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/
Laboratory diagnosis of HTLV infection: techniques & challenges

Dr Clarice Neuenschwander, PhD

Laboratory of Virology, Oswaldo Cruz Foundation, Brazilian Ministry of Health, Brazil
Introduction

Brazil is endemic but the actual prevalence is unknown.

Stigmatizing disease

Haematogenous transmission

Disабlisible chronic diseases

Associated coinfections

There is no rapid tests

There is no antiviral drugs

There is no vaccines
Transmission

Mother to Child transmission (vertical or by breastfeeding)

Sexual transmission

Sharing needles

Blood and organs transplantations

*In Brazil, screening for blood donors became mandatory in 1993, and for and organs/tissue donors, in 2009.

Early diagnosis is critical to:

- Stop ways of transmissions in community and within families
- Advise infected people and family, focusing in the life quality
- Identify HTLV associated comorbidities, to provide an Integral clinical management
- Knowledge the actual prevalence and distribution of HTLV infection

**WHY testing for HTLV infection?**
WHO should test for HTLV?

- Pregnant women
- Blood, milk and organ/tissue donors
- Organ receptors
- Family and sexual partner of PLWHTLV
- Offspring of women with HTLV
- People with HTLV associated diseases

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WHO should test for HTLV?

Differential diagnosis of myopathies

People with sexual and hematogenous infections

People with tuberculosis

Patients with Strongyloides stercoralis

Patients with lymphomas or leukemias

Accidents with blood or other biological material and drug addicts

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HOW to do the HTLV infection diagnosis?

Step I - Screening Tests

Step II - Confirmatory Tests and tests to discriminate the viral type
Step I - Screening Tests

- ELISA (Enzyme Immunoassay) ou CLIA (Chemiluminescence Immunoassay)
- Antibodies against recombinant proteins of HTLV-1/2 evelop (gp46 e gp21)
- High Sensibilities and variable Specificities (92-99,5%)
- False positive and inconclusive results rise costs
- They don't discriminate the viral type, and so need a confirmatory test (test sample pools is a strategy)
Step II - Confirmatory Tests

- **SEROLOGICAL**
  - Western Blot
  - Line Immunoassay

Detect antibodies against:
- rgp46-I of HTLV-1
- rgp46-II of HTLV-2
- GD21 of bot virus

Cost higher than molecular tests

Fonte: DCCI/SVS/MS, 2021
## Interpretacion of WB

<table>
<thead>
<tr>
<th>RESULTADO</th>
<th>BANDAS ENCONTRADAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positivo para HTLV-1</td>
<td>p19 e/ou p24 + GD21 + rgp 46-I</td>
</tr>
<tr>
<td>Positivo para HTLV-2</td>
<td>p19 e/ou p24 + GD21 + rgp 46-II</td>
</tr>
<tr>
<td>Positivo para HTLV-1 e HTLV-2</td>
<td>p19 e/ou p24 + GD21 + rgp 46-I + rgp 46-II</td>
</tr>
<tr>
<td>Positivo para HTLV (não tipado)</td>
<td>p19 e p24 + GD21</td>
</tr>
<tr>
<td>Indeterminado</td>
<td>Qualquer combinação de bandas que não as descritas acima</td>
</tr>
<tr>
<td>Negativo</td>
<td>Nenhuma reatividade</td>
</tr>
</tbody>
</table>

Fonte: DCCI/SVS/MS.
Step II - Confirmatory Tests

• MOLECULAR

- Detect pro-viral DNA integrated in white blood cells of host genome

- High Specificity and Sensibility

- PCR (qPCR, nPCR, LAMP)

- qPCR can be used for qualitative diagnosis or to quantify pro-viral burden

- Protocols are in house (i.e. clinically unvalidated)

- Useful when WB is inconclusive and in children under 18 months

Fonte: DCCI/SVS/MS, 2021
Algorithm to confirm the HTLV infection by serologic test

Fonte: DCCI/SVS/MS, 2021
When results of WB may be inconclusive

- Seroconversion period - Immunologic window (around 90 days from infeccion)
- Cepas of HTLV different from that used to manufacturer the commercial tests
- Defective viral particles
- Viral mutations in gene regions which codify the structural or regulator ptns (mainly env ptns)
- Low pro-viral burden, mainly in HTLV-2 infections

Fonte: DCCI/SVS/MS, 2021; CAMPOS et al., 2017, 2020; JACOB et al., 2008, 2009; KURAMITSU et al., 2017; MARTINS et al., 2010; MORIMOTO et al., 2005)
Algorithm to confirm the HTLV infection by molecular test

 amostra de sangue total

triagem sorológica (EIA 3ªG ou CLIA)

Reagente/indeterminado

Não

Descarta a infecção por HTLV-1/2

Sim

confirmatório molecular (nPCR, PCR-RFLP, qPCR ou LAMP)

dNA proviral positivo para HTLV-1 ou HTLV-2

Confirma a infecção por HTLV-1 ou por HTLV-2

Recomendado confirmatório sorológico (LIA ou WB) para excluir falso-negativo

DNA proviral não detectado

Sem a infecção por HTLV-1/2 ou DNA proviral abaixo do limite de detecção do teste utilizado

Fonte: DCCI/SVS/MS, 2021
Calenges

- Rise knowledge about HTLV and associated diseases among the general population and healthcare professionals
- Train healthcare professionals to welcome, advice and conduct cases
- Rise investment in clinical and basic research
- Rapid tests: in Brazil, there is 2 in validation phase, and other one in developing phase (our research group)
- Public policies to test broadly in prenatal routines: Brazil had recent advances in national guidelines, but is still not routinely testing pregnant women
Motivacion - Love - Guarantee Integral Care to PLWHTLV

XVI International Symposium on HTLV in Brazil.
João Pessoa, Paraíba, Oct 2023
Thank you.

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