

# Imported hantavirus cardiopulmonary syndrome in an Italian traveller returning from Cuba

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## SUMMARY

Hantavirus hemorrhagic fever with renal syndrome is endemic in Europe and Asia, while hantavirus cardiopulmonary syndrome (HCPS) is endemic in Northern, Central and Southern America. The first case of imported HCPS involving an Italian traveller returning from Cuba is reported.

**KEY WORDS:** Hantavirus, Hantavirus Cardiopulmonary Syndrome, 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 (Nichol *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 13<sup>th</sup> to 30<sup>th</sup> 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 17<sup>th</sup> 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 21<sup>st</sup> 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

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TABLE 1 - *Hantavirus values with hantavirus cardiopulmonary syndrome imported from Cuba.*

Assay	Time after onset of HPS symptoms	
	4 days	90 days
IgM <sup>1</sup> (IFA)	<b>positive</b>	negative
IgM <sup>2</sup> (ELISA)	negative	negative
IgG <sup>3</sup> (ELISA)	<b>positive</b>	<b>positive</b>
Real-time RT-PCR <sup>4</sup>		
Sin Nombre	<b>positive</b>	ND
Andes	negative	ND
Tula	negative	ND
Dobrava	negative	ND
Puumala	negative	ND
Hantaan/Seoul	negative	ND

<sup>1</sup>Anti-Hantavirus IIFT IgM, EUROIMMUN Lübeck, DE (Sin Nombre and Andes virus antigens). <sup>2</sup>Anti-Hanta Virus Pool ELISA IgM, EUROIMMUN, Lübeck, DE (Hantaan, Dobrava and Puumala virus antigens). <sup>3</sup>Anti-Hanta Virus Pool ELISA IgG, EUROIMMUN, Lübeck, DE (Hantaan, Dobrava and Puumala virus antigens). <sup>4</sup>Hantavirus real-time reverse transcription-PCR (Kramski *et al.*, 2007).

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 29<sup>th</sup> September, the man was discharged with an improved chest radiological picture. Three months later, on 17<sup>th</sup> 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

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

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