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Review Article

Chapare mammarenavirus - a new deadly virus outbreak: a review

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ABSTRACT

In 2003 an emerging mammarenavirus (formerly arenaviruses) was discovered in Bolivia and named Chapare (CHAPV). It was related to severe and fatal haemorrhagic fever, being similar in clinical features to Machupo (MACV). In mid-2019, CHAPV was the explanation for a cluster of 5 cases, two of them laboratory confirmed, three of them fatal. Reverse transcription polymerase chain reaction (RT-PCR) analysis and subsequent analysis of the entire virus S and L ribonucleic acid (RNA) segment sequences identified the virus as a member of the New World Clade B arenaviruses, which includes all the pathogenic South American arenaviruses. The virus was shown to be most closely associated with Sabia´ virus, but with 26% and 30% nucleotide difference within the S and L segments, and 26%, 28%, 15% and 22% aminoalkanoic acid differences for the L, Z, N, and GP proteins. LUJV, CHAPV, GTOV, and SABV, which are geographically restricted, have been associated with only a few to a few dozen cases. They are, therefore, relatively unimportant to clinicians compared to many other viruses that are usually co-endemic. However, MACV, JUNV, and especially LASV have caused large outbreaks (LASV has caused hundreds of thousands of infections per year). Visitors to countries in which these viruses are endemic, or war-fighters that are deployed to these countries, need to be aware of how to prevent and suspect a mammarenavirus infection.

Keywords: Chapare virus, Mammarenavirus, New world epidemiology

INTRODUCTION

Mammerenavirus has gained specific interest in researchers and bio scientists in the last few years worldwide. Mammarenavirus is also known as arenavirus. It is mostly found in mammals but human transmission was not much appreciated before. Now it has gained an new fame in the virology as its human transmission case was reported in Bolivia has significantly improved worldwide.[1,2] In many countries of South America and abroad, the amplitude and therefore the magnitude of Mammarenavirus outbreaks has been increasing and detected. Metagenomic and metatranscriptomic are different techniques by whcih different novel viruses are

identified.[3] This also includes Mammarenaviruses, Machupo (MACV), Latino (LATV) and Chapare (CHAPV).[4]

In 2003 to 2004, CHAPV was recovered from one fatal case of viral haemorrhagic fever within the Chapare River region in rural Bolivia. Additional cases were reported from this outbreak; however, details and laboratory confirmation are lacking. Rodents of the Muroidea are the natural hosts of most mammarenaviruses. Old World mammarenaviruses are found in rodents of the Muridae, subfamily Murinae. New World mammarenaviruses are found in rodents of the Cricetidae, subfamily Sigmodontinae. Mammarenavirus human transmission is also reported via animals only especifically rodents. Rodents blood, excreta or secreta, or body parts caught in mechanical harvesters. Only small quantities of MACV can be isolated from human blood or from throat or oral swabs of infected patients.[5]

VIRAL LIFE CYCLE

Arenaviruses produce enveloped and spherical to pleomorphic virions, ranging from 50 to 300 nm in diameter. The particles' sandy appearance in microscopy sections earned these viruses their name (Latin arena=sand). The arenavirus genome consists of two single-stranded RNA (RNA) molecules, designated L (large) and S (small). Virus particles initially enter the host through inhalation of aerosolized particles. It is hypothesized that alveolar macrophages are the first cell types infected due to the route of infection and virus present in macrophages early in infection.[6] The life cycle of mamerenavirus is shown in Figure 1.

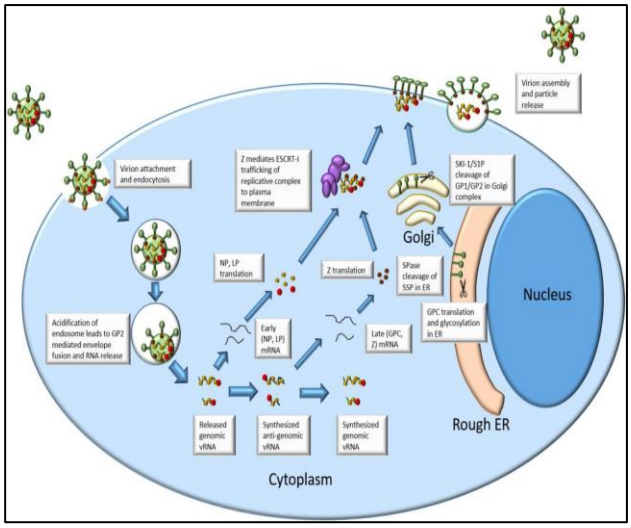

Figure 1: Life cycle of Mamarenavirus.

CLINICAL FEATURES

New World mammarenaviral hemorrhagic fevers caused by CHAPV, GTOV, JUNV, MACV, or SABV are clinically similar. Disease begins insidiously after an incubation period of 1 to 2 weeks. Initial symptoms/signs often include fever and malaise, headache, myalgia, epigastric pain, or anorexia. After 3 to 4 days, signs become increasingly severe with multisystem involvement: prostration; abdominal pain; nausea and vomiting; constipation; or mild diarrhoea. In some cases, dizziness, photophobia, retro-orbital pain, or disorientation may also appear, as well as the earliest signs of vascular damage, such as conjunctival injection, skin petechiae, mild (postural) hypotension, or flushing over the head and upper torso. About 30% of patients develop more severe hemorrhagic or prominent neurologic manifestations (convulsions, tremor of the hands or tongue, coma) or secondary bacterial infections during the second week of illness. Hemorrhagic manifestations, such as bleeding from mucous membranes (gums, nose, vagina/uterus, gastrointestinal tract) and ecchymoses at needle puncture sites, are common in these patients. However, blood loss is minor overall. Capillary leakage may be a hallmark of disease, and elevated haematocrit occurs during the height of capillary leak syndrome. Death usually occurs 7 to 12 days after disease onset from organ failure and shock. Patients who survive begin to enhance during the second week of disease onset. Convalescence often lasts several weeks with fatigue, hair loss, dizziness, or Beau's lines in digital nails. "VHF" convalescent symptoms also include pharyngitis or pharyngitis.[7]

DIAGNOSIS

For virus detection by either virus isolation, antigen detection, or RNA detection early samples got to be taken (1–2 days after onset, during the fever period): several biological products can potentially harbour virus material including whole blood (sera and cells buff coat). Mammarenavirus antibodies are often detected by enzyme-linked immunosorbent assays (ELISAs), virus neutralization tests, and fluorescence microscopy assays (IFAs). RT-PCR, real-time PCR, and real-time RT-PCR tests are valuable tools for rapid and early diagnosis of mammarenavirus infections. However, the use of these assays in a clinical or environmental setting for the early detection of human cases has been limited by the expense of equipment and by expertise. Virus isolation is that the gold standard for diagnosis of mammarenavirus infections. Mammarenaviruses can easily be recovered in cell cultures, particularly from Vero cells.[8] (Table 1)

PROPHYLAXIS AND TREATMENT

Few prophylactic and therapeutic treatments are approved for use against mammarenaviral hemorrhagic fevers. Treatment, therefore, consists primarily of supportive care and passive antibody therapy. Transfusion of immune convalescent plasma with defined doses of JUNV-neutralizing antibodies is that the present therapeutic intervention and treatment method against AHF. Current anti-mammarenaviral therapy is limited to an off-label use of the non-immunosuppressive guanosine analogue, ribavirin (1-β-d-ribofuranosyl- 1-H-1,2,4-triazole-3-

carboxamide), an IMP dehydrogenase inhibitor. Despite the bioterrorism and public health risks associated with pathogenic mammarenavirus infection, FDA-licensed vaccines are currently not available.[9]

Table 1: Lab diagnosis of Chapare Mammarenavirus.

Lab diagnosis	
Sample collection	• Virus isolation, antigen detection, or RNA detection- early samples need to be taken (1–2 days after onset, during the fever period, whole blood (sera and cells buff coat) • Free viral RNA-sera, urine, sperm • Antibody detection-early (1–5 days after onset) and late blood samplings are useful (2 weeks after onset)
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	•
Sample handling	Class II biological safety cabinet, tubes with 1 ml of Trizol, in freezer
Detection procedures	• Neutralization test using TC ID50 Method – with neutral red in pretitered antiserum • Ag capture ELISA • Immunohistochemical staining. • IFA • Antibody detection ELISA • Neutralization test • RT-PCR-Real-time reverse transcription (RT)-PCR assay based on fluorescence resonance energy transfer (FRET) probes

*TCID - tissue culture infectious dose

CONCLUSION

Arenaviruses represent a large and taxonomically diverse group of animal viruses that are maintained by small rodents, bats, and snakes in nature. Seven mammarenaviruses, however, are the etiological agents of severe viral hemorrhagic fevers related to high case fatality rates. Distance from or safe handling of rodents and their bodily fluids or tissues and general rodent control around human settlements or camps should be the first priority to prevent mammarenavirus infections.

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