MRI Contributes to the Differentiation Between MS and HTLV-I Associated Myelopathy in British Columbian Coastal Natives

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ABSTRACT: *Background:* Human T-cell lymphotropic virus type I (HTLV-I)-associated myelopathy/tropical spastic paraparesis (HAM/TSP) in British Columbian Coastal Natives has, to date, been a clinical and laboratory diagnosis. However, magnetic resonance imaging (MRI) abnormalities have been well-described in other populations in which HAM/TSP is endemic. *Methods:* In order to assess the usefulness of MRI as a diagnostic tool in this population, we compared scans of HAM/TSP patients with those of HTLV-I positive non-HAM/TSP British Columbian Coastal Natives (carriers) and multiple sclerosis patients presenting with progressive paraparesis. *Results:* The typical nonspecific findings of thoracic cord atrophy and increased signal in the periventricular and subcortical white matter on T2-weighted images were confirmed in the HAM/TSP patients. Despite a lack of specificity of the MRI findings between HAM/TSP patients and HTLV-I carriers, criteria that could effectively differentiate HAM/TSP patients from multiple sclerosis patients with similar clinical presentations were determined. *Conclusions:* Clinical and radiological correlations suggest that longitudinal MRI investigations charting the course of HAM/TSP may reveal the clinical significance of these lesions and further define the role of MRI in the diagnosis of this entity. Magnetic resonance imaging is an important supplement to immunological and clinical data in differentiating multiple sclerosis from HAM/TSP.

RÉSUMÉ: L'IRM contribue à la différentiation de la MS et de la myélopathie associée au HTLV-1 chez les autochtones de la région côtière de la Colombie Britannique. *Contexte:* La myélopathie associée au HTLV-1/paraparésie spastique tropicale (HAM/TSP) chez les autochtones de la région côtière de la Colombie Britannique était jusqu'à ce jour un diagnostic basé sur la clinique et le laboratoire. Cependant, les anomalies observées à l'imagerie par résonance magnétique (IRM) ont été bien décrites dans d'autres populations chez qui le HAM/TSP est endémique. *Méthodes:* Nous avons comparé les scans de patients atteints de HAM/TSP avec ceux de patients autochtones de la région côtière de la Colombie Britannique HTLV-1 positifs sans HAM/TSP et de patients atteints de sclérose en plaques (SEP) présentant une paraparésie progressive afin d'évaluer l'utilité de l'IRM comme outil diagnostique dans cette population. *Résultats:* L'atrophie de la moelle thoracique et l'augmentation du signal dans la substance blanche périventriculaire et sous-corticale sur les images pondérées en T2, qui sont des observations non spécifiques typiques, ont été confirmées chez les patients atteints de HAM/TSP. Malgré le manque de spécificité des observations à l'IRM entre les patients atteints de HAM/TSP et les porteurs de HTLV-1, des critères qui pourraient permettre de différentier les patients atteints de HAM/TSP des patients atteints de SEP présentant un tableau clinique similaire ont été établis. *Conclusions:* Des corrélations cliniques et radiologiques suggèrent que l'investigation longitudinale par IRM documentant l'évolution de la HAM/TSP peut révéler la signification clinique de ces lésions et aider à définir le rôle de l'IRM dans le diagnostic de cette maladie. L'IRM ajoute de l'information supplémentaire importante aux données immunologiques et cliniques pour distinguer la SEP de la HAM/TSP.

Human T-cell lymphotropic virus type I (HTLV-I)-associated myelopathy/tropical spastic paraparesis (HAM/TSP) is a chronic viral-induced neurological disorder.[1,2] It is considered endemic in populations in Japan, the West Indies, the Seychelles, and Colombia.[3,4] HTLV-I infection of an endemic level with disease association has most recently been described in North America, among British Columbian Coastal Natives.[5,6] Regardless of geography, the clinical picture of HAM/TSP is consistent and includes a triad of (i) motor dysfunction (spasticity and weakness of the legs, with increased tone and extensor plantar responses), (ii) sensory dysfunction (pain of the neuritic type at the level of the back, which is often the initial manifestation,[7] and minor sensory deficits in the legs), and (iii) bladder dysfunction (neurogenic bladder with chronic retention).[8] Satisfaction of the

above clinical criteria together with HTLV-I immunoreactivity in the serum confirm the diagnosis of HAM/TSP.[9]

Several authors have described typical magnetic resonance imaging (MRI) findings of thoracic cord atrophy[10-13] in up to 74% of patients[14] and increased signal in periventricular and subcortical white matter.[15-18] The nonspecific nature of these findings, which occur in as many as 58% of patients with HAM/TSP on cranial MRI, has been discussed.[8] Ogata et al[19] suggested that abnormalities seen on MRI in patients with multiple sclerosis are indistinguishable from those seen in HAM/TSP patients. Other studies have stressed specific criteria in evaluating the MRI image to differentiate the areas of increased signal in multiple sclerosis (MS) and HAM/TSP by location, number, and size of the lesions.[20,21] These criteria include more extensive abnormalities on MRI of the brain and cervical spine in MS, such as: focal increases in signal intensity in posterior fossa structures and the cervical cord;[12] irregular extensions of periventricular signal changes into the deep white matter;[22] more than three lesions larger than 3 mm;[23] a single lesion larger than 5 mm;[24] a periventricular lesion larger than 3 mm.[25] Godoy et al[26] found that patients with primary progressive MS, a form of MS most similar to HAM/TSP clinically, had a considerably greater number of lesions in all brain regions than HAM/TSP patients. The MRI lesions reported in HAM/TSP have also been compared to[27] and distinguished from[28] those seen in healthy carriers of the HTLV-I virus. Opinions also differ on whether HAM/TSP patients' lesions can be effectively distinguished from signal changes due to aging, collagen vascular disease, or small lacunar infarcts.[26,28,29] There is still considerable debate about the correlation between the extent of cerebral MRI abnormalities and the severity of the spastic paraparesis in HAM/TSP,[25,28] as well as the correlation between spinal cord atrophy and the duration of disease.[30]

These questions concerning the use of MRI in HAM/TSP have yet to be asked in the British Columbian Coastal Natives. Our objectives were to describe any MRI abnormalities; to test the sensitivity of MRI in diagnosing HAM/TSP in this population; to apply the existing MRI criteria to the differentiation of HAM/TSP, MS, and HTLV-I carriers in order to examine the specificity of the MRI lesions seen in HAM/TSP; and to correlate the degree of abnormalities seen on MRI with the severity of disease. We retrospectively reviewed MRIs of patients at various stages of HAM/TSP, seropositive family members or contacts of these HAM/TSP patients who did not satisfy criteria for HAM/TSP, and patients with MS who presented with a progressive paraparesis clinically resembling the picture of HAM/TSP.

MATERIALS AND METHODS

Twelve patients with HAM/TSP, nine non-HAM/TSP HTLV-I carriers, and 13 MS patients with progressive paraparesis who attended the clinics at the University of British Columbia were studied. All patients and carriers had clinical examinations, MRI, and cerebrospinal fluid (CSF) or serum enzyme-linked immunoabsorbant assay (ELISA) studies performed. All tests for the presence of antibodies in serum and CSF using ELISA technique or Western blot were confirmed, and all polymerase chain reaction (PCR) amplifications of viral DNA from blood

and CSF were performed in Dr. G. Dekaban's laboratory at the John P. Robarts Research Institute in London, Ontario.[31]

Patients with HAM/TSP were classified according to their Expanded Disability Status Scale (EDSS) of Kurtzke.[32]

Magnetic resonance imaging scans from seven centres using a variety of scanners (0.15 Tesla to 1.5 Tesla) were available for review. A number of pulse sequences were used, with all patients having at least a conventional spin echo or fast spin echo proton density and T2 images (TR, repetition time = 2000-2729 msec; $TE(eff)_1$, echo time = 17-60 msec; $TE(eff)_2$ = 90-150 msec). The hard copy films of the MRI examinations of head, cervical cord, and thoracic cord were separately examined, in random order, by one of us (D.L.), who was blinded to the clinical details of the cases. The cord MRIs were examined for the presence of diffuse atrophy (resolution would not allow more focal measurements) and areas of increased signal intensity. The cranial MRIs were analyzed for the location (brainstem, cerebellum, corpus striatum, white matter, periventricular), number, and size of lesions using criteria previously reported.[20,23,25] These were: 1) at least one lesion larger than 6 mm; 2) presence of three or more lesions larger than 3 mm; 3) at least one periventricular lesion larger than 3 mm; and 4) at least one infratentorial lesion larger than 3 mm. A diagnosis probable for MS by Paty criteria was defined as the presence of three or more white matter lesions greater than 3 mm.[23] A diagnosis of MS by Fazekas criteria was defined as three areas of increased signal with at least two of the following: 1) a lesion abutting the lateral ventricle; 2) an infratentorial lesion; 3) a lesion exceeding 5 mm in size.[24] Of note is that part of the Fazekas criteria have now been incorporated in the McDonald International Panel's criteria for the diagnosis of MS.[33]

The extent of white matter lesions was classified by number and by size (0=no lesions; 1=one lesion; 2=multiple lesions extending beyond one lobe; 3=confluent lesions forming multiple large patches), and the extent of periventricular lesions by degree of extension (0=no lesions; 1=discontinuous lesions – bilateral, symmetrical, rounded foci of hyperintensity in the anterior horns or anterior to the ventricles; 2=continuous lesions – diffuse continuous hyperintensity surrounds the ventricles; 3=periventricular halo – smooth halo of hyperintensity completely surrounds the bodies of the lateral ventricles; 4=diffuse white matter abnormality – diffuse periventricular hyperintensity with irregular lateral margins) as in prior studies.[16]

The sensitivity and specificity of MRI as a diagnostic test in HAM/TSP was assessed by comparing the incidence of cord atrophy and increased signal on cervical and thoracic cord MRIs, and the frequency, number and location of areas of increased signal on head MRIs in HAM/TSP patients with carriers, using the chi-square test. In order to determine the usefulness of the MRI criteria documented to distinguish MS and HAM/TSP, we calculated the statistical difference in the incidence of each criterion between the HAM/TSP and MS patients using the chi-square test, and calculated the sensitivity and specificity of each criterion individually and of combinations of the criteria. We used a one-way analysis of variance to assess any differences in the extent of MRI abnormalities between the three patient groups, within age subgroups, and within HAM/TSP symptom severity subgroups. Statistical significance was reached if $p<.05$. For combinations of criteria, p was appropriately reduced.

Table 1: Demographic and virology data of the three subject groups

	HAM/TSP patients (12)	Non-HAM/TSP HTLV-I carriers (9)	MS progressive paraparesis patients (13)
Males	4 (33%)	3 (33%)	8 (62%)
Females	8 (67%)	6 (66%)	5 (38%)
Coastal Natives	11 (91%)*	9 (100%)	1 (8%)
Mean age of onset of disease (range)	48 yrs. (19-68) s.d.=14	N.A.	37 yrs. (15-56) s.d.=12
Duration of symptoms before MRI	6 yrs.	N.A.	12 yrs.
Mean age at time of MRI (range)	54 yrs. (33-75) s.d.=13	48 yrs. (30-62) s.d.=9	49 yrs. (32-65) s.d.=9
HTLV-I serology	12/12	9/9	0/13
PCR on blood	11/11	6/8	0/10
CSF serology	11/11	2/5**	Not done
PCR on CSF	5/7	1/4**	Not done

N.A.   Not applicable

*   significant difference between HAM/TSP and MS group, p<.005 (chi-square test)

**   no clinical evidence of HAM/TSP despite presence of HTLV-I antibodies or virus in the CNS

Table 2: Clinical data of the three subject groups

	HAM/TSP patients (12)	Non-HAM/TSP HTLV-I carriers (9)	MS myelopathy Patients (13)
Symptoms			
Leg weakness	11 (92%)[+]	2 (22%)*	9 (69%)
Urinary urgency, incontinence	10 (83%)[+]	2 (22%)**	8 (62%)
Lumbar, buttock, or leg pain	9 (75%)[+]	3 (33%)***	7 (54%)
Paraesthesiae:			
Lower extremities	7 (58%)[+]	1 (11%)	3 (23%)
Upper extremities	3 (25%)	1 (11%)	6 (46%)
Signs			
Spastic gait	10 (83%)[+]	— (0)	7 (54%)
Increased tone	10 (83%)[+]	22% (2)	8 (62%)
Upgoing plantar response‡	9 (75%)[+]	1 (11%)****	10 (77%)
Increased knee-jerk reflex	9 (75%)[+]	2 (22%)*****	11 (85%)
Decreased ankle-jerk reflex	2 (17%)	1 (11%)	2 (15%)
Sensory deficits	7 (58%)[+]	— (0)	6 (46%)

[+]   significant difference (p < .05) between HAM/TSP and HTLV-I carriers, chi-square test

*   includes one patient with polymyositis and one patient with MCA stroke

**   includes one patient with a neurogenic bladder due to cauda equina compression, and one patient with chronic urinary retention (with no neurogenic component on urodynamic studies)

***   includes one patient with musculoskeletal chronic back pain, one patient with disc herniations and lumbar stenosis, and one patient with disc pain and leg cramps

****   includes one patient with MCA stroke with a unilateral upgoing toe

*****   includes brisk reflexes in one asymptomatic carrier and hyperactive reflexes in one patient with MCA stroke

‡   of note is the relative frequency of a normal plantar response even in this group of spastic paraparesis

RESULTS

Clinical

Demographic and virology data are summarized in Table 1.

On clinical examination, eight of the HAM/TSP patients had Kurtzke scores of 6.0 or less at the time of their MRI scans, while five of the HAM/TSP patients had Kurtzke scores of 6.5 or more. One patient who had scans taken three years apart was represented in both groups.

The 13 patients in the MS group presented to the MS clinic with a history of a chronic progressive paraparesis and were diagnosed with clinically probable MS as previously defined.[34] Five of the MS patients had vague past histories of an additional previous attack and their courses could be described as secondary progressive. They were not, however, excluded from the study as the lack of a clearly defined previous relapse maintained primary progressive MS as a possible diagnosis at the time of MRI. All of the MS patients were negative for HTLV-I antibodies by ELISA. Three characteristics differentiated the paraparesis of HAM/TSP from that of primary MS: the intensity of spasticity relative to motor deficit, the subtleness of sensory findings, and the high frequency of bladder dysfunction. However, there were no significant differences in the incidence of symptoms or signs between the HAM/TSP and MS myelopathy groups (Table 2). Complaints of leg weakness, bladder dysfunction, back and leg pain, and evidence of hyperreflexia occurred in some carriers due to polymyositis, lumbar disc disease, diabetic neuropathy, and hemiparesis from middle cerebral artery stroke.

MRI abnormalities (Table 3)

Cord

Magnetic resonance imaging demonstrated a significantly higher frequency of abnormalities of the cervical cord of patients with MS than patients with HAM/TSP or carriers (Figure 1). Although the cervical cord of four of eight HAM/TSP patients were abnormal (Figure 2) while none of the carriers' cervical cords were abnormal, the difference was not statistically significant.

Abnormalities on MRI of the thoracic cord were seen in five of eight HAM/TSP patients. Three of four carriers and three of four MS patients also had abnormal scans and there were no statistically significant differences between the groups.

Brain

All of the HAM/TSP and MS patients and 78% of the carriers who had MRI of the brain had at least one area of increased signal (Figure 3). As a group, the MS patients had a significantly greater number of lesions (mean 13.7) than HAM/TSP patients (mean 3.9) and HTLV-I carriers (mean 3.5). Although the groups did not differ significantly in the extent of the subcortical or periventricular lesions, brainstem lesions were significantly more common in MS patients than in HAM/TSP patients, while periventricular halos were more common in HAM/TSP patients. White matter and periventricular lesions were common in both HAM/TSP patients and carriers. Although periventricular lesions larger than 3 mm were found twice as often in HAM/TSP patients than in carriers, there was no statistically significant difference between the number or location of white matter lesions in the HAM/TSP patients compared with the carriers.

The correlation between age and number of lesions on head MRI in the HAM/TSP patients and HTLV-I carriers yielded a Spearman's r (rank correlation) of only .10; the three patients over the age of 60 had a higher mean number of lesions than the 17 patients under the age of 60 in the HAM/TSP and HTLV-I carrier groups (p<.05).

Specificity of brain lesions: MS and HAM/TSP

Four parameters were studied in an attempt to differentiate white matter lesions seen on MRIs of the head of HAM/TSP patients and MS. All of the criteria and all possible combinations of the criteria were found at a higher frequency in the MS patients than in the HAM/TSP patients, including two commonly used criteria: Paty and Fazekas criteria (Table 4). The most specific criteria for MS was a combination of a lesion greater than 6 mm and an infratentorial lesion greater than 3 mm (Figure 4). The permutation with the highest combined sensitivity and specificity for MS patients' lesions was a combination of a lesion greater than 6 mm and a periventricular lesion greater than 3 mm.

Clinical and radiological correlations in HAM/TSP

When HAM/TSP patients were segregated by severity of disability (EDSS < 6.0 and EDSS ≥ 6.5), those with more severe disease had twice the number of white matter lesions (5.2 ± 4.3 vs. 2.6 ± 1.5) and more extensive periventricular abnormalities (mean score 2.0 ± 1.4 vs. 1.2 ± 1.1), but those differences were not significant. One patient who had two MRIs three years apart showed an increase in the number of white matter lesions from 3 to 11.

DISCUSSION

This is the first study to compare the specificity of MRI abnormalities in British Columbian Coastal Natives with HAM/TSP and in patients presenting with the progressive paraparetic MS. A number of our HAM/TSP patients were originally thought to have MS, which further exemplifies the clinical significance of this differential diagnosis. Our study demonstrated that having a lesion greater than 6 mm on MRI of the head and an infratentorial lesion greater than 3 mm is reliably predictive of MS rather than HAM/TSP. Our results also support previous studies indicating that brainstem lesions, large periventricular lesions, and cervical spine hyperintensities are more characteristic of MS than HAM/TSP.[12,22,26] Fazekas criteria, which have been used to differentiate MS from HAM/TSP in Japanese patients, were confirmed in our population, although the criteria proved somewhat less effective in our British Columbian Coastal Native population (80% specificity, 73% sensitivity) than previously reported by Offenbacher et al[20] in Japanese patients (96%, 81% respectively). When we applied Paty criteria, MS patients and HAM/TSP patients were also correctly distinguished a significant proportion of the time (specificity 70%, sensitivity 73%), although again less effectively than in Japanese patients as reported by Kuroda et al[25] (93%, 86% respectively).

While MRI is helpful in differentiating patients with MS and HAM/TSP when read by a radiologist blinded to clinical details, our results indicate that MRI plays a more limited role in the actual diagnosis of HAM/TSP. Magnetic resonance imaging
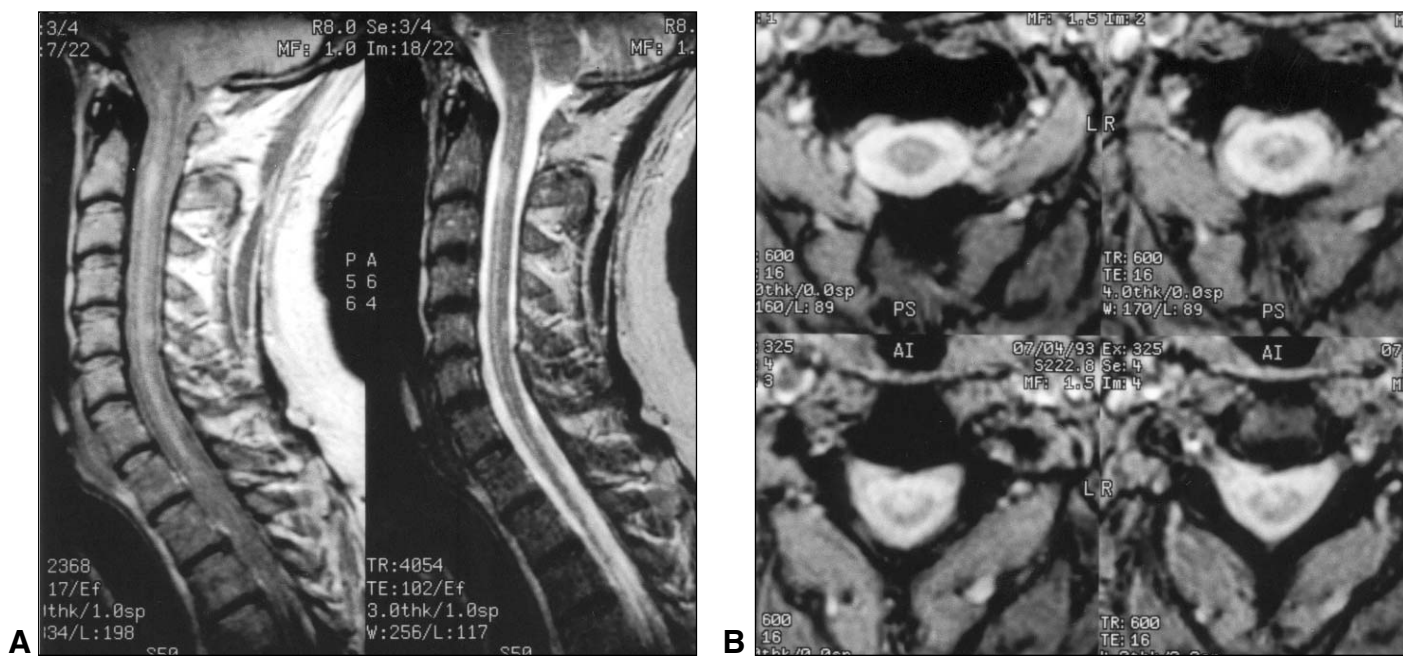
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*Figure 1: Increased signal is shown in proton density and T2-weighted sagittal (**a**) and T2-weighted axial (**b**) MRIs of the cervical cord in a 49-year old Caucasian with a chronic progressive MS who presented with bilateral leg weakness, bilateral paraesthesiae, and a spastic paraparetic gait. This finding was present in all the MS patients studied and in only three of eight HAM/TSP patients.*
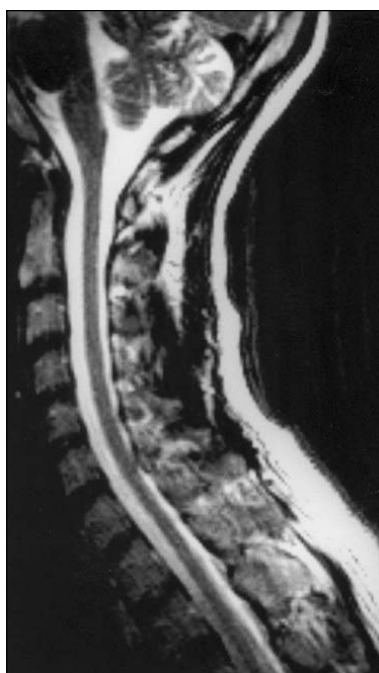

Figure 2: T2-weighted sagittal MRI of the cervical cord demonstrates atrophy in a 32-year old patient with urinary retention, spastic paraparesis, and HTLV-I detectable in the CSF. This finding has been described previously in HAM/TSP. Atrophy was found at a similar rate in the MS patients we studied.
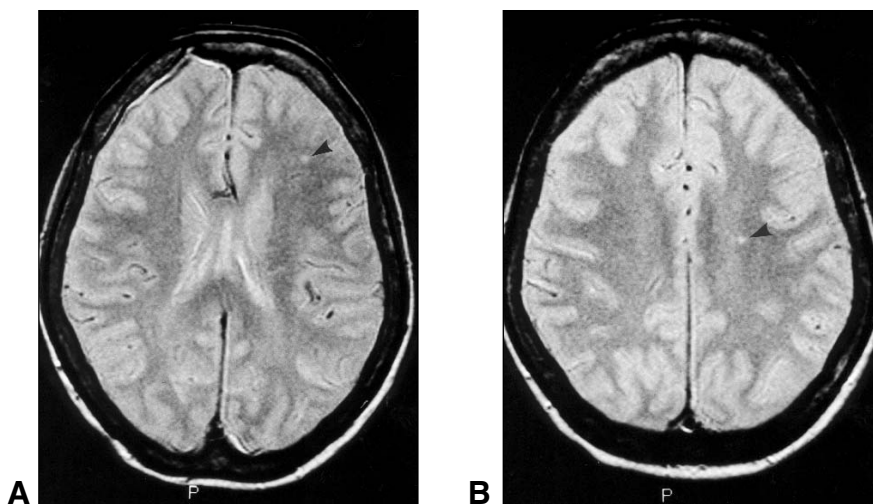

*Figure 3 (**a**) and (**b**): Proton density axial MRIs of the head show two areas of increased signal (arrows) in the cerebral white matter of a 45-year old patient with a spastic, wide-based gait, urinary symptoms, and CSF positive for HTLV-I.*

abnormalities were consistently present where there was clinical disease. These lesions, in order of most to least common, were increased signal in periventricular regions on MRI of the head; increased signal in subcortical white matter regions on MRI of the head; atrophy of the thoracic cord; increased signal in the cervical cord; increased signal in the thoracic cord; and atrophy of the cervical cord. The frequency of these patterns of MRI abnormalities in our patients reflects what has been reported

Table 3: MRI data from the three subject groups

	HAM/TSP Patients (12)	HTLV-I carriers (9)	MS myelopathy patients (13)
Cervical cord –			
# examined	8	4	8
Increased signal	3 (38%)	0 (—)	8 (100%)*
Atrophy	1 (13%)	0 (—)	2 (25%)
Thoracic cord -			
# examined	8	4	4
Increased signal	2 (25%)	2 (50%)	2 (50%)
Atrophy	4 (50%)	3 (75%)	2 (50%)
Head –			
# examined	10**	9	11
Normal scans	0 (—)	2 (22%)	0 (—)
Areas of increased signal:			
Brainstem	1 (10%)	2 (22%)	6 (55%)***
Cerebellum	0 (—)	0 (—)	1 (9%)
Corpus striatum	0 (—)	4 (44%)****	3 (27%)
White matter	7 (70%)	7 (77%)	9 (82%)
Periventricular	8 (80%)	4 (44%)	11 (100%)*****

*   significant difference between MS group and HAM/TSP group; p<.01, chi-square test
**   9 HAM/TSP patients had cranial MRIs; one patient had 2 scans 3 years apart
***   significant difference between MS group and HAM/TSP group; p<.05, chi-square test
****   significant difference between carrier group and HAM/TSP group; p<.05, chi-square test
*****   significant difference between MS group and carrier group; p<.025, chi-square test

Table 4: Criteria differentiating cranial MRI of HAM/TSP and MS patients

Criteria	HAM/TSP patients (10)	MS patients (11)	Sensitivity of criteria for MS	Specificity of criteria for MS	Chi-square test: MS vs. HAM
I. 1 lesion > 6 mm	3 (30%)	10 (91%)	91%	70%	p<.01
II. 3 lesions>3 mm	3 (30%)	8 (73%)	73%	70%	p<.05
III. 1 periventricular lesion > 3 mm	6 (60%)	11 (100%)	100%	40%	p<.025
IV. 1 infratentorial lesion > 3 mm	1 (10%)	6 (55%)	55%	90%	p<.05
I. and **II.**	2 (20%)	8 (73%)	73%	80%	p<.025*
I. and **III.**	2 (20%)	10 (91%)	91%	80%	p<.001
I. and **IV.**	0 (—)	6 (55%)	55%	100%	p<.01
II. and **III.**	3 (30%)	8 (73%)	73%	70%	p<.05*
II. and **IV.**	1 (10%)	6 (55%)	55%	90%	p<.05*
III. and **IV.**	1 (10%)	6 (55%)	55%	90%	p<.05*
I. II. and **III.**	2 (20%)	8 (73%)	73%	80%	p<.025*
I. II. and **IV.**	0 (—)	6 (55%)	55%	100%	p<.01
II. III. and **IV.**	1 (10%)	6 (55%)	55%	90%	p<.05*
I. II. III. and **IV.**	0 (—)	6 (55%)	55%	100%	p<.01
Suggestive of MS:					
Fazekas criteria (**II** + 2 of: **I, III, IV**)	2 (20%)	8 (73%)	73%	80%	p<.025
Suggestive of MS: Paty criteria (**II**)	3 (30%)	8 (73%)	73%	70%	p<.05

* not statistically significant (combined probabilities not originally hypothesized) unless p<.01
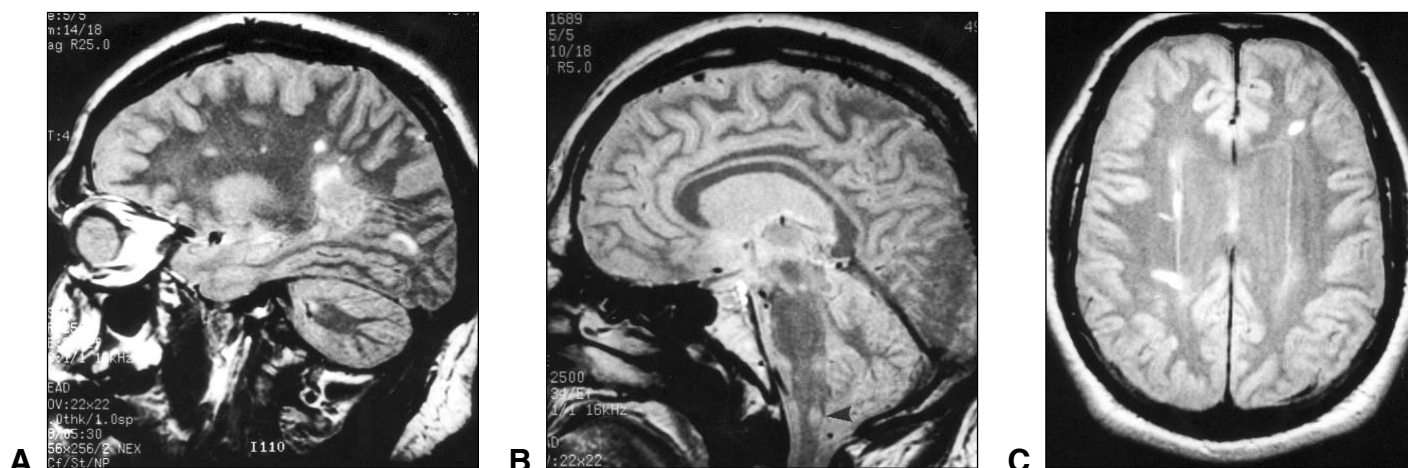
Figure 4: *Proton density sagittal (**a** and **b**) and axial (**c**) MRIs of the head of a 50-year old British Columbian Coastal Native. Multiple white matter abnormalities including a lesion > 6 mm, a brainstem lesion (arrow), and a periventricular lesion > 3 mm make these images suggestive by both Paty and Fazekas criteria of multiple sclerosis. The patient presented with a progressive myelopathy and a family history positive for HAM/TSP despite having CSF and serum that tested negative for HTLV-I.*

from other areas of the world.[10,12,14,15] In some reports, patients with clinical disease have had normal scans[8] or atypical features such as cord swelling,[30] but this was not seen in our study. This may be due to the fact that the disease presents later or is detected later in British Columbian Coastal Natives and therefore the clinical picture may be more advanced in the subjects whose scans we analyzed.

The lack of significant differences between HAM/TSP patients and nonaffected carriers implies that lesions seen on MRI in HAM/TSP may not be indicative of the underlying pathology. This agrees with a previous study that found brain lesions on MRI in an asymptomatic seropositive individual.[27] We found a trend towards a greater frequency of increased signal in the cervical spine and periventricular region in HAM/TSP patients than in carriers, findings similar to those reported when comparing HAM/TSP patients with those with other neurological disease, particularly spondylitic myelopathy and spinocerebellar degeneration.[26] However, nonspecificity is consistent among studies of MRI in HAM/TSP.[15,17] It has been suggested that, if one controls for age and cerebrovascular risk factors, patients under 60 with HAM/TSP have a higher incidence of multiple deep and subcortical white matter lesions than non-HAM/TSP carriers.[28] As predicted, patients over 60 in our study did have more white matter lesions than those under 60, even though we did not control for cerebrovascular risk factors. However, we found no significant difference in the number of white matter lesions between the HAM/TSP patients and HTLV-I carriers in the British Columbian Coastal Natives, regardless of age.

Due to the already small sample size, patients were not selected that had disease attributed to HAM/TSP alone. In several of the HAM/TSP patients, spondylotic changes and spinal stenosis were evident on MRIs of the cervical spine. As well, although the diagnosis of HAM/TSP had been excluded in the carriers on a purely clinical basis, neurological complaints were not uncommon. Therefore subclinical disease, even early HAM/TSP, and other neurological pathology might have been

responsible for some of the abnormalities seen on the carriers' MRIs, for example the thoracic cord abnormalities and the four MRIs that demonstrated corpus striatum lesions.

It has been suggested that the degree of disability, using the Kurtzke scale, and the length of the history of disease, but not the age of onset, are related to the number (more than two) and appearance of brain lesions.[28] We did see one patient who progressed clinically and had a greater number of lesions on the later examination. Although patients with EDSS ≥ 6.5 had more lesions and more confluent periventricular areas of increased signal, these results did not achieve statistical significance in our series. However, dividing our HAM/TSP sample into subgroups left us with very small sample sizes which made interpretation of these results difficult. Incomplete MRI sets (for example four of five patients with advanced HAM/TSP had no thoracic cord MRIs) and the challenge of bringing in asymptomatic individuals for radiological studies further limited our numbers, making significant distinctions between groups a challenge to demonstrate. We thus support the view that, in HAM/TSP, the correlation remains unclear between the severity/prognosis of the spastic paraparesis and the extent of cerebral MRI abnormalities.[8,25]

Future studies within the British Columbian Coastal Native population should assess larger samples of subjects in order to differentiate more accurately radiological abnormalities in HAM/TSP patients and HTLV-I carriers. With the advent of better health care in areas in which the disease is endemic, improvement in the access to medical technology, and the dissemination of information to both doctors and patients about HAM/TSP, this will become more practical. Newer radiological techniques might help improve the sensitivity and specificity of MRI as a diagnostic tool in HAM/TSP[35] particularly in cases of dissociation between clinical and antibody status. Longitudinal investigations, evaluating MRI lesions in HAM/TSP patients as their disease progresses, are required to help elucidate further the nature and extent of radiological abnormalities. Our investigation showed that it was easier to detect changes in an

individual patient over a period of time than differences between small numbers of patients assigned to groups based on their immunological and clinical status.

In summary, MRI demonstrates, with excellent sensitivity, abnormalities in British Columbian Coastal Natives suffering from HAM/TSP. Its use as a reliable first-line diagnostic modality is limited by the nonspecific nature of the lesions seen, which may be attributed to subclinical pathology, other neurological disease, vascular abnormalities, or age-related changes in carriers. Until the specificity of our radiological assessments improves, HAM/TSP will primarily remain a clinical and laboratory diagnosis. However, in the differentiation of multiple sclerosis and HAM/TSP, particularly in populations in which HAM/TSP is endemic, MRI is an important supplement to immunological and clinical data, and the criteria tested herein can now be applied to make a more confident radiological diagnosis.

REFERENCES

1. Gessain A, Barin F, Vernant JC, et al. Antibodies to human T-lymphotropic virus type-I in patients with tropical spastic paraparesis. Lancet 1985; ii: 407-410.
2. Cumming WJ. Myelitis and toxic, inflammatory and infectious disorders. Curr Opin Neurol Neurosurg 1992; 5: 549-553.
3. Osame M, Matsamuto M, Usuku K, et al. Chronic progressive myelopathy associated with elevated antibodies to human T-lymphotropic virus type I and adult T-cell leukemialike cells. Ann Neurol 1987; 21: 117-122.
4. Roman GC. The neuroepidemiology of tropical spastic paraparesis. Ann Neurol 1988; 23(suppl): S113-S120.
5. Oger J, Lai H. Demyelination and ethnicity: experience at the University of British Columbia multiple sclerosis clinic with special reference to HTLV-I-associated myelopathy in British Columbian North Pacific Amerindians. Ann Neurol 1994; 36: S22-S24.
6. Oger J, Werker DH, Foti D, Dekaban GA. HTLV-I associated myelopathy: an endemic disease of Canadian Aboriginals of the Northwest Pacific Coast? Can J Neurol Sci 1993; 20: 302-306.
7. McFarlin DE, Blattner WA. Non-AIDS retroviral infections in humans. Annu Rev Med 1991; 42: 97-105.
8. Gessain A, Gout O. Chronic myelopathy associated with human T-lymphotropic virus type I (HTLV-I). Ann Int Med 1992; 117: 933-946.
9. McKendall RR, Oas J, Lairmore MD. HTLV-I-associated myelopathy endemic in Texas-born residents and isolation of virus from CSF cells. Neurology 1991; 41: 831-836.
10. Kermode AG, Rudge P, Thompson AJ, et al. MRI of thoracic cord in tropical spastic paraparesis [letter]. J Neurol Neurosurg Psychiatry 1990; 53: 1110-1111.
11. Melo A, Moura L, Rios S, et al. Magnetic resonance imaging in HTVL-I associated myelopathy. Arq Neuropsiquiatr 1993; 51: 329-332.
12. Rudge P, Ali A, Cruickshank JK. Multiple sclerosis, tropical spastic paraparesis, and HTLV-I infection in Afro-Caribbean patients in the United Kingdom. J Neurol Neurosurg Psychiatry 1991; 54: 689-694.
13. Levin MC, Jacobson S. HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP): a chronic progressive neurologic disease associated with immunologically mediated damage to the central nervous system. J Neurovirology 1997; 3: 126-140.
14. Ferraz AC, Gabbai AA, Abdala N, Nogueira RG. Magnetic resonance in HTLV-I associated myelopathy. Leukoencephalopathy and spinal cord atrophy. Arq Neuropsiquiatr 1997; 55: 728-736.
15. Alcindor F, Valderrama R, Canavaggio M, et al. Imaging of human T-lymphotropic virus type-I associated chronic progressive myeloneuropathies. Neuroradiology 1992; 35: 69-74.
16. Fukushima T, Ikeda T, Uyama E, et al. Cognitive event-related potentials and brain magnetic resonance imaging in HTLV-I-associated myelopathy (HAM). J Neurol Sci 1994; 126: 30-39.
17. Gout O, Gessain A, Bolgert F, et al. Chronic myelopathies associated with human T-lymphotropic virus type I. A clinical, serologic, and immunovirologic study of ten patients in France. Arch Neurol 1989; 46: 255-260.
18. Power C, Weinshenker BG, Dekaban GA, et al. HTLV-I associated myelopathy in Canada. Can J Neurol Sci 1989; 16: 330-335.
19. Ogata A, Nagashima K, Tashiro K, et al. MRI-pathological correlate of brain lesions in a necropsy case of HTLV-I associated myelopathy. J Neurol Neurosurg Psychiatry 1993; 56: 194-196.
20. Offenbacher H, Fazekas F, Schmidt R, et al. Assessment of MRI criteria for a diagnosis of MS. Neurology 1993; 43: 905-909.
21. Paty DW. Magnetic resonance in multiple sclerosis. Curr Opin Neurol Neurosurg 1993; 6: 202-208.
22. Cruikshank JK, Rudge P, Dalgleish AG, et al. Tropical spastic paraparesis and human T cell lymphotropic virus type 1 in the United Kingdom. Brain 1989; 112: 1057-1090.
23. Paty DW, Oger JJF, Kastrukoff LF, et al. MRI in the diagnosis of MS: a prospective study with comparison of clinical evaluation, evoked potentials, oligoclonal banding, and CT. Neurology 1988; 38: 180-185.
24. Fazekas F, Offenbacher H, Fuchs S, et al. Criteria for an increased specificity of MRI interpretation in elderly subjects with suspected multiple sclerosis. Neurology 1988; 29: 1822-1825.
25. Kuroda Y, Matsui M, Yukitake M, et al. Assessment of MRI criteria for MS in Japanese MS and HAM/TSP. Neurology 1995; 45: 30-33.
26. Godoy AJ, Kira J, Hasuo K, Goto I. Characterization of cerebral white matter lesions of HTLV-I-associated myelopathy/tropical spastic paraparesis in comparison with multiple sclerosis and collagen-vasculitis: a semiquantitative MRI study. J Neurol Sci 1995; 133: 102-111.
27. Mattson DH, McFarlin DE, Mora C, Zaninovic V. Central nervous system lesions detected by magnetic resonance imaging in an HTLV-I antibody positive symptomless individual [letter]. Lancet 1987; 2:49.
28. Kira J, Fujihara K, Itoyama Y, et al. Leukoencephalopathy in HTLV-I associated myelopathy/tropical spastic paraparesis: MRI analysis and a two year follow-up study after corticosteroid therapy. J Neurol Sci 1991; 106: 41-49.
29. Furukawa Y, Une H, Osame M. Magnetic resonance imaging findings of HTLV-I associated myelopathy. Rinsho Shinkeigaku 1989; 29: 154-158.
30. Shakudo M, Inoue Y, Tsutada T. HTLV-I-associated myelopathy: acute progression and atypical MR findings. Am J Neuroradiol 1999; 20: 1417-1421.
31. Dekaban GA, Oger JJF, Foti D, et al. HTLV-I infection associated with disease in aboriginal Indians from British Columbia: a serological and PCR analysis. Clin Diag Virol 1994; 2: 67-78.
32. Wade DT. Measurement of Neurological Rehabilitation. Oxford: Oxford University Press, 1992; 285-290.
33. McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the Diagnosis of Multiple Sclerosis. Ann Neurol 2001; 50: 121-127.
34. Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 1983; 13: 227-231.
35. Tourbah A, Deschamps R, Stievenart JL, et al. Magnetic resonance imaging using FLAIR pulse sequence in white matter disease. J Neuroradiol 1996; 23: 217-222.