ARENAVIRUS: A FATAL OUTCOME

ABSTRACT

A new case of Arenavirus infection, with fatal outcome, in São Paulo State, Brazil, is reported. On May 17th, 1999, a 32-year-old-man, an coffee-grain machine operator, resident in the rural area of Espírito Santo do Pinhal, presented a illness with clinical suspicion of hantavirus infection. High fever, myalgia, malaise, abdominal pain, nausea, vomiting and cough characterized the disease. The patient worsened with hemoptysis and hematuria. He developed dyspnea, tachycardia, mental confusion and low fever (36-37°C). On May 21st, the patient was transferred to the Hospital Santa Casa de Misericórdia of São João da Boa Vista city. Death occurred on May 28th. Differential diagnosis included: leptospirosis, hepatitis, yellow fever, herpes simplex, cytomegalovirus, mononucleosis, HIV 1 and 2 and hantavirus; for which serological tests were negative. Rabies virus detection by immunofluorescence was also negative. A blood sample, taken before death, was inoculated intracerebrally into newborn mice. Liver, lungs, heart, kidney and spleen samples were submitted to histological examination; the liver showed severe acute hepatitis with extensive lobular necrosis; lungs presented a discrete interstitial inflammation. All other organs were virtually normal. An agent was isolated from the brains of sick mice on the 11th day after inoculation. For its serological characterization the virus (SPH 185338) was tested by complement fixation (CF) and neutralization (N). By CF and N tests, the agent was classified as a member of Tacaribe complex closely related to Sabia virus.

INTRODUCTION

The first case of Arenavirus infection in Brazil was detected in São Paulo State, in 1990, when a new arenavirus, called Sabia virus, was isolated from an agricultural engineer who presented hemorrhagic fever syndrome and died (1). The arenaviruses are generally associated with chronic infection but clinically benign in rodents native from Europe, Africa and Americas, and perhaps other continents. These viruses have been isolated from diverse groups of mammalian hosts in defined geographic areas. They are clinically responsible for human infections and have been

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used as experimental models to study acute and persistent infections. Man usually becomes infected by contact with contaminated rodent excreta (2).

Arenaviruses have been identified in Old World (LCMV, Lassa and Mobala) and in New World. The first arenavirus discovered was lymphocytic choriomeningitis virus (LCMV) in 1933 during a St. Louis encephalitis epidemic. It was associated with aseptic meningitis and identical to an agent that chronically infected mouse colonies (2). After the isolation of Tacaribe virus from Artibeus bat and mosquitoes in Trinidad in 1956 and 1958, respectively, no subsequent isolations were reported for a long period. New arenaviruses have been discovered in the Americas on the average of one every three years, including two highly lethal, Guanarito and Sabia (1, 2, 5), both in 1990. In Brazil other arenaviruses, such as Amapari and Flexal, were isolated in Evandro Chagas Institute. Flexal was responsible for two laboratory infections and should be regarded as potentially dangerous. Tacaribe virus was implicated in a single example of febrile disease with mild central nervous symptomatology (2, 3, 6).

Junin, Machupo, Guanarito, and Sabia viruses are associated with hemorrhagic fevers and high mortality in Argentina, Bolivia, Venezuela and Brazil, respectively. By this reason, they represent a local public health impact of rodent-borne viral diseases, and are considered emerging diseases. Arenaviruses are divided into two complexes: an American or Tacaribe complex and an Old World or LCM complex, based on serology and phylogenetic analysis of viral RNA. The Tacaribe complex is associated with American rodents, whereas LCM, Lassa, and Mobala are associated with Old-world rodents.

**CASE REPORT**

On May 17th, 1999, a 32-year-old man, a coffee-grain machine operator, resident in the rural area of Espirito Santo do Pinhal - SP, presented an illness with clinical suspicion of hantavirus infection. The clinical manifestations were characterized by a febrile illness accompanied by high fever, myalgia, malaise, abdominal pain and epigastric pain, nausea, vomiting and cough. He worsened with hemoptysis and hematuria. The patient developed dyspnea, tachycardia, mental confusion and low fever (36°-37°C). Paleness, tremors, sweating, edema on the face and neck were also present. On May 21st, during the course of the illness, there was an aggravation, and the patient was transferred to Hospital Santa Casa de Misericórdia, in São João da Boa Vista city. Death occurred on May 28th.

Differential diagnosis included: leptospirosis, hepatitis, yellow fever, herpes simplex, cytomegalovirus, mononucleosis, HIV 1 and 2 and hantavirus; for which serological tests were negative. Rabies virus detection by immunofluorescence was also negative.

**MATERIAL AND METHODS**

Suckling mice were inoculated intracerebrally with 0.02 ml of patient's blood sample collected in the 11th day of disease, before death. Mice liver, lung, heart, kidney and spleen samples were submitted to histological examination. According to histological examination, the liver showed severe acute hepatitis with extensive lobular necrosis and the lungs presented a discrete interstitial inflammation. All other organs were virtually normal.

An agent was isolated from the brains of sick mice on the 11th day after inoculation. The serologic characterization of the virus identified as SPH-185338 was made by complement fixation (CF) (7) and neutralization (N) (8) tests. A test for sensitivity to the delipidizing action of sodium deoxycholate (SDC) was also done (9).

**RESULTS AND DISCUSSION**

Cross-CF tests revealed that the SPH-185338 virus is classified as belonging to Tacaribe complex, based on its relationships with Sabia, Amapari and Flexal viruses. By N tests, the virus is closely related to Sabia virus. The virus was shown to be sensitive to SDC. The titer of the virus in the untreated controls was found to be $10^{-6.3} \text{LD}_{50}$ and after SDC treatment, $10^{-2.5} \text{LD}_{50}$, a behavior similar to Tacaribe virus which titer in the (untreated $\geq 10^{7.2} \text{LD}_{50}$ and treated $\leq 10^{-2.5} \text{LD}_{50}$).

The patient of the case here reported was probably infected in the area where he lived and worked, where there is a high risk of exposure to rodent excreta, as consequence of agricultural occupation. Laboratory infections caused by arenaviruses have also been reported. Therefore,
human and rodent specimens should be processed with appropriated precautions in BSL-4 and/or BSL-3 laboratories, but with additional precautions, since the transmission can occur through aerosols. In Brazil, Flexal virus had caused two laboratory infections and Sabia virus was responsible for two laboratory infections, one in Brazil in 1992 and other in the USA in 1994 (2, 3, 4, 6).

In conclusion, the current difficulty in diagnosing arenavirus infections, and distinguish them from other viral infections, especially when they become hemorrhagic, will be possible only with a better characterization of these viruses.

REFERENCES


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