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

Ministério da Saúde
FIOCRUZ Fundação Oswaldo Cruz
HTLV Brasil
NAP Retrovírus (USSP)
NEAS
JOHNS HOPKINS MEDICINE
Enabling research by sharing knowledge
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/
Other neurological manifestations of HTLV

Dr Prof Carlos A. Pardo, MD

Johns Hopkins Myelitis & Myelopathy Center
Divisions of Neuroimmunology, Neuroinfectious Disorders and Advanced Clinical Neurology, Johns Hopkins University School of Medicine, USA
HTLV-1 in the nervous system: More than TSP/HAM!!

Retroviruses may target diverse groups of cells and structures of the nervous system!!

- HTLV-1-associated neurological disorders
  - HTLV-1-Associated Myelopathy (HAM)
    - Acute/subacute HAM
    - Chronic HAM
  - HTLV-1-Associated Encephalopathy
  - HTLV-1-leukoencephalitis/white matter disease
  - HTLV-1-associated optic neuritis
A 54-yo woman with a remote history of optic neuritis and concerns for a demyelinating disorder

HTLV-1 in the nervous system: More than TSP/HAM!!

<table>
<thead>
<tr>
<th>Year</th>
<th>Symptom</th>
<th>MRI</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>Optic neuritis</td>
<td></td>
<td>IV MTP Copolymer</td>
</tr>
<tr>
<td>2011</td>
<td>Aseptic meningitis</td>
<td></td>
<td>IV MTP</td>
</tr>
<tr>
<td>2016</td>
<td>Gait problems</td>
<td>MRI: Meningeal Foci + Gad</td>
<td>Oral Prednisone</td>
</tr>
<tr>
<td>2018</td>
<td>Bladder symptoms</td>
<td>MRI: Concerns About MS</td>
<td>Anti-CCR4 IVIG</td>
</tr>
<tr>
<td>2019</td>
<td>MRI: Multiple WM lesions</td>
<td>Gait Problems progressed</td>
<td></td>
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<tr>
<td>2020</td>
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Brain MRI T2W 2019
A 54-yo woman with a remote history of optic neuritis and concerns for a demyelinating disorder

HTLV/1 proviral load in blood was 9% (up from 6.9%), 48% in CSF, protein 60 mg/dL, 4 WBC, positive oligoclonal bands.
HTLV-1 in the nervous system: More than TSP/HAM!!

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  - Chronic HAM
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<td>HTLV-1 Serum+ CSF</td>
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- HTLV-1-associated neurological disorders
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  - HTLV-1-associated optic neuritis

From: Dixon L. et al. Imaging Spectrum of HTLV-1-Related Neurological Disease
Neurology: Clinical Practice
HTLV-1 in the nervous system: More than TSP/HAM!!

- **HTLV-1-associated neuromuscular disorders**
  - HTLV-1-associated myositis
  - HTLV-1-associated neuritis/neuropathy

**HTLV-1 Associated Myositis**
- Prolonged clinical course
- Prominent endomysial infiltrates
- Infrequent necrotic fibers
- Prominent regenerative activity
- Cytochrome c oxidase deficiency
- Mitochondrial abnormalities


HTLV-1 in the nervous system: More than TSP/HAM!!

Retroviruses may target diverse groups of cells and structures of the nervous system!!

- **HTLV-1-associated neuro-ophthalmologic disorders**
  - Acute T-cell leukemia/lymphoma (ATL) ocular disease
  - HTLV-1-associated uveitis
  - HTLV-1-associated optic neuritis

- **HTLV-1-associated neuromuscular disorders**
  - HTLV-1-associated myositis
  - HTLV-1-associated neuritis/neuropathy

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**HTLV-1 Uveitis**

From Koju Kamoi. Frontiers in Microbiology
Doi: 10.3389/fmicb.2020.00388

<table>
<thead>
<tr>
<th>ATL-related ocular manifestations</th>
<th>n = 44</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracocular irritation</td>
<td>22</td>
<td>45.8</td>
</tr>
<tr>
<td>Opportunistic infection</td>
<td>19</td>
<td>39.6</td>
</tr>
<tr>
<td>(Cytomegalovirus)</td>
<td>(19)</td>
<td>(100.0)</td>
</tr>
<tr>
<td>(Herpesvirus)</td>
<td>(2)</td>
<td>(10.0)</td>
</tr>
<tr>
<td>(Toxocara)</td>
<td>(1)</td>
<td>(5.3)</td>
</tr>
<tr>
<td>Dry eye</td>
<td>3</td>
<td>6.8</td>
</tr>
<tr>
<td>Scleritis</td>
<td>2</td>
<td>4.5</td>
</tr>
<tr>
<td>Uveitis</td>
<td>1</td>
<td>2.3</td>
</tr>
<tr>
<td>Anomalous retinopathy</td>
<td>1</td>
<td>2.3</td>
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HTLV-1 in the nervous system: More than TSP/HAM!!

The problem of overlapping syndromes

- HTLV-1-associated neurological disorders may overlap with:
  - Multiple sclerosis
  - Neuromyelitis optica
  - HIV/AIDS
  - Others

Differentiation of HAM/TSP from patients with multiple sclerosis infected with HTLV-I.

The high proviral load in peripheral blood mononuclear cells or in CSF or both may be a good marker of human T lymphotropic virus type I (HTLV-I)-associated myelopathy/tropical spastic paraparesis (HAM/TSP) and can differentiate patients with HAM/TSP from patients with multiple sclerosis infected with HTLV-I.
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  - HIV/AIDS
  - Others

HIV/HTLV-1 coinfection:
- Accelerated progression to AIDS
- Worse outcomes of HIV-related opportunistic infections.
- HTLV-1 induces HIV viral replication and the transition from M- to T-tropic HIV phenotype
- HIV/HTLV-1-coinfected individuals have higher production of proinflammatory cytokines, most notably interleukin 2 and interferon-γ
- Neurological manifestations like encephalopathy, peripheral neuropathy, and HAM/TSP were more frequently reported in coinfected patients.
