Imported hantavirus cardiopulmonary syndrome in an Italian traveller returning from Cuba

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INTRODUCTION

Hantaviruses are rodent-borne enveloped negative-sense RNA viruses belonging to the Bunyaviridae family transmitted primarily through inhalation of virus-contaminated aerosols from rodent excreta. Hantavirus hemorrhagic fever with renal syndrome (HFRS) is caused by European and Asian strains (Jonsson et al., 2010), while hantavirus cardiopulmonary syndrome (HCPS) is caused by North, Central and South American strains (Nicol et al., 1993, Jonsson et al., 2010) but no HCPS has been previously reported in the Caribbean region. In this report, a case of HCPS imported from Cuba is described.

CASE REPORT

From 13th to 30th August 2010 a 59 year-old Italian visited the city of Havana, as well as rural areas, natural reserves and caves in Cuba. During his visit to rural Cuba, the traveller stayed in households or family-run bed-and-breakfasts. Some days after his return to Italy, the man exhibited a mild respiratory syndrome. On 17th September, he was hospitalized for high fever, dyspnea and diffuse nodular infiltrates associated with lymphadenopathy.

On admission, monocytosis, slight alterations in aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), erythrocyte sedimentation rate (ESR) and C-reactive protein concentration were shown. Respiratory secretions were negative for common bacterial and viral agents. Less common viral agents were then suspected and serum samples were sent to our Institution for further analysis.

Taking into account the possible exposure to rodent excreta during the journey, HCPS was hypothesized and serum samples were tested for hantavirus antibody determination. On 21st September, hantavirus IgM tested positive by an IFA assay (Anti-Hantavirus IIFT IgM, EUROIMMUN Lübeck, Germany) utilizing antigens from American (Sin Nombre and Andes) virus strains while they tested negative by an ELISA assay using antigens for European and Asian strains (Anti-Hanta Virus Pool ELISA IgM, EUROIMMUN) (Table 1).

Hantavirus IgG were positive by a broadly reactive ELISA assay (Anti-Hanta Virus Pool ELISA IgG, EUROIMMUN). In addition, a real-time RT-PCR signal (threshold cycle 36.5) was observed.
in the serum sample using primers and probes to Sin Nombre virus (the prototype American strain), whereas no signal was observed using primers and probes to other European and Asian strains (Kramski et al., 2007) (Table 1).

Unfortunately, the low viral load did not allow the typing to be confirmed by sequencing.

On 29th September, the man was discharged with an improved chest radiological picture. Three months later, on 17th December, IgM and viral RNA were no longer detectable in the man’s serum, while IgG positivity was confirmed (Table 1). Taken together, the results suggested an imported hantavirus infection.

DISCUSSION

In recent years, the emergence and spread of hantavirus diseases has been associated with an increase in international travel, ecological changes and global dissemination of rodent vectors (Jonsson et al., 2010). The main risk factors for travellers are: accommodation in abandoned or derelict facilities and trekking or camping outside recommended areas (Castillo et al., 2007). After the first outbreak in the United States in May 1993 (Nichol et al., 1993), many clusters of HCPS sustained by a variety of hantavirus strains (CDC) have occurred in different countries of North (Canada, United States), Central (Panama) and South America (Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay) (Murgue et al., 2002) due to the broad hantavirus reservoir, consisting of several susceptible species of rodents (CDC).

While no information is available on hantavirus infections in Cuba in WHO, CDC and ECDC databases, HCPS has been reported in nearby regions (Panama, Florida). In addition, serological evidence of hantavirus infection was documented on the islands of Barbados (Groen et al., 2002), Trinidad and Tobago (Adesiyun et al., 2011). The clinical picture is generally accepted as a criterion to differentiate hantavirus infections by Old and New world strains, as the former are associated with HFRS and the latter with HCPS. On the other hand, a significant number of patients with HFRS may show respiratory symptoms mimicking HCPS (Vaheri et al., 2012). This report presents some limitation on virus typing. Firstly, the broad cross-reactivity of commercial serology assays makes it difficult to differentiate infections sustained by different hantavirus strains. Neutralization assays could be more informative for hantavirus serotyping, but require high-level containment laboratories that are not widely available. Secondly, while real-time RT PCR confirmed the hantavirus infection, the presence of the prototype American hantavirus strain remains just a suggestion if unconfirmed by sequencing.

Taking into account:
- the endemicity of HCPS in neighboring countries (Nichol et al., 1993, Khan et al., 1996, Matheus et al., 2010);
- a clinical picture compatible with HCPS;
- hantavirus-specific IgM, IgG and virus RNA during the acute phase;
- the disappearance of hantavirus IgM and RNA in the convalescent phase, while retaining the IgG positivity, it is reasonable to conclude that

<table>
<thead>
<tr>
<th>Assay</th>
<th>Time after onset of HPS symptoms</th>
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<tbody>
<tr>
<td></td>
<td>4 days</td>
</tr>
<tr>
<td>IgM¹ (IFA)</td>
<td>positive</td>
</tr>
<tr>
<td>IgM² (ELISA)</td>
<td>negative</td>
</tr>
<tr>
<td>IgG³ (ELISA)</td>
<td>positive</td>
</tr>
<tr>
<td>Real-time RT-PCR⁴</td>
<td>positive</td>
</tr>
<tr>
<td>Sin Nombre</td>
<td>Andes</td>
</tr>
<tr>
<td>Tula</td>
<td>negative</td>
</tr>
<tr>
<td>Dobrava</td>
<td>negative</td>
</tr>
<tr>
<td>Puumala</td>
<td>negative</td>
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<tr>
<td>Hantaan/Seoul</td>
<td>negative</td>
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</tbody>
</table>

this is the first report of HCPS in Italy imported from Cuba.

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REFERENCES
Center for Diseases Control, Atlanta, USA: http://www.cdc.gov/ncidod/diseases/hanta/hps/index.htm