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Short Communication

## Serological diagnosis of hantavirus pulmonary syndrome in a febrile patient in Colombia



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### SUMMARY

Hantavirus pulmonary syndrome (HPS) is an often fatal rodent-borne zoonosis caused by any of at least 20 hantavirus genotypes distributed throughout the Americas. Although HPS has been documented in several bordering countries, it has not been reported in Colombia. Here we report seroconversion to a hantavirus in paired samples from a hospitalized patient with symptoms compatible with HPS from Montería, Córdoba Department, north-western Colombia. Tests for regionally endemic agents including *Plasmodium*, *Leptospira*, *Salmonella*, dengue virus, *Brucella*, *Rickettsia*, human immunodeficiency virus and hepatitis viruses were negative. Because the patient was enrolled in a clinical trial for hemorrhagic fevers conducted by the University of Córdoba, serum samples were collected on admission and at discharge. Testing using Sin Nombre virus ELISA showed IgG and IgM seroconversion between samples. The eventual finding of this first clinical case of hantavirus infection in Colombia is consistent with the high prevalence of hantavirus antibodies in humans in the region and the likely exposure of the patient to rodents. The clinical presentation was similar to that found in neighbouring Panama.

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## 1. Introduction

Hantavirus pulmonary syndrome (HPS) is an often fatal rodent-borne zoonosis caused by any of at least 20 hantavirus genotypes distributed throughout the Americas. The disease was first identified in the USA where the newly described etiological agent, Sin Nombre virus (SNV), has caused approximately 600 cases with a fatality rate of 36%.<sup>1</sup> Although HPS is documented in several bordering countries, it has not been reported in Colombia. In 2004, we detected IgG antibodies to SNV by ELISA in 14% of serum samples from 88 rural volunteers in north-western Colombia.<sup>2</sup> In 2013, we detected IgG antibodies to Maciel or Araraquara hantaviruses in 8.4% of 286 agricultural workers in Córdoba Department.<sup>3</sup> These prevalences are much higher than those found in serosurveys in North America and suggest that rural workers in north-western Colombia are frequently exposed

to one or more hantaviruses.<sup>2–5</sup> Nevertheless, no HPS cases had been reported in Colombia.

## 2. Methods

In May 2013, a 26-year-old man from Montería, Colombia (Figure 1) was admitted to the emergency ward (San Jerónimo Hospital, Montería) complaining of fever, headache, arthralgia, myalgia, asthenia, malaise, and dyspnoea of 7-day duration. He was tested for regionally endemic agents, *Plasmodium*, *Leptospira*, *Salmonella*, dengue virus, *Brucella*, *Rickettsia*, human immunodeficiency virus and hepatitis viruses. Because the patient was enrolled in a clinical trial for hemorrhagic fevers conducted by the University of Córdoba, serum samples were collected on admission and at discharge. These serum samples were tested by ELISA for antibodies reactive to SNV. The SNV ELISA detects (cross-reacts with), but does not distinguish between all known hantaviruses hosted by New World cricetid rodents.

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**Figure 1.** Map of South America showing the location of the city of Montería, within Córdoba Department, Colombia. Note the proximity to Panama.

### 3. Results

The patient lived in a rural natural habitat bordering cultivated areas where people live alongside rodents and in poor sanitation conditions. On admission, he was febrile (40 °C) and had a heart rate of 76 beats/min and respiratory rate of 23 breaths/min. He had icteric sclera, no lymphadenopathy, normal cardiac and pulmonary

auscultation findings, painful splenomegaly, no rash, and a normal neurological examination. A chest X-ray was normal. Pancytopenia and hyperbilirubinemia were seen on haematological analysis. Tests for regionally endemic agents in acute phase samples were all negative (Table 1). The patient remained febrile for 3 days; he was discharged on day 5 without a definitive diagnosis. ELISA testing of the stored admission and discharge sera showed IgG and IgM seroconversion to SNV. Tests for *Leptospira*, dengue virus, *Brucella* and *Rickettsia* repeated on convalescent samples were negative (Table 1).

### 4. Discussion

We did not find it unusual that the case patient did not have pulmonary oedema and only had a mild respiratory symptoms. In a study done in bordering Panama, 21% of diagnosed HPS patients did not show pulmonary oedema and 44% had mild HPS with mild oedema but no respiratory insufficiency.<sup>6</sup> The investigators in Panama described three categories of hantavirus infection: hantavirus fever (absence of dyspnoea, normal chest X-ray, not requiring oxygen therapy), mild HPS (occasional or no dyspnoea, abnormal chest X-ray), and moderate to severe HPS (marked dyspnoea, abnormal chest X-ray, mechanical ventilation required).<sup>6</sup>

The present serologically confirmed HPS case is compatible with hantavirus fever, as described above. In Colombia we have observed other cases that are compatible with hantavirus fever, but none have been confirmed serologically. The rodents, *Zygodontomys brevicauda* (reservoir of Calabazo virus in Panama) and *Oligoryzomys fulvescens* (reservoir of Choclo virus, a known agent of HPS in Panama), are also found in adjacent Colombia,<sup>7</sup> including Córdoba. In 2011, investigators from Antioquia Department (adjacent to Córdoba) found 14% of sampled *Z. brevicauda* to be antibody-positive to SNV and Maciel viruses.<sup>4</sup> Sequencing of PCR amplicons from their lung tissue revealed a virus closely related to Calabazo virus from Panama.<sup>4</sup> This is the only report of the genetic characterization of a hantavirus in rodents in Colombia.

Confirmation of the case we describe was in accordance with one US Centers for Disease Control and Prevention laboratory criterion for the diagnosis of HPS – the detection of hantavirus-specific IgM or rising titres of hantavirus-specific IgG.<sup>8</sup> Nevertheless, hantavirus infection in humans in Colombia has not been diagnosed by culture or molecular techniques. The eventual finding of this first clinical case of hantavirus infection in Colombia is consistent with the high prevalence of hantavirus antibodies in humans in the region and the likely exposure of

**Table 1**  
Potential etiological agents evaluated in a hantavirus pulmonary syndrome patient in north-western Colombia

Etiological agent	Diagnostic method	Result in acute phase sample	Result in convalescent phase sample	Interpretation
<i>Plasmodium</i> sp	Blood smear	Negative for parasitic forms	Not performed	Infection ruled out
<i>Leptospira</i> sp	MAT <sup>a,b</sup>	<1:100	<1:100	Without seroconversion
<i>Salmonella</i> sp	Blood culture	Negative	Not performed	Infection ruled out
Dengue virus	IgM/Ns1 antigen	Negative/negative	Negative/not performed	Infection ruled out
<i>Brucella</i> sp	Rose Bengal test	Negative	Negative	Infection ruled out
<i>Rickettsia</i> sp	<i>R. rickettsii</i> / <i>R. typhi</i> IFA IgG test, Focus Diagnostics <sup>®a</sup>	<1:64/<1:64	<1:64/<1:64	Without seroconversion
HIV	ELISA	Negative	Not performed	Infection ruled out
Hepatitis B virus	HBsAg	Negative	Not performed	Infection ruled out
Hantavirus	ELISA IgM/IgG <sup>c</sup>	0.74/0.5	12.6/3.5	Positive seroconversion

MAT, microscopic agglutination test; IFA, immunofluorescence antibody test; HBsAg, hepatitis B surface antigen.

<sup>a</sup> Positive cut-off values: *Leptospira* MAT titre  $\geq 1:100$ ; *Rickettsia* IFA IgG titre  $\geq 1:64$ .

<sup>b</sup> ELISA *Leptospira*-IgM was also negative.

<sup>c</sup> Sin Nombre virus (SNV) ELISA IgM and IgG optical density ( $\geq 1.10$ , positive;  $< 0.9$ , negative).

the patient to rodents. Furthermore, the clinical presentation was similar to that found in neighbouring Panama.<sup>6</sup> Finally, although there is strong evidence of a broad geographic distribution of HPS in the Americas and in neighbouring countries,<sup>2–5,9</sup> a high prevalence of hantavirus infection in local rodent populations, and associated risk factors for HPS (exposure to rural rodents), the apparent incidence of HPS in Colombia is low. One reason for this disparity is likely poor surveillance within Colombia. It is also possible that the strain of virus infecting humans in Colombia is relatively benign and only rarely causes symptomatic disease.

The demonstration of HPS in Colombia is important information for Colombian public health and medical personnel; this case report should help physicians to suspect and diagnose HPS.

*Conflict of interest:* None declared.

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### References

1. US Centers for Disease Control and Prevention. Hantavirus. Atlanta, GA: CDC; 2013. Available at: <http://www.cdc.gov/hantavirus/> (accessed February 2014).
2. Mattar S, Parra M. Serologic evidence of hantavirus infection in humans, Colombia. *Emerg Infect Dis* 2004;**10**:2263–4.
3. Guzmán C, Mattar S, Levis S, Pini N, Figueiredo LT, Mills J, et al. Prevalence of antibody to hantaviruses in humans and rodents in the Caribbean region of Colombia determined using Araraquara and Maciel virus antigens. *Mem Inst Oswaldo Cruz* 2013;**108**:167–71.
4. Londono A, Diaz F, Agudelo P, Levis S, Rodas J. Genetic evidence of hantavirus infections in wild rodents from northwestern Colombia. *Vector Borne Zoonotic Dis* 2011;**11**:701–8.
5. Aleman A, Iguaran H, Puerta H, Cantillo C, Mills J, Ariz W, et al. Primera evidencia serológica de infección por hantavirus en roedores en Colombia. *Rev Salud Publica* 2006;**8**:1–12.
6. Armien B, Pascale J, Munoz C, Marinas J, Nunez H, Herrera M, et al. Hantavirus fever without pulmonary syndrome in Panama. *Am J Trop Med Hyg* 2013;**89**:489–94.
7. Eisenberg JF. Mammals of the neotropics: the northern neotropics. Chicago, IL: University of Chicago Press; 1989.
8. US Centers for Disease Control and Prevention. Hantavirus pulmonary syndrome (HPS) case definition. Atlanta, GA: CDC; 2012. Available at: <http://www.cdc.gov/hantavirus/health-care-workers/hps-case-definition.html> (accessed January 2014).
9. Jonsson CB, Figueiredo LT, Vapalahti O. A global perspective on hantavirus ecology, epidemiology, and disease. *Clin Microbiol Rev* 2010;**23**:412–41.