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Human T-Cell Lymphotropic Virus Type I and Neurologic Disease in Panama, 1985 and 1986

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• **Human T-cell lymphotropic virus type I (HTLV-I) causes adult T-cell leukemia and has recently been associated with HTLV-associated myelopathy/tropical spastic paraparesis. The HTLV-I is endemic throughout the Caribbean basin and parts of South America, and HTLV-associated myelopathy/tropical spastic paraparesis also seems to be common in this area. This 2-year study, 1985 and 1986, was designed to evaluate the occurrence of HTLV-I infection in all newly diagnosed cases of selected neurologic diseases in Panama City, Panama. Six (8%) of 71 patients had antibody to HTLV-I detected by immunofluorescence, enzyme-linked immunosorbent assay, radioimmunoassay, and Western blot assays; 5 patients' conditions were diagnosed as spastic paraparesis, and all 5 were seropositive and also had HTLV-I antibody in cerebrospinal fluid. The remaining seropositive patient had multiple sclerosis, and no antibody was detected in her cerebrospinal fluid. Clinical and electrophysiologic studies indicated that HTLV-I–associated spastic paraparesis is a multifocal, primarily demyelinating disease that principally involves the spinal cord.**

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The human T-cell lymphotropic virus type I (HTLV-I) is highly associated with adult T-cell leukemia (ATL).[1] Several studies have indicated that both HTLV-I and ATL are endemic in the Caribbean basin.[2,3] Observational studies in Martinique,[4] Jamaica,[5] Trinidad[6] the Americas, and other areas have indicated a possible association between HTLV-I infection and spastic paraparesis.

Panama physically and culturally links Central America, South America, and the Caribbean. We have previously reported that the prevalence of HTLV-I antibody in Panama City is similar to that of other countries in the region.[7] We have initiated population-based, descriptive, seroepidemiologic studies to define the occurrence of HTLV-I–associated diseases in Panama. This report concerns HTLV-I infection in selected newly diagnosed neurologic diseases, and its results confirm that infection is highly associated with spastic paraparesis.

PATIENTS AND METHODS

Population Base

Panama has approximately 2 million inhabitants; more than 30% of the population lives in the Panama City metropolitan area. Public health care services are the responsibility of the Ministry of Health and Social Security Administration. Two government tertiary care hospitals, Santo Tomas and the Complejo Hospitalario Metropolitano-CSS (CHM-CSS), provide approximately 81% of all inpatient and outpatient services in the metropolitan area.

Study Patients

This study enrolled all patients with specified neurologic diseases that were diagnosed in the Neurology Clinics at Santo Tomas Hospital and the Social Security Metropolitan Medical Center (CHM-CSS) between January 1985, and December 1986. Eligible diagnoses included idiopathic degenerative nervous system disorders possibly caused by retroviruses (Table 1); patients with epilepsy, stroke, migraine, back pain, and similar common diagnoses were not included. Standard data were abstracted from charts, and serum was collected from all participants. Serologic results were not known at the time of diagnosis and were not used as diagnostic criteria.

Family Contacts

We attempted to locate household contacts of all HTLV-I–seropositive patients. Gorgas Memorial Laboratory Division of Epidemiology staff in Panama City visited the home, explained the study, solicited informed consent, obtained demographic and familial data, and collected 10 mL of venous blood from household residents older than 1 year. In addition, we attempted to contact, enroll, and bleed all blood relatives (children, siblings, and parents) and sexual partners of seropositive study patients regardless of current residence.

Laboratory Studies

Sera were tested independently under code in three HTLV-I antibody assays: indirect immunofluorescence antibody assay (IFA), enzyme-linked immunosorbent assay (ELISA), and solid-phase radioimmunoassay. Positives were confirmed by Western blot. Cerebrospinal fluid specimens from seropositive patients were tested by IFA and Western blot. Sera were also tested for human immunodeficiency virus antibody by an HTLV type III ELISA kit (VIRGO, Columbia, Md).

Indirect Immunofluorescence.—Sera were tested at the Gorgas Memorial Laboratory by using an IFA kit. Specimens were diluted 1:10 in phosphate-buffered saline solution and tested against HTLV-I–infected HUT-102B cells and uninfected HUT-78 controls. Positive sera were titrated by using four-fold dilutions, starting at 1:10; the end point was defined as the highest positive dilution.

ELISA.—An ELISA kit (Du Pont/NEN Medical Products, North Billerica, Mass) was used according to the manufacturer's instructions.[8]

Solid-Phase Radioimmunoassay.—Finally, sera were tested at Program Resources, Inc, Frederick, Md, by radioimmunoassay to measure antibody against the HTLV-I p24 antigen.[9]

Western Blot Assay.—All sera positive in either the IFA or ELISA were retested at Biotech Research Laboratory, Rockville, Md, by Western blot.[10] The Western blot used an HTLV-I lysate prepared from a singly banded virus, from a culture supernatant of HUT-102 cells.

Ancillary Studies

All seropositive patients had additional studies, including the following ones: (1) radiology—radiographs of the skull and cervical, thoracic, and lumbar spine, panmyelogram, and brain computed tomographic scan; (2) hematology—complete blood cell counts and peripheral blood smears were examined by a hematologist for morphologic abnormalities; (3) blood chemistry studies and serologic tests for syphilis (Brewer diagnostic rapid plasma reagin card test, Becton Dickinson Microbiology Systems, Cockeysville, Md); and (4) lumbar puncture—collecting cerebrospinal fluid for cell count and description, protein/glucose determination, HTLV-I antibody testing, syphilis serology, and oligoclonal band determination. For oligoclonal band measurements, cerebrospinal fluid was concentrated with a filter (Micon-B, Amicon Corp, Scientific System Division, Donovers, Mass) and subjected to agarose gel electrophoresis (Titan gel high-resolution protein system, Helena Laboratories, Beaumont, Tex).

The HTLV-I-seropositive patients underwent the following neurophysiology testing: visual and somatosensorial evoked responses, electromyography, and nerve conduction studies. For the visual evoked responses, the absolute abnormal latency of p100 in our laboratory is up to 116 milliseconds for a 31-minute angle; the left-to-right maximal normal difference is 9 milliseconds for a 31-minute angle and 11 milliseconds for a 15-minute angle. Motor and sensory nerve conduction velocities in the upper and lower extremities were measured, including distal latencies. Shahani's latency vs height curves were used for the F response and H-reflex.

REPORT OF CASES

Table 1.—Patients With Eligible Neurologic Disease Diagnoses Identified and Enrolled in Panama, 1985 and 1986

Diagnosis	No. of Patients		
	Diagnosed	Enrolled	Seropositive
Parkinson's disease	32	14	0
Trigeminal, facial, other cranial nerve disorders	26	14	0
Guillain-Barré syndrome	17	13	0
Anterior horn cell disease	10	7	0
Multiple sclerosis	8	8	1
Spastic paraparesis	5	5	5
Myasthenia gravis	5	4	0
Encephalitis, myelitis, encephalomyelitis	1	1	0
Cerebral degenerations	1	1	0
Extrapyramidal disease not Parkinson's disease	1	1	0
Spinocerebellar disease	1	1	0
Demyelinating diseases not multiple sclerosis	1	1	0
Muscular dystrophies and other myopathies	1	1	0

Case 1.—The condition of this 31-year-old mestizo woman was diagnosed as spastic paraparesis in 1985. She was born in Colón City, Panama, where she resided for 23 years before moving permanently to Panama City. She had no family history of neurologic disease and had never received a transfusion. Her neurologic problems began in 1979, when she noted progressive weakness of both legs, following a normal delivery of her first child. By 1981, urinary incontinence, distal lower-limb numbness, constipation, and back pain had developed in the patient. Her general physical examination results were unremarkable. On neurologic examination, cognitive functions were intact, and cranial nerves, sensory function, and coordination were normal. She had a paraparetic spastic gait, patellar and Achilles hyperreflexia, bilateral ankle clonus, and a positive Babinski's sign. Results of a muscle biopsy and nerve conduction studies, an electromyogram, and somatosensory and visual evoked responses were normal. Her neurologic status has remained stable for the last 2 years.

Case 2.—This 37-year-old mestizo woman had spastic paraparesis that was diagnosed in 1985. She was born and resided in Panama City her entire life. She denied a family history of neurologic problems and denied previous transfusions. Her neurologic problems began in 1974, when she noted progressive difficulty with walking, due to weakness and stiffness in both legs. Urinary incontinence and constipation subsequently developed in the patient. General physical examination findings were normal. A neurologic evaluation showed normal cognitive functions and cranial nerves; there were no cerebellar or sensory abnormalities. She had a spastic paraparetic gait, with bilateral patellar and Achilles hyperreflexia, bilateral ankle clonus, and a positive Babinski's sign. Results of a muscle biopsy and nerve conduction studies, an electromyogram, and visual and somatosensory evoked potentials were normal. Her last neurologic evaluation in July 1987 showed a mild worsening of the spastic paraparesis.

Case 3.—This 33-year-old mestizo man's condition was diagnosed as spastic paraparesis in 1986. He had no family history of neurologic disease and had never received a transfusion. He was born and resided in Panama City his entire life. His neurologic problems began in 1981, when he noted progressive weakness and stiffness in both legs. By 1986, urinary incontinence, constipation, and sexual impotence had developed in the patient. General physical examination findings were normal. The neurologic evaluation revealed cognitive functions and cranial nerves to be normal. He had a spastic paraparetic gait, with patellar and Achilles hyperreflexia, bilateral ankle clonus, and a Babinski's sign. He had no sensory or cerebellar abnormalities. Visual and somatosensory evoked responses, results of nerve conduction studies, and an electromyogram were normal. His neurologic abnormalities, in particular urinary incontinence, have slowly progressed through July 1987.

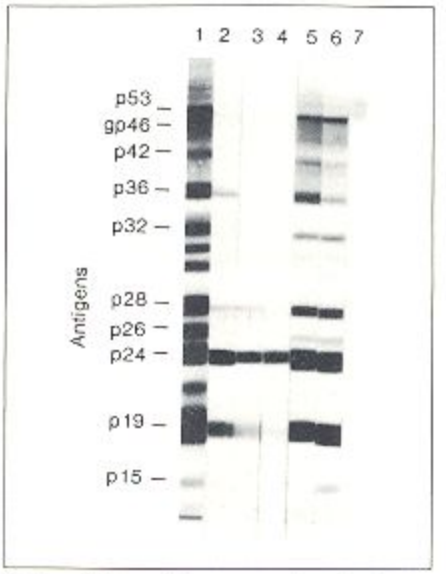

Fig 1.—Western blot assays of antibodies to human T-cell lymphotropic virus type I proteins in sera from patients with spastic paraparesis in Panama, 1985 and 1986. 1 indicates positive control; 2 through 6, patients 2 through 6 with spastic paraparesis; and 7, patient 7 with multiple sclerosis.

Case 4.—This 56-year-old black woman's condition was diagnosed as spastic para-

Table 2.—HTLV-I Antibody Assays in Patients With HTLV-I-Seropositive Neurologic Disease Paraparesis*

	Patient					
	1	2	3	4	5	6
Diagnosis	SP	SP	SP	SP	SP	MS
Serum antibody titer						
ENI IFA†	640	160	40	640	640	10
Du Pont ELISA‡	Pos	Pos	Pos	Pos	Pos	Pos
RIA p24§	Pos	Pos	Pos	Pos	Pos	Pos
Western blot‖	Pos	Pos	Pos	Pos	Pos	Pos
Cerebrospinal fluid antibody titer						
ENI IFA†	40	Neg	10	40	160	Neg
Western blot‖	Pos	Pos	Pos	Pos	Pos	Neg

*HTLV-I indicates human T-cell lymphotropic virus type I; SP, spastic paraparesis; MS, multiple sclerosis; Pos, positive; and Neg, negative.

†ENI IFA indicates Electronucleonics, Inc (Columbia, Md) indirect immunofluorescence antibody assay.

‡Du Pont ELISA indicates Du Pont/NEN Medical Products (North Billerica, Mass) commercial enzyme-linked immunosorbent assay for HTLV-I.

§RIA p24 indicates Biotech Research Laboratory (Rockville, Md) radioimmunoassay for antibody against p24.

‖See Fig 1.

Table 3.—Clinical, Laboratory, Radiologic, Neurophysiologic Studies of Patients With HTLV-I-Seropositive Neurologic Disease Paraparesis*

	Patient					
	1	2	3	4	5	6
Diagnosis	SP	SP	SP	SP	SP	MS
Age, y	31	37	33	56	40	49
Sex	F	F	M	F	F	F
Duration of symptoms, y	7	13	6	9	8	5
Hx of transfusion	No	No	No	No	No	No
Neurol examination results						
Spastic gait	+	+	+	+	+	−
Hyperreflexia	+	+	+	+	+	−
Babinski's sign	+	+	+	+	+	−
Clonus	+	+	+	−	+	−
Neurogenic bladder	+	+	+	+	+	+
Sexual impotence	NA	NA	+	NA	NA	NA
Electrophysiologic findings						
Nerve conduction	Norm	Norm	Norm	ABN	ABN	ND
Electromyogram	Norm	Norm	Norm	Norm	ABN	ND
Evoked responses						
Visual	Norm	Norm	Norm	ABN	ABN	ABN
Somatosensorial	Norm	Norm	Norm	ABN	ABN	Norm
CSF						
VDRL	NR	NR	NR	NR	NR	NR
WBCs, 10^6/L	2	3	0	5	0	2
Protein, g/L	0.40	0.31	0.35	0.55	0.16	0.32
Glucose, mmol/L	2.8	3.0	2.7	3.7	ND	ND
Oligoclonal bands	Neg	Neg	Neg	Neg	Neg	Pos

*HTLV-I indicates human T-cell lymphotropic virus type I; SP, spastic paraparesis; MS, multiple sclerosis; Hx, history; plus sign, physical finding present; minus sign, physical finding absent; NA, not applicable; Norm, normal; ABN, abnormal; ND, not done; CSF, cerebrospinal fluid; NR, not reactive; Neg, negative; and Pos, positive.

paresis in 1986. She was born in Almirante, Panama, a small town on the Caribbean border with Costa Rica, where she resided until moving permanently to Panama City at 39 years of age. She had no family history of neurologic disease and had never received a transfusion. She presented with a 9-year history of progressive gait disturbance, stiffness of both legs, urinary incontinence, and mild back pain. General physical examination findings, higher cortical functions, and cranial nerve examination results were normal. A neurologic examination revealed a mild hypertonia of the lower extremities with hyperreflexia, a bilateral Babinski's sign, and spastic gait. She had no sensory or cerebellar abnormalities. Visual evoked responses showed prolonged p100 in the right eye (120 milliseconds on the right vs 112 on the left eye, with a 31-minute angle). Bilateral sural and superficial peroneal nerve stimulation did not evoke cortical responses. An electromyogram was normal. Results of nerve conduction studies were abnormal, with a bilateral prolonged soleus F wave and H-reflex. Her spastic paraparesis has slowly worsened through her last follow-up in July 1987.

CASE 5.—This 40-year-old black woman's condition was diagnosed as spastic paraparesis in 1986. She was born and lived for 11 years in a small town in the Darien province. Between the ages of 11 and 28 years, she lived in Turbo, Colombia, where she first married and had two children. She has resided in Panama City since the age of 28 years, where she married for the second time and had two more children. She had no family history of neurologic disease and had never received a transfusion. Her problems began in 1979 with progressive difficulty with walking and weakness in both legs. By 1982, she was no longer able to walk and, in addition, had urinary frequency and paresthesia in both legs. General physical examination results were normal. A neurologic evaluation revealed normal cognitive functions and cranial nerves. She had no sensory or cerebellar abnormalities. She was able to walk only with difficulty and had a marked spastic gait with bilateral ankle clonus and a positive Babinski's sign. Visual evoked response showed a prolonged left p100 with normal visual acuity (116 milliseconds on the left eye vs 109 milliseconds on the right for a 31-minute angle). Somatosensory cortical responses of sural and peroneal nerves in both lower limbs showed a prolonged latency. Results of nerve conduction studies were normal, except for delayed soleus and posterior tibial F waves and H-reflex. A lower-limb electromyogram was abnormal with giant and polyphasic motor unit potentials in the tibialis anterior and gastrocnemius muscles.

CASE 6.—This 49-year-old mestizo woman's condition was diagnosed as multiple sclerosis in 1985. She had never received a blood transfusion and had no family history of neurologic disease. She first noted visual disturbances and an unsteady gait in 1980; by 1981, a right hemiparesis, severe incoordination of both hands, and urinary incontinence had developed in the patient. Results of a neurologic examination revealed bilateral optic atrophy, bilateral internuclear ophthalmoplegia, right hemiparesis and bilateral dysmetria, trunk and gait ataxia, and scanning dysarthria. Results of cerebrospinal fluid studies were normal, except that IgG levels were elevated with oligoclonal bands. Findings from radiologic studies were normal. Somatosensory evoked responses were normal. Visual evoked potentials showed a prolongation of p100 with a reduced amplitude bilaterally. Neurologic signs and symptoms improved transiently following the diagnosis, but in late 1986, she experienced a relapse with an exacerbation of her cerebellar syndrome.

RESULTS

Eligible Patient Population

One hundred nine eligible patients' conditions were diagnosed at the Santo Tomas or CHM-CSS Neurology Services during 1985 and 1986 (Table 1). Parkinson's disease was the most frequent diagnosis (32 patients [30% of the total]), followed by facial nerve palsy (26 patients [24%]), Guillain-

Barré syndrome (17 [16%]), anterior horn cell disease (10 [9%]), multiple sclerosis (8 [7%]), spastic paraparesis (5 [5%]), myasthenia gravis (5 [5%] patients), and assorted other diseases (6 [6%] patients).

HTLV-I Antibody—Cases

Seventy-one (65%) of the eligible patients were recruited into the clinical epidemiology study (Table 1). Thirty-eight eligible patients were not enrolled; 24 had registered fictitiously and could not be located; 7 did not return because they had moved and we elected not to follow them up; and 7 died of other causes.

Six patients had HTLV-I antibody detected by all assays and confirmed by Western blot (Fig 1); seropositivity was limited to patients with spastic paraparesis (five of five patients) and multiple sclerosis (one [13%] of eight) (Table 2). The five patients with spastic paraparesis also had HTLV-I antibody detected in cerebrospinal fluid, but the patient with multiple sclerosis did not. None of the study patients had human immunodeficiency virus antibody.

All six seropositive patients had normal serum glucose, urea nitrogen, creatinine, aminotransferase, and electrolyte levels. Syphilis tests on blood and cerebrospinal fluid were negative, and results of radiologic studies were normal. In addition, white blood cell counts, differential cell counts, and morphologic features were normal in the six seropositive patients. Clinical findings and laboratory results are summarized in Table 3.

HTLV-I Antibody—Family Members

We located and enrolled 37 contacts for the 5 seropositive patients with spastic paraparesis (Fig 2); we were unable to locate 9 grandchildren and 3 parents in index cases. No sexual partners had HTLV-I antibody nor did 13 children. Only one family (patient 1) had seropositive individuals: a brother (age, 35 years), mother (age, 55 years), and father (age, 57 years), but 2 younger siblings were negative. The 3 seropositive family members had normal neurologic examination results.

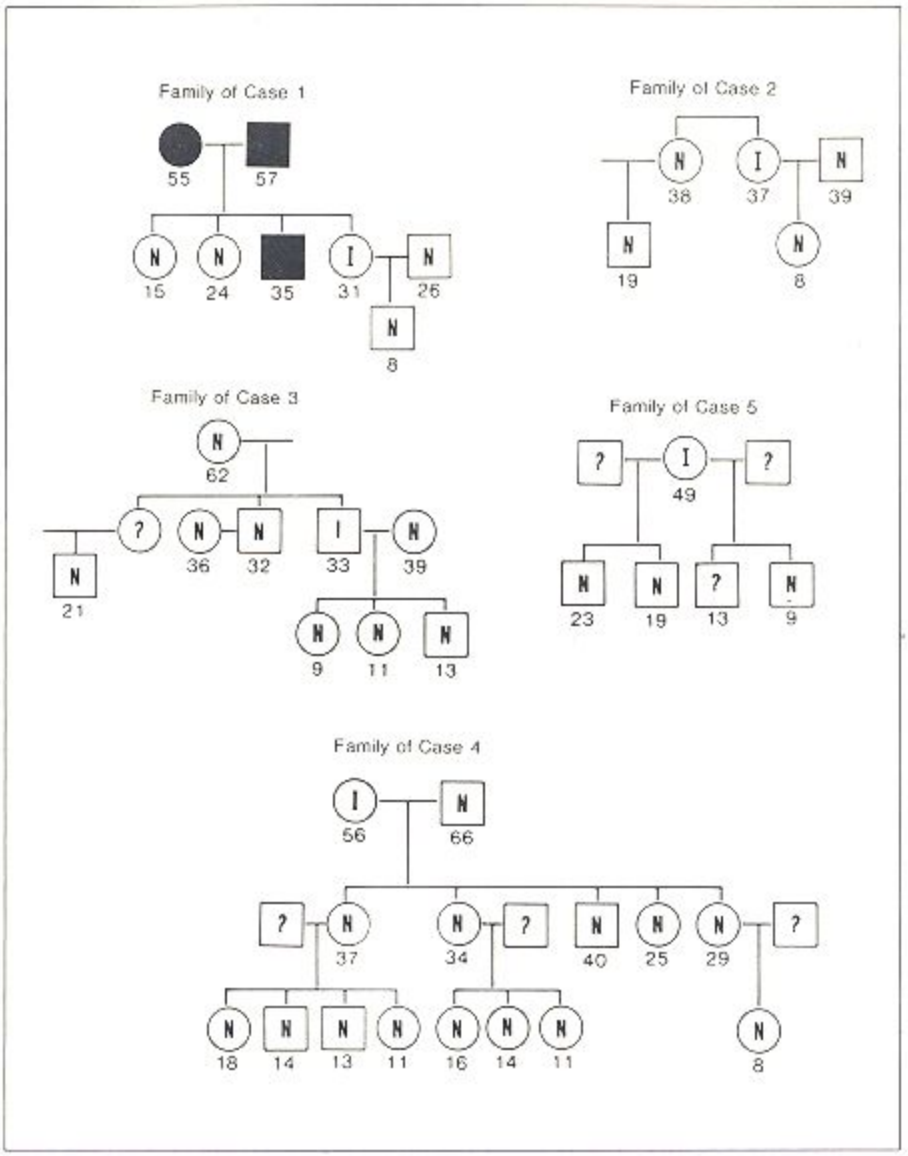

Fig 2.—Human T-cell lymphotropic virus type I serologic studies in family members of patients with spastic paraparesis in Panama, 1985 and 1986. Open squares indicate male; open circles, female; N, seronegative; I, seropositive index case; closed circle, seropositive; closed squares, question mark, unable to locate or obtain blood; and number below symbol, age in years.

COMMENT

This study of patients with incident neurologic disease significantly strengthens the previously hypothesized association of HTLV-I infection and spastic paraparesis and argues against an association with multiple sclerosis. All five patients with spastic paraparesis whose conditions were diagnosed in Panama City between 1985 and 1986 had serum and cerebrospinal fluid HTLV-I antibody. The only other seropositive patient had classic multiple sclerosis and did not have cerebrospinal fluid antibody. Previously reported studies have been based on prevalent cases of spastic paraparesis in which the patients had been followed up in neurology clinics for many years, and these studies have not measured HTLV-I infection in defined, representative neurologic disease groups. Prevalent disease studies cannot be generalized to a population since they include patients with recent diagnoses and variable-term survivors, who have remained under follow-up. At the same time, as our study illustrates, usual definitions of incidence cannot be strictly applied to chronic neurologic disease syndromes. Patients in our study experienced worsening neurologic signs for an average of 8.6 years before finally seeing a neurologist and having their conditions diagnosed as spastic paraparesis. Other neurologic diseases present with a more acute onset so that patients seek medical attention and their conditions are diagnosed more rapidly.

Despite these limitations, data from published observational studies have been similar and are consistent with our conclusions. To our knowledge, the first published report used clinic records from Martinique and found that 10 (59%) of 17 patients with spastic paraparesis and 13 (4%) of 303 assorted controls had HTLV-I antibody.[5]

The study was extended[11] to include the following subjects: 32 patients with spastic paraparesis identified between 1973 and 1985 and enrolled for study from 1984 through 1986; 139 other neurology clinic patients enrolled from 1984 through 1986; 48 assorted (nondefined) family members; and 296 other controls. Seventy-eight percent of patients with spastic paraparesis were seropositive by ELISA, and this was confirmed by Western blot assay, and 11 patients, who could be tested, had antibody in cerebrospinal fluid; 13% of the other patients with neurologic disease were seropositive, and 3 (5%) of 56 also had cerebrospinal fluid antibody; and 8 family members (17%) were seropositive, as were 2% of the normal population. Similar seroprevalence rates have been reported in pilot studies from Kingston, Jamaica, and Tumaco, Colombia,[5] but the referent populations and time periods were not described. Thirty-two Jamaican patients with spastic paraparesis were studied; 16 (67%) of 24 serum specimens and 15 (60%) of 25 cerebrospinal fluids had HTLV-I antibody detected by ELISA. From the patients in Tumaco, 3 of 3 serum specimens and 16 (73%) of 22 cerebrospinal fluid specimens had antibody. A similar study that used available specimens has been published from Trinidad where 3 of 6 patients had serum antibody and 2 of 6 had cerebrospinal fluid antibody to HTLV-I detected by ELISA.[5]

Two recent studies have been published concerning HTLV-I infection and spastic paraparesis in other geographic areas. Roman and collaborators[12] conducted a study of all patients with symptoms suggestive of paraparesis on Mahé Island, Seychelles. Fifty-six possible cases were evaluated; 20 met clinical criteria for spastic paraparesis, and 17 (85%) were seropositive (ELISA confirmed by IFA). In contrast only 2 of 16 controls were seropositive. A second study of 6 patients with paraparesis from Japan (clinical source unspecified) found that all 6 had both serum and cerebrospinal fluid HTLV-I antibody detected by ELISA, particle agglutination, and Western blot. In contrast, 12 (15%) of 78 other neurology clinic patients (also from an unspecified source) were seropositive, and none had antibody in cerebrospinal fluid.[11]

Finally, a pilot study found evidence of active HTLV-I infection in six of seven patients with spastic paraparesis from Jamaica, Haiti, and Colombia. This unique study established T-cell lines from both peripheral blood and cerebrospinal fluid cells and used an IFA test against p19.[14] The HTLV-I has also been isolated from the cerebrospinal fluid of a Japanese patient with HTLV-associated myelopathy.[15]

Our study in Panama also obtained detailed clinical data that defined HTLV-I–associated spastic paraparesis. It is important to stress that the study included all eligible patients with neurologic disease, and all clinical diagnoses were made before serologic testing. Patients with spastic paraparesis presented a chronic progressive syndrome similar to that reported previously.[16-18] All were adults aged 33 to 56 years, and four were women. Major abnormalities involved the lower corticospinal tracts. Two patients showed abnormal evoked visual potentials with prolonged p100 latencies. Other workers have reported clinical optic nerve involvement,[19] but electrophysiologic studies indicating optic nerve demyelination have not been reported, to our knowledge. Nerve conduction studies and electromyograms in these same two patients revealed signs of denervation with alterations of the spinal roots (delayed H-reflex and F wave with normal peripheral nerve conduction and giant polyphasic potentials), similar to others' findings.[20,21] These clinical and neurophysiologic findings, in conjunction with limited neuropathologic studies,[22] suggest that HTLV-I–associated spastic paraparesis is a multifocal primarily demyelinating disease that principally affects the spinal cord, but which can also involve at least optic and spinal nerve roots.

None of our patients with spastic paraparesis had abnormal lymphocytes in either peripheral blood or cerebrospinal fluid. This is similar to a report from Tumaco,[18] but contrasts to HTLV-I–associated paraparesis in Japan.[13]

Several transmission mechanisms for HTLV-I have been hypothesized, but our study did not clarify this important problem. No seropositive patient had received transfusions or had unusual parenteral exposures. We obtained blood from regular sexual partners of four patients, and all were seronegative. One patient had two regular male sex partners, neither of whom could be located. We also tested serum from 13 of the patients' 14 children, and all were negative. In only one instance were antibody patterns compatible with vertical transmission; the index patient, her older brother, and both parents were seropositive. These seropositive family members did not have detectable neurologic abnormalities.

Several studies of spastic paraparesis in the Caribbean have failed to document familial transmission patterns, but these studies have not adequately documented sampling frames.[11,12,23] In contrast, studies in Japan indicate HTLV-I transmission from husband to wife and mother to child in normal populations[24] and among families with ATL.[25,26] A recent case-control study of spastic paraparesis in Tumaco showed that children of seropositive patients were significantly more likely to be infected than children of controls, but numbers were small, and sampling was incomplete and not adequately documented.[27] The study also showed that 75% of spouses of seropositive patients had HTLV-I antibody and that this was highly associated with the number of years of marriage.

It is difficult to interpret our negative serologic results in the children of index patients since the incubation period between HTLV-I infection and development of neurologic disease is not known; 10 children were born 2 to 20 years before their mother first noted neurologic symptoms; 2 women noted neurologic problems immediately following delivery of their presently 8- and 9-year-old seronegative children; and another woman became ill a year before birth of a currently 13-year-old child (who refused to give blood) and 4 years before birth of a seronegative 9-year-old child. Newly developed laboratory methods, such as the polymerase chain reaction, which detects HTLV infection irrespective of host immune response, may resolve many of these issues.

Finally, mention should be made concerning the relative occurrence of spastic paraparesis and ATL in Panama. Our study did not attempt to document all neurologic diseases, but spastic paraparesis occurred at essentially the same incidence as multiple sclerosis. Five patients with spastic paraparesis were enrolled, through the two Panama City hospitals, during the 2-year study. The minimum crude annual incidence of spastic paraparesis in Panama City was 0.26/100 000, and the minimum annual incidence in the adult population aged 30 years or older was 0.73/100 000. Only three HTLV-I antibody-positive ATL cases were documented in the country between 1984 and 1986. Thus, in Panama, neurologic manifestations seem to be a more common sequela of HTLV-I infection than hematologic malignancy.

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