

## CASE REPORT

### HANTAVIRUS PULMONARY SYNDROME IN ANAJATUBA, MARANHÃO, BRAZIL

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#### SUMMARY

The authors report a confirmed case of hantavirus pulmonary syndrome in the rural area of the municipality of Anajatuba, state of Maranhão. Two other suspected cases from the same region are also described. The confirmed case involved a previously healthy young woman who died with signs and symptoms of acute respiratory insufficiency 5 days after presenting fever, myalgia and a dry cough. The patient was a student who was helping her parents with work in the fields; it was a habit of the family to store rice inside the house. The suspected cases involved two first-degree relatives working as field hands who died of acute respiratory insufficiency 24 and 48 hours, respectively, after presenting fever, myalgia and a dry cough. Both stored rice and corn inside their home. People living in the region reported massive infestations with rats in the woods and fields.

**KEYWORDS:** Hantavirus disease; Hantavirus pulmonary syndrome; Brazil.

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#### INTRODUCTION

Since it was first described in 1993<sup>3,11</sup>, hantavirus pulmonary syndrome (HPS) has become a source of concern at the public health level in several countries due to its severity and to the limited control measures. More than 14 viruses belong to the genus *Hantavirus*, family Bunyaviridae, have been implicated in human disease, with at least 9 of them being associated with HPS<sup>14</sup>. The disease is characterized by the onset of fever, myalgia and abdominal pain, rapidly accompanied by cough and dyspnea, which are habitually followed by acute respiratory insufficiency, circulatory collapse and death in most cases<sup>6</sup>. The natural reservoirs of the disease are mainly represented by wild rodents that harbor the virus apparently without developing the disease. These rodents can eliminate large amounts of the virus through the feces, urine and saliva. Human infection can occur by inhalation of aerosols containing the virus, by contact with a rodent's saliva during a bite, or by contact of non-intact skin with rodent excreta<sup>12</sup>. Person-to-person transmission was suggested in Argentina<sup>8,17</sup>, but subsequent investigations indicated that this possibility is highly improbable<sup>12</sup>. As of May 2001, 114 HPS cases had been reported in Brazil (Fundação Nacional de Saúde, written communication): 36 from Paraná, 23 from São Paulo, 18 from Rio Grande do Sul, 16 from Minas Gerais, 11 from Santa Catarina, 05 from Mato Grosso, 02 from Pará, 01 from Maranhão, 01 from Bahia and 01 from Goiás. In Brazilian cases so far the fatality rate is 44.7% (Fundação Nacional de Saúde, written communication).

#### CASE REPORT

The municipality of Anajatuba, located about 120 km from São Luís in the microregion of Baixada Ocidental Maranhense (Western State of Maranhão Floodplain) has a population of 20,316 inhabitants and a territory of 1,137 km<sup>2</sup>. The climate is semihumid tropical with a relatively uniform temperature ranging from 26 to 28 °C. Rainfall ranges from 2,000 to 25,000 mm/year and predominates in the months from January to July. The soil is of the hydromorphic type, with the characteristics of periodic flooding, when vast alluvial fields occur in the shape of an immense fresh water sheet called the "Pantanal Maranhense" (Floodplain of the State of Maranhão). In the summer these waters recede considerably, draining into the rivers of the region and leaving vast grassy fields exposed. Part of the population lives in mud huts along the margins of these fields. The main economic activities are manioc, rice and corn culture, cattle grazing and hook and line fishing. The Quebra site, where the confirmed HPS case was detected, is located in the rural area of the municipality of Anajatuba. The population is of 535 inhabitants and very poor acquisitive power who basically live at manioc plantation and fishing in the flooded lowlands.

On May 20, 2000, M.C.R., a 19-year-old girl, a student who helped her parents in the fields, presented a fever of 39 °C, accompanied by shivering and intense generalized myalgia predominating in the lumbar region, followed by persistent dry cough. On May 22 she sought medical care and was treated with diclofenac and gentamicin and sent back home.

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Fig. 1 - Location of the Municipality of São Luís and of Anajatuba on the Map of the State of Maranhão

About 36 hours later she was admitted to the municipal hospital with intense dyspnea, cyanotic extremities and tachycardia. Auscultation revealed diffuse crepitant and bubbling stertors in both lungs and the patient presented petechia on the limbs (except for the extremities). There were no signs of meningeal irritation. Profuse diarrhea occurred during hospitalization. She was transferred to a hospital in São Luís, where she died 30 minutes after admission, before laboratory or radiologic tests could be performed. The presence of IgM and IgG class antibodies were detected by enzyme-linked immunosorbent assay (ELISA) using an Andes recombinant nucleocapsid protein antigen, performed at the Instituto Evandro Chagas, Belém, Pará. Blood specimens were diluted to 1:100 through 1:6,400. Samples were tested against the recombinant nucleocapsid antigen and a recombinant control antigen. A conjugate of anti-rabbit immunoglobulin G was used to detect bound of IgM and a conjugate of anti-human immunoglobulin G was used to detect bound of IgG. On each assay were included one positive and three negative controls. The optical densities (OD) were corrected by subtracting the OD value of the antigen control from the OD value of the sample with the antigen. The cutoff was established by adding 3 standard deviations (SD) to the mean of the negative controls. If the cutoff value was inferior to 0.3 these values were taken as the cutoff, so if the samples corrected OD values were superior to that they were considered positive.

Two additional suspected cases of HPS were observed. Both were laborers from São Jerônimo, a village located about 8 km from the place of residence of M.C.R. The first, C.C.D., was a 25-year-old man who was admitted to the municipal hospital on March 16, 2000 complaining of high fever, not measured, which had started five days before, with shivering and generalized myalgia predominating in the lumbar region, in addition to periorbital headache and dry cough. About 12 hours after the onset of symptoms he had experienced important dyspnea and profuse sweating. Clinical examination revealed a temperature of 36 °C, severe dyspnea, tachypnea, and tachycardia. Arterial pressure was 40 x 20 mmHg, and the pulse was rapid and filiform. The extremities were cold and cyanotic and petechia were present on the limbs. Pulmonary auscultation revealed diffuse crepitant and bubbling stertors in both lungs. The patient died 40 minutes after admission to the hospital. The second patient, E.L.D., a 19-year-old boy, a nephew of C.C.D., was admitted to the municipal hospital on May 6, 2000 complaining of fever, not measured, of 2 days duration, with shivering, myalgia predominating in the lumbar region, and periorbital headache. About 24 hours after the onset of symptoms he started to have a dry cough accompanied by vomiting and watery diarrhea and followed by progressive dyspnea, general malaise and agitation. Upon admission, he had a temperature of 39.9 °C, arterial pressure of 80 x 50 mmHg, intense dyspnea, cyanotic extremities, and crepitant and bubbling stertors in both lungs, and he died about 24 hours after admission. No laboratory tests were performed because they were not available at the health unit of admission. In these cases no autopsy was performed. On May 25, 2000, blood samples were gathered from 17 family contacts, all asymptomatic, of the two cases, for tests of the presence of IgG and IgM using the Andes antigen. Positivity of IgG was detected in 14 (82%). All were negative for IgM. A population study, currently in progress in the region, should determine the local prevalence.

## DISCUSSION

Although only patient M.C.R. can be considered a confirmed case on the basis of the criteria for case definition of the CDC<sup>4</sup>, the clinical course of the three patients was consistent with that described for severe forms of

HPS. The early symptoms of fever, myalgia and dry cough, followed by severe and rapidly progressive respiratory insufficiency, represented a pattern which is consistently repeated in the cases reported in the literature<sup>1,2,6,9,10,15</sup>. In general, HPS presents three phases<sup>12</sup>: the first, the prodromic phase, is nonspecific and is characterized by high fever, myalgia and headache, with the possible occurrence of nausea, vomiting and diarrhea; the second, the cardiopulmonary phase, starts with dry or productive cough followed by dyspnea, cyanosis and tachycardia and progresses to severe respiratory insufficiency and signs of circulatory collapse. The death rate is elevated during this phase. The third phase, of convalescence, is characterized by the disappearance of respiratory symptoms and by hemodynamic recovery. In clinical practice, the diagnosis can be confirmed by the presence of IgM class antibodies or by the increase in IgG class antibodies against hantavirus by ELISA<sup>3,4,12</sup>. The detection of viral genome by reverse transcription and polymerase chain reaction, indirect immunofluorescence, neutralization, passive hemagglutination and Western blot technique are also used for diagnostic.

The region where the confirmed and suspected cases occurred belongs to the rural area and its economy is based on agriculture and fishing. Rodent infestation both in flooded fields and in the forest area is significant. It is common to identify dwellers who use the flesh of these rodents as bait for fishing. Field studies involving the capture and identification of these rodents are currently underway. An abnormally high rainfall was recorded in the Baixada Ocidental Maranhense during the months that preceded the occurrence of these cases. Thus, the fields were flooded at levels above the habitual ones and the waters reached the residences, most of which are located along the margins of these fields. The association between climatic and environmental characteristics and hantavirus transmission has been studied and was documented in the Four Corners region in the United States<sup>5,6,7,19</sup>. The population density of rodents, influenced by environmental conditions, seems to be an important link in this association<sup>13</sup>. In the rural zone of the municipality of Anajatuba, rodent excreta are easily identified inside human dwellings, which in general have dirt floors. The high prevalence of IgG antibodies (82%) against hantavirus identified in family contacts of the patients strongly suggests that hantavirus circulates in the region. In the rural area of Juquitiba, São Paulo, the serologic survey of 49 people living in the neighbourhood of the patients with SPH detected 4 persons (8.2%) with IgG or IgM antibodies against the antigen of the Hantaan virus and three persons (6.1%) with IgG antibodies against the antigen of the Sin Nombre virus<sup>16,18</sup>. In Franca, São Paulo, serologic tests carried out in 12 workers of the exhibition park, IgG antibodies against the antigen of the Sin Nombre virus were positive in 3 individuals (25%)<sup>9</sup>. An epidemiological study is currently being set up in the municipality of Anajatuba to define the prevalence of hantavirus infection, to assess the dynamics of transmission and to identify asymptomatic or oligosymptomatic forms of the disease. Flooding of the Baixada Maranhense fields is a seasonal phenomenon that is repeated every year during the rainy season, suggesting that the epidemiologic conditions that permitted the occurrence of a human case of HPS may be reproduced every year.

## RESUMO

### Síndrome pulmonar por Hantavírus em Anajatuba, Maranhão, Brasil

Os autores descrevem um caso confirmado de síndrome pulmonar por hantavírus ocorrido na área rural do município de Anajatuba, estado

do Maranhão. Outros dois casos suspeitos da mesma região são também descritos. O caso confirmado era de uma mulher jovem, previamente saudável, que foi a óbito com quadro de insuficiência respiratória aguda 5 dias após haver iniciado quadro de febre, mialgia e tosse seca. Trata-se de uma estudante que trabalhava com os pais na lavoura, os quais tinham a prática de estocar arroz dentro de casa. Os casos suspeitos são de dois lavradores, parentes diretos, que foram a óbito com insuficiência respiratória 24 horas e 48 horas, respectivamente, após início de febre, mialgia e tosse seca. Ambos armazenavam grãos de arroz e milho dentro da residência. Os moradores da região relatam grande infestação por ratos na região de mata e campo.

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