Webinário

Vírus linfotrópico de células T humanas (HTLV): a ameaça silenciosa e suas manifestações neurológicas

30 Nov, 2023, 13:00 GMT/10:00 BR/AR

Registre-se

Tradução simultânea
PT-ESP-ING
Panel

Chair: Augusto César Penalva de Oliveira - Supervising Physician, Neurology Medical Team, Emílio Ribas Infectious Diseases Institute, Brazil

Steven Jacobson - Senior Investigator, Viral Immunology Section, Neuroimmunology and Neurovirology Division (NND), National Institutes of Health (NIH), USA

Lucia Brito - Neurophysiologist, Reference Center for the Care of Patients with Demyelinating Diseases, Restauração Hospital, Ministry of Health, Brazil

Carlos Pardo - Director, Johns Hopkins Myelitis & Myelopathy Center, Baltimore, Maryland, USA

Clarice Neuenschwander - Senior Researcher at the Laboratory of Virology and Experimental Therapy, Fiocruz Pernambuco, Fiocruz, Brazil.

Cristiane Campello Bresani – Senior Researcher at the Laboratory of Virology and Experimental Therapy, Fiocruz Pernambuco, Fiocruz, Brazil.
Resources

- https://portal.fiocruz.br/en
- https://fiocruz.tghn.org/
- https://lac.tghn.org/
- https://www.instagram.com/HTLVBrasil/
- https://fiocruz.tghn.org/health-topics/neuroinfeccoes/grupo-neuroinfeccoes/
Neurological manifestations of HTLV infection

Dr Lucia Brito, MD

Reference Center for the Care of Patients with Demyelinating Diseases, Restauração Hospital, Brazilian Ministry of Health, Brazil
CONFLICT OF INTEREST

ANVISA Resolution No. 102 of 30/11/2000 republished on 01/06/2001 and CFM Resolution No. 1595/2000

Institutions that supported lectures, research presented at conferences and scientific publications in 2016-2023:

• Merck Serono
• Bayer Schering
• Baxter
• Novartis
• Teva
• Biogen
• Genzyme/Sanofi Aventis
• Brazilian Academy of Neurology
• Paraná State Government
• University of Liverpool and Glasgow (ZIKA PLAN)
• State Reference Center for the Care of Patients with Demyelinating Diseases - Restauração Hospital - Pernambuco State Government.
CLINICAL CASE

• First appointment - 03/May/2003 – LRS
• BD- 30/March/1981 (22 years old)
• High school
• From Recife - Non-Caucasian

• In 1999 (18 years old) motor complaint in lower limbs, urinary incontinence - **progressive condition**
• Father with positive symptomatic HTLV. Mother – positive asymptomatic
• Patient was breastfed

• **Normal clinical examination**
• **Neurological examination** - Lower limbs (MRC 4, Ashworth scale G-1, Reflexes 3+, hypopalesthesia), bilateral clonus feet, spastic paretic gait, altered sphincters
RESEARCH AND MANAGEMENT

1999

- Positive western blot test on serum for HTLV
- Other serological tests normal
- Urodynamics - detrusor hyperactivity, decreased bladder capacity, normal bladder compliance and sensitivity

- Symptomatic treatment, monthly MTP
- Periodic - densitometry, ophthalmologic evaluation, TB application
DIAGNOSTICS

❖ **Syndromic** - bilateral pyramidal syndrome, lower limbs hypopalaeesthesia, sphincters

❖ **Topographical** - thoracic spinal cord

❖ **Etiological** – viral

❖ **Nosological** - HTLV myelopathy
Approximately 4% will manifest HAM/PET

20 to 40 million infected worldwide

## Epidemiology of Infection

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Place</th>
<th>Number of Patients</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Grassi MFR et al.</td>
<td>2011</td>
<td>Ceará e Bahia</td>
<td>281</td>
<td>32.7</td>
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<tr>
<td>Slater CMSA et al.</td>
<td>2012</td>
<td>Rio de Janeiro - RJ</td>
<td>128</td>
<td>26.0</td>
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<tr>
<td>Castilhos RM et al.*</td>
<td>2012</td>
<td>Porto Alegre - RS</td>
<td>38</td>
<td>28.9</td>
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<tr>
<td>Adry RARC et al.†</td>
<td>2012</td>
<td>Bahia e São Paulo</td>
<td>45</td>
<td>100.0</td>
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<tr>
<td>Sequeira CG et al.‡</td>
<td>2012</td>
<td>Belém – PA</td>
<td>13,382</td>
<td>0.3</td>
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<tr>
<td>Starling ALB et al.</td>
<td>2013</td>
<td>Belo Horizonte - MG</td>
<td>87</td>
<td>100.0</td>
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<tr>
<td>Ferreira MLB</td>
<td>2013</td>
<td>Recife – PE</td>
<td>163</td>
<td>100.0</td>
</tr>
</tbody>
</table>
NEUROLOGICAL COMPLEX

Myopathy

Motor neuron disease like

Sub-clinical HAM/PET

Polyneuropathy

Cognitive deficit

Dysautonomia

Araújo AQC, Silva MTT, Lancet Neurol, 2006;5:1068-1076
Motor neuron disease like CLINICAL COMPLEX

HAM/PET

Pulmonary alveolite
Uveitis
Vasculitis
Monoclonal gammopathy
Thyroiditis
Ichthyosis
Sjögren's syndrome
Arthropathy
Cryoglobulinemia
Adult T-cell leukemia / lymphoma

Verdonck et al., Lancet Inf Dis, 2007; 7:266-281
The HTLV-1 virus

C virus, enveloped double-stranded RNA

Family Retroviridae

Subfamily Orthoretroviridae

Genus Deltaretroviridae

- p19 matrix
- Nucleocapsid p15
- Capsid P24
- Reverse transcriptase p62/p32
- GP21 Transmembrane
- Surface GP46
Thoracic region

- Low blood flow
- Increased adhesion molecules (VCAM-1)
- Increased adhesion of CD4+ and CD8+ to the endothelium
- Increased synthesis of metalloproteinases 2 and 9 (MMP-2 and MMP-9)
- Disruption of the blood-brain barrier
- Increased synthesis of pro-inflammatory cytokines, IL1, IL6, TNF-a, INF-g by glial cells, (CD4+ and CD8+)
- Increased lesions in the thoracic region

References:
**DIAGNOSTIC CRITERIA**

**Presence of HTLV-1 antibody in serum or CSF confirmed by Western blot or PCR**

**Exclusion of other mimicking diseases**

- Definitive Diagnosis
- Probable Diagnosis
- Possible Diagnosis
Criteria for suspicion of diagnosis in a non-endemic area

Clinical features

Risk factors for HTLV-1
- Being born in an area endemic for the virus
- Having a sexual partner from an endemic area
  - Descent from an endemic area

RESEARCH

Clinical and neurological examination

Complementary research

Assessment of the degree of disability
NEUROLOGICAL EXAMINATION

AFFECTED FUNCTIONAL SYSTEMS

PYRAMIDAL
- Spasticity
- Exalted reflexes

CEREBELLAR
- Ataxia

SENSORY
- Paresthesia
- Dysesthesia
- Alteration of deep sensitivity

SPHINTERIC
- Urinary
- Anal

PERIPHERAL NERVES
- Complaint of distal sensory disturbance

MUSCLES
- Myopathy
LESS FREQUENT NEUROLOGICAL MANIFESTATIONS

ISOLATED SIGN
Hand tremor
Absence or depression of patellar

OTHER SYMPTOMS
Seizure
Cognitive Impairment
Dementia
Altered consciousness

CRANIAL NERVES
Optic atrophy
Nystagmus
Deafness
Other deficits

Araújo AQC, Silva MTT, Lancet Neurol, 2006;5:1068-1076
COMPLEMENTARY NEUROLOGICAL INVESTIGATION - OLIGOSYMPTOMATIC AND SYMPTOMATIC PATIENTS

MRI
CSF
Electromyography
Biochemical dosages, viral tests

Urinary tract ultrasound
Urodynamic study
Tilt table test
ASSESSMENT OF DISABILITY

SCALES

- Kurtzke
- IPEC
- OSAME
- Barthel
- JOA
- Ashworth
EDSS (EXPANDED DISABILITY STATUS SCALE)

Final EDSS established based on walking distance with or without support

- **0**: Normal neurological examination
- **1.5**: Minimal disability
- **2**: Moderate disability
- **2.5**: Impaired ambulation
- **3**: Need assistance
- **3.5**: Wheelchair restriction
- **4**: Moderate disability
- **4.5**: Bedridden patient
- **5**: Full ambulation
- **5.5**: Wheelchair restriction
- **6**: Death

**Full ambulation** to **Bedridden patient**
IPEC DISABILITY SCALE
Evandro Chagas Clinical Research Institute

**MOTOR ASSESSMENT**
- Gait (1 – 11)
- Ability to run (0 – 1)
- Ability to climb stairs (0 – 2)
- Ability to jump (0 – 3)

**SPASTICITY**
- Clonus (0 – 2)
- Espasmo flexor-extensor (0 – 1)

**SENSIBILITY**
- Paresthesia (0 – 2)
- Low back or lower limb pain (0 – 2)

**SPHINCTERS**
- Bladder control (0 – 3)
- Bowel control (0 – 2)

**Total Score**
Zero - 29
IPEC DISABILITY SCALE
Evandro Chagas Clinical Research Institute

Quartil = \frac{\text{"Sum of Points"}}{\text{"Sickness time in years"}}

1° Quartil – score < 25%
Slow progression

3° Quartil - score > 75%
Rapid progression
OTHER DISABILITY ASSESSMENT SCALES

**OSAME Motor Disability Score**
- Evaluates motor function
- Graduation from zero to 13 (highest index = highest commitment)

**JOA – Japanese Orthopedic Association**
- Evaluates motor, sensory and sphincter function
  - Graduation from -2.0 to 17.0 (higher index = higher commitment)

**Barthel**
- Evaluates degree of independence in activities of daily living
- Graduation from zero to 20 (lowest index = highest commitment)

**Ashworth**
- Grades muscle tone
- Graduation from zero to 4 (highest index = highest commitment)

CLINICAL COURSE OF HAM/PET

- Very fast progression
- Slow progression
- Slower progression
- Mild progression

Period since onset of disease

Motor disability

Severe

Yamano Y, Sato T. Frontiers in Microbiology 2012;3;389:1-10
THE EXPERIENCE

REFERENCE CENTER FOR THE CARE OF PATIENTS WITH DEMYELIZING DISEASES AND NEUROINFECTION
EPIDEMIOLOGICAL DATA OF THE CRAPPDD-HR

Period of Time:
1994 to 2023 (29 years old)

Number of patients followed:
265 patients

Reference
Spontaneous Search
Hemotherapy Center of Pernambuco
Other Services
DISTRIBUTION BY GENDER

Female:male ratio = 3.2:1
AGE DISTRIBUTION ACCORDING TO GENDER

FEMALE
Average 55.75 ± 1.42 years

MALE
Average 53.63 ± 2.81 years

There was no significant difference in age between the sexes

F = 0.417

p_{unicaudal left} = 0.520
HTLV NEUROLOGICAL COMPLEX

- ed with uveitis and Sjögren's syndrome (1)
- ed with non-Hodgkin's lymphoma (1)
- ed with hair cell leukemia (6)

PERIOD OF TIME: 1994-2023 (29 years)
CLINICAL AND NEUROLOGICAL EXAMINATION

ASYMPTOMATIC
Periodic follow-up (semi-annual)

OLIGOSSYMPTOMATIC

SYMPTOMATIC
Follow-up with variable periodicity
Treatment
Physiotherapy
COUNSELLING

REFRAIN FROM DONATING:
- Blood
- Organs
- Milk
- Sperm

DISCUSS WITH SEXUAL PARTNER:
- Sexual transmission
- Preventive Measures

REFRAIN FROM THE SHARED USE OF:
- Needles
- Syringes
- Perfuro-shear

AVOID
- Breastfeeding
Thank you