 27 patients who clinically had the AIDS dementia syndrome (16). In a prospective evaluation of HIV(+) individuals by Post et al, 20 (17%) of 119 subjects had white matter lesions, although none were considered diffuse. Small focal lesions were not distinguished from larger lesions (14). These previous reports, however, did not note that subtle, early signal changes of DWM lesions in patients seropositive for HIV may be difficult to distinguish from normal white matter using high-field MR. Once we realized this difficulty, we attempted to document our observation by testing, in a blinded fashion, the reliability of our diagnosis of DWM lesions in a subgroup of 14 subjects. Our initial diagnostic impression changed in 3/10 seropositives. In general, areas of abnormal signal that we consistently felt to represent DWM lesions were found in the parietal lobes and forceps major. However, restricting lesion identification to this anatomic localization alone did not improve the reproducibility of our diagnosis. Subtle DWM lesions remained difficult to identify. It remains possible that clearly identifiable DWM lesions may be present with more severe disease. Our study, which focused on minimally symptomatic subjects in this initial phase, would include few of these individuals. Our ongoing longitudinal examination of this group will test this hypothesis.

Linear measurements of the ventricles, brain, and calvaria using procedures previously described by Hahn et al and Lemay et al were made in an attempt to quantitate variations in ventricular size in this group of HIV(+) and HIV(-) men (17, 18). We also compared the results of our subjective visual assessment of ventricular size to the measured sizes. We found that subjective visual inspection correlated well with linear measurements of ventricular size, as has been noted previously (19). Linear measurements provide a quantitative reproducible evaluation; nevertheless, we realize that linear measures are fraught with potential error due to lack of standardization of the areas measured, volume averaging, difficulties defining edges, and a large range of sizes in normal populations. Additionally, in HIV infection, tissue loss may occur in, as yet, unpredictable locations, which may result in ventricular

measurements being performed at locations inappropriate for detection of decreased number of cells. Software was not available to reliably perform volume measures.

Grant et al and Olson et al described focal punctate lesions in patients with AIDS or ARC (12, 16). We currently feel that most of the lesions that we identified as punctate foci are, in reality, prominent perivascular spaces. These have now been shown to be present in the midbrain as well as in the basal ganglia (20). Even though this type of lesion is more common in older patients (>50 years) the high incidence of these foci in the HIV(-) group supports our belief that the lesions have no pathologic significance. McArthur et al also recently suggested that the focal areas of increased T2 signal without mass effect did not appear to relate to neuropsychologic abnormalities (21). It is possible, however, that these lesions are predecessors of brain pathology, a possibility that will be clarified by longitudinal analysis.

Neuropsychologic evaluation of our minimally symptomatic HIV(+) population showed a trend toward slowed completion of perceptual tasks in HIV(+) subjects, while neurologic evaluation demonstrated mild cranial nerve and sensory abnormalities present in both HIV(+) and HIV(-) individuals. At the univariate level of analysis, we are in close agreement with recent multicenter studies which have also suggested that subjects seropositive for HIV do not evidence significant increase in neuropsychologic impairment over HIV seronegative controls (7-9, 22, 23). It is not as well established whether asymptomatic HIVs(+) will differ from HIVs(-) in analysis based upon domains of cognitive function corrected for confounding variables such as educational levels.

Enlarged adenoids and increased T2 signal in the nasopharyngeal soft tissues tended to correlate inversely with T4 values, were often associated with lymphadenopathy by history, and tended to be present in patients with palpable adenopathy and lower T4 values. Barzan et al found similar correlations in 66 HIV(+) patients who underwent clinical assessment of nasopharyngeal tissues (24). We felt that nasopharyngeal changes were a manifestation of generalized lymphadenopathy. The presence of sinus involvement, although frequently present, appeared to be unrelated to HIV status in this group of seropositive and seronegative subjects.

A number of conclusions can be drawn from early review of our study group: 1) MR is normal

to minimally abnormal during early stages of HIV infection. 2) Subtle neuropsychologic abnormalities do not statistically correlate with abnormalities on MR. 3) The abnormal white matter changes, consisting of diffuse increased signal that have been reported by others in HIV(+) persons, were uncommon in our study population and, more importantly, could not be reliably identified. 4) Sixty-two percent of our HIV(+) subjects without ongoing opportunistic infections demonstrated enlargement of adenoidal tissue. This most likely represents a manifestation within the nasopharynx of the more generalized lymphadenopathy present in this population.

This is an ongoing longitudinal study. The patients currently entered into the study will be reevaluated at 6-month intervals for 3–5 years. Serial MR examinations of these patients should yield information regarding the clinical course of CNS involvement with HIV infection.

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