HANTAVIRUS CARDIOPULMONARY SYNDROME IN RIBEIRÃO PRETO, BRAZIL, 2010-2011

Glauciane Garcia de Figueiredo, Michelly de Pádua, Gilberto Sabino dos Santos Júnior, Alex Martins Machado, Marília Farignoli Romero, Daniela Leitão Delsin, Ana Carolina Dias de Carvalho, Soraya Jabur Badra, Luiz Tadeu Moraes Figueiredo*

Centro de Pesquisa em Virologia da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo

ABSTRACT

Cardiopulmonary Syndrome (HCPS) is a severe disease caused by Hantaviruses. In the present study, we have analyzed sera of 62 HCPS suspected cases from the region of Ribeirão Preto, São Paulo, in the period of 2010-2011. Clinical samples of twelve patients were positive, based on both RT-PCR and IgM-ELISA. Hantavirus-infected patients included 8 males and 4 females, 16-57 years old, 3 of whom were rural workers (25%) and one of them related direct contact with wild rodents. The majority of the other patients (75%) lived in the periphery of cities and reported the presence of rodents in their homes. The case fatality ratio of these 12 HCPS cases was 41.6%. Our results confirm that hantaviruses are endemic, with occurrence of HCPS and fatalities, every year, in the region of Ribeirão Preto. More educational and preventive measures are necessary in order to prevent human infections by hantavirus in the region, and other parts of Brazil.

Keywords: hantavirus, cardiopulmonary syndrome, Ribeirão Preto, Brazil

INTRODUCTION

Hantavirus is a genus in the family Bunyaviridae that includes more than 20 virus genotypes. These viruses are enveloped with three single-stranded segments of negative-sense RNA genome, defined as small (S), medium (M) and large (L) (Plyusnin et al.1996). The S segment encodes a nucleocapsid protein; the M segment encodes 2 glycoproteins (Gn and Gc); and the L segment encodes the viral RNA polymerase (Schmaljohn & Hooper 2011).

Hantaviruses can produce two distinct diseases: Hemorrhagic Fever with Renal Syndrome in the Old World and Hantavirus Cardiopulmonary Pulmonary Syndrome (HCPS) in the Americas. The viruses are carried by rodent hosts and transmitted in infectious aerosols of animal excreta (Lee et al. 1982, Nichol et al 1993).

Five hantavirus genotypes have been reported causing HCPS in Brazilian patients: Anajatuba, Araraquara (ARAV), Castelo dos Sonhos, Juquitiba/Araucária, and Laguna Negra-like. In Brazil, approximately 1400 Hantavirus cases have been reported from 1993 to 2011, with a 41% case fatality ratio (Ministério da Saúde do Brasil 2011). In the Ribeirão Preto region, Northeast of São Paulo, Brazil, HCPS cases have been reported since 1998. The aim of this work is to analyze the diagnosis and some epidemiological aspects of HCPS cases that occurred in the Ribeirão Preto region from 2010 to 2011.

MATERIAL AND METHODS

Human Samples

Laboratorial diagnosis of hantavirus infections in clinical samples of HCPS suspected cases from Ribeirão Preto and other cities in the region has been performed at the Virology Research Center of the Escola de Medicina of the Universidade de São Paulo in Ribeirão Preto (VRC-EMUSP-RP). From 2010 thru July of 2011, clinical samples of 62 HCPS suspected cases were analyzed at the VRC-EMUSP-RP.

Serology

Serum or blood samples from HCSP suspect cases were tested by IgM-ELISA and IgG-ELISA using a recombinant nucleocapsid protein of ARAV as antigen, as previously reported by Figueiredo et al. 2008, 2009a.

RT-PCR

RNA was extracted from sera, blood samples,
and human lung tissues using the Extraction Kit (Qiagen, USA). RT-PCRs for partial genomic amplification of S and M segments of viral RNA were performed as previously described (Moreli et al. 2004).

RESULTS

Samples from all 62 HCPS suspect cases were analyzed by IgG-ELISA, IgM-ELISA and RT-PCR. Twelve individuals had positive results in all 3 tests, as shown in Table 1. These hantavirus infected patients were all adults, 8 males (66.6%) and 4 females. Three patients were rural workers (25%) and one of them related direct contact with wild rodents. The majority of the other cases (75%) lived in the periphery of urban areas and referred contact with rodents in their homes. The case fatality ratio of these HCSP cases was 41.6%.

Clinical samples were collected from patients 3 to 27 days after the onset of symptoms, as shown in Table 1. The majority of the cases occurred in the dry season, from April to July.

Table 1. General data of 12 hantavirus cardiopulmonary syndrome cases diagnosed in Virology Research Center of the Escola de Medicina of the Universidade de São Paulo in Ribeirão Preto, 2010-2011.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Collection time (days)*</th>
<th>IgG (+)</th>
<th>IgM (+)</th>
<th>Patient outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>AYG</td>
<td>Male</td>
<td>31</td>
<td>4</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>ALR</td>
<td>Male</td>
<td>25</td>
<td>4</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>RLC</td>
<td>Male</td>
<td>23</td>
<td>27</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>HESH</td>
<td>Male</td>
<td>16</td>
<td>4</td>
<td></td>
<td></td>
<td>Died</td>
</tr>
<tr>
<td>CMFS</td>
<td>Male</td>
<td>28</td>
<td>14</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>LSC</td>
<td>Male</td>
<td>34</td>
<td>4</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>CAB</td>
<td>Male</td>
<td>30</td>
<td>3</td>
<td></td>
<td></td>
<td>Died</td>
</tr>
<tr>
<td>MISP</td>
<td>Female</td>
<td>33</td>
<td>3</td>
<td></td>
<td></td>
<td>Died</td>
</tr>
<tr>
<td>AASC</td>
<td>Female</td>
<td>40</td>
<td>4</td>
<td></td>
<td></td>
<td>Died</td>
</tr>
<tr>
<td>EAR</td>
<td>Female</td>
<td>39</td>
<td>3</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>AKFN</td>
<td>Female</td>
<td>29</td>
<td>3</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>SRB</td>
<td>Male</td>
<td>57</td>
<td>3</td>
<td></td>
<td></td>
<td>Died</td>
</tr>
</tbody>
</table>

+ Positive test; - Negative test.
*Time of sample collection after onset of symptoms.

DISCUSSION

In the last six years, the diagnosis of hantavirus infections has been done in VRC-EMUSP-RP by using 2 RT-PCRs that amplify part of the N gene in the S viral RNA segment and part of Gn gene in the M viral segment and also IgM and IgG-ELISAs, using an N recombinant protein of ARAV as antigen. All these techniques were developed in our laboratory, which allowed the possession of sensitive, fast and reliable tools for diagnosis of these infections (Moreli, et al. 2004; Figueiredo et al. 2008, 2009a).

More than 70 HCPS cases have been reported in the Ribeirão Preto region since 1998 (Ministério da Saúde do Brasil 2011). The causative of HCPS in the region is ARAV, and its rodent-reservoir is Necromys lasiurus, a wild rodent of the Cerrado landscape (Suzuki et al. 2004; Sousa et al. 2008).

We show here that cases of HCPS have kept occurring in the Ribeirão Preto region since 1998, six or more cases per year. Our results corroborate previous reports, from Chile, Argentina, USA and Brazil, showing that the majority of HCPS cases occur in male adults, mostly agricultural workers or people in contact with a rural environment (Campos et al. 2009; Sotomayor et al. 2009; Martinez et al. 2010, MacNeil et al. 2011, Travassos da Rosa et al. 2011).

In the present study, 25% of the HCPS cases occurred in agricultural workers and the presence of rodents at home was related by 75% of the HCPS patients, all living in peripheral urban areas, which probably, enhanced the hantavirus infection. A serologic study in the Amazon region, Brazil, showed that the majority of HCPS cases were associated with a previous exposure to rodents in the field and in dwellings (Mendes et al. 2010). Limongi et al. (2007) observed in Minas Gerais, Brazil, that HCPS cases predominated among agricultural workers and those living in peripherial urban areas.

Clinical samples were collected from the patients 3 to 27 days after the onset of symptoms (Table 1). IgM antibodies to hantavirus were observed in all clinical samples independently of time of collection. As previously reported, most of our HCPS cases occurred in the dry season, April to August (Suzuki et al. 2004, Campos et al. 2009). Only 2 cases occurred at a different time of the year. According to Donalisio et al. 2008, in the cerrado areas, human cases of hantavirus infection occur in the dry season because this is the harvest season that requires intense agricultural work and this worker population is probably more exposed to infected rodents.

The case fatality ratio of the 12 HCPS cases was 41.6%. This fatality ratio is lower than others reported in previous studies in the region of Ribeirão Preto, which was approximately 50% (Campos et al. 2009, Figueiredo et al. 2009b Figueiredo et al. 2010). ARAV, the causative of HCPS in the region of Ribeirão Preto is, probably, the most virulent among all Brazilian hantaviruses (Figueiredo et al. 2009b). Despite the low amount of cases analyzed, it is possible that the number of fatal HCPS cases is slowly decreasing in the region of Ribeirão Preto, which could be, in part, a consequence of HCPS information offered to health officers in recent years.
Thus, attendant physicians could suspect the disease earlier and admit these patients immediately to hospitals that could provide suitable respiratory and hemodynamic support. In short, we show here that the laboratory is fundamental for diagnosis of hantavirus infection and that most of the HCPS suspected cases analyzed in the study were, probably, infections by other pathogens. We also show that HCPS is an endemic disease that keeps occurring in the region of Ribeirão Preto, mainly in the dry season. Further educational campaigns teaching the population about hantavirus transmission by wild rodents and preventive measures to reduce contact with these animals and their excreta could reduce occurrence of HCPS cases in the region, as well as in other parts of Brazil.

ACKNOWLEDGMENTS

We would like to thank the Epidemiological Surveillance Teams of the Health Departments of Ribeirão Preto and Sertãozinho cities for supplying most of the clinical samples and information on the HCPS patients. We also thank FAPESP for supporting this work.

REFERENCES


