

UNKNOWN DISEASE IN SOUTH AFRICA IDENTIFIED AS ARENAVIRUS INFECTION

H Zeller (herve.zeller@ecdc.europa.eu)¹, K Leitmeyer¹, C Varela Santos¹, D CouLombier¹

1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Introduction

On 12 September 2008, a tourist guide organising safari trips, residing in Lusaka, Zambia, was evacuated in a critical condition to Johannesburg, South Africa. She was admitted to a clinic where she died on 14 September about 10 days after the onset of symptoms. The symptoms included a prodromal phase with fever, myalgia, vomiting, diarrhoea, followed by rash, liver dysfunction and convulsions [1]. Cerebral oedema was detected on scan examination. No laboratory specimen was available for investigation.

The paramedic who had cared for the index case during her evacuation to Johannesburg developed prodromal symptoms similar to the index case. He was hospitalised on 27 September. His condition deteriorated and he died on 2 October. An intensive care unit nurse who cared for the index case in Johannesburg developed similar flu-like symptoms and was hospitalised on 1 October. Her condition deteriorated on 4 October and she died on 5 October of acute respiratory distress syndrome. In both cases, the incubation period is estimated to have been about one week. On 13 October, the World Health Organization (WHO) posted a website update informing about a fourth case affecting a nurse who had been in contact with the paramedic [2].

On 12 October 2008, the National Institute for Communicable Diseases (NICD) in South Africa provided preliminary evidence that the causative agent of the disease was a virus from the Arenaviridae family [3]. Specimens were shipped to the United States Centers for Disease Control and Prevention (CDC) in Atlanta for additional investigations.

Arenavirus taxonomy

Arenaviruses are enveloped viruses (about 120 nm diameter) with a bi-segmented negative strand RNA genome. The typical image in electronic microscopy showing grainy ribosomal particles ("arena" in latin) inside the virions gave the name to this family of viruses. The prototype is the Lymphocytic Choriomeningitis (LCM) virus, isolated in 1933 in North America from a human case with aseptic meningitis. Cases caused by LCM occur worldwide. Other arenaviruses causing hemorrhagic fevers were reported in South America, causing sporadic cases or limited outbreaks: Junin virus in 1958 in Argentina, Machupo virus in 1963 in Bolivia, Guanarito virus in 1990-1991 in Venezuela, Sabia virus in 1990 in Brazil and more recently Chapare virus in 2004 in Bolivia [4]. In West Africa, Lassa virus was identified in Nigeria in 1969. It causes

thousands of cases each year in Sierra Leone, Liberia, Guinea and Nigeria. However, only limited data are available to assess the real incidence of Lassa fever in Africa.

Clinical symptoms of arenavirus infections, treatment and vaccine

Two types of clinical presentations are described: neurological and haemorrhagic fever. However, asymptomatic arenavirus infection may be frequent. The incubation period is about 10 days (3-21 days). LCM viruses cause aseptic meningitis or meningoencephalitis with an overall case fatality <1%. Foetal infections can result in congenital abnormalities or death. Transmission of arenaviruses via organ transplantation has been documented; immunosuppressed recipient patients can develop fatal haemorrhagic fever-like disease [5,6]. The Lassa viral haemorrhagic fever usually presents as a non-specific illness with symptoms including fever, headache, dizziness, asthenia, sore throat, pharyngitis, cough, retrosternal and abdominal pain, and vomiting. In severe forms, facial oedema is associated with haemorrhagic conjunctivitis, moderate bleeding (from nose, gums, vagina, etc.) and exanthema. Neurological signs may develop and progress to confusion, convulsion, coma and death. Severe prognosis is associated with a high viraemia, elevated aspartate aminotransferase (AST) liver enzymes, bleeding, encephalitis and oedema. There is a very high risk of foetal mortality in pregnant women during the third trimester of pregnancy. Case fatality rates range from 5 to 20% for hospitalised cases. Clinical symptoms of infection by arenaviruses in South America are similar to those described for Lassa fever in Africa.

Ribavirin has been shown to be an effective treatment for Lassa fever, especially when started within the first six days of illness [7,8]. There is currently no vaccine for Lassa fever but several candidates are under development studies with successful trials in primates [9]. One available vaccine is licensed in Argentina for Junin virus.

Reservoir of arenavirus and transmission

Arenaviruses are associated with rodents, their natural hosts. Some of these viruses can be transmitted to humans by contact with faeces, urine, blood or saliva of infected rodents or with dust containing infective particles. In South America, Machupo and Junin viruses were identified in *Calomys* rodent, and Guanarito virus was found in a *Sigmodon* cotton rat [10]. In West Africa, *Mastomys natalensis* (a peridomestic rodent) is the reservoir of Lassa virus. Its geographic distribution is much wider in sub-Saharan Africa than the presently known area of Lassa transmission [11]. Other

arenaviruses such as Mopeia virus in Mozambique had been isolated from rodents without evidence of disease in humans [10].

Fatal nosocomial and laboratory infections by arenaviruses have been reported. Contamination occurs via direct contact with body fluids or via droplets. Since the 1970s special procedures for handling these viruses (now categorised as class 4 agents) have been put in place, including the building of dedicated biosafety laboratories (BSL-4), with containment equipment for all activities involving the virus, infectious or potentially infectious body fluids or tissues.

Conclusion

In the cluster reported here, four cases have been identified including an index case and three cases of subsequent nosocomial transmission among health workers. The clinical presentation was consistent with neurological symptoms of arenavirus infection. As the incubation period for arenaviruses is up to three weeks, secondary cases may still be identified as part of the follow-up of contacts established in response to this event.

The professional activities of the index case could have favoured possible exposure to rodent excreta in a rural area.

This is the first identification of an arenavirus causing human disease in a southern African country. Further laboratory investigation will allow characterisation of the virus associated with this outbreak and its relation with the existing Lassa virus present in West Africa.

Since 1969, at least 24 cases of Lassa fever are known to have been exported outside Africa, including 16 cases imported to Europe [12,13]. However, in none of these cases has secondary transmission resulted in a symptomatic disease.

Acknowledgements

We gratefully acknowledge the openness, the collaboration and the information provided by the National Institute for Communicable Diseases in South Africa, as well as the International and Tropical Department of the French Institute for Public Health Surveillance (Institut de veille sanitaire, InVS).

References

1. National Institute for Communicable Diseases (NICD). Outbreak of an acute disease, ex-Zambia. Communicable Diseases Communique volume 7 alert 1; October 2008. Available from: http://www.nicd.ac.za/pubs/communique/2008/NICDSpecialCommOct_alert01.pdf
2. WHO website: http://www.who.int/csr/don/2008_10_13/en/index.html
3. ProMED-mail. Undiagnosed fatalities - S. Africa ex Zambia (7): arenavirus. Archive Number 20081012.3234. 12 October 2008. Available from: http://www.promedmail.org/pls/otn/f?p=2400:1001:3702875069304837::NO::F2400_P1001_BACK_PAGE,F2400_P1001_PUB_MAIL_ID:1000,74346
4. Delgado S, Erickson BR, Agudo R, Blair PJ, Vallejo E, Albariño CG, et al. Chapare virus, a newly discovered arenavirus isolated from a fatal hemorrhagic fever case in Bolivia. *PLoS Pathog.* 2008;4(4):e1000047.
5. Brief report: Lymphocytic choriomeningitis virus transmitted through solid organ transplantation - Massachusetts, 2008. *MMWR Morb Mortal Wkly Rep.* 2008 Jul 25;57(29):799-801
6. Palacios G, Druce J, Du L, Tran T, Birch C, Briese T, et al. A new arenavirus in a cluster of fatal transplant-associated diseases. *N Engl J Med.* 2008;358(10):991-998.
7. McCormick JB, King IJ, Webb PA, Scribner CL, Craven RB, Johnson KM, et al. Lassa fever. Effective therapy with ribavirin. *N Engl J Med.* 1986;314(1):20-6.
8. World Health Organization. Lassa fever - fact sheet. April 2005. Available from: <http://www.who.int/mediacentre/factsheets/fs179/en/>
9. Lukashevich IS, Carrion R Jr, Salvato MS, Mansfield K, Brasky K, Zapata J, Cairo C, Goicochea M, Hoosien GE, Ticer A, Bryant J, Davis H, Hammamieh R, Mayda M, Jett M, Patterson J. Safety, immunogenicity, and efficacy of the ML29 reassortant vaccine for Lassa fever in small non-human primates. *Vaccine.* 2008 Sep 26;26(41):5246-54.
10. Charrel RN, de Lamballerie X. Arenaviruses other than Lassa virus. *Antiviral Res.* 2003 Jan;57(1-2):89-100.
11. Fichet-Calvet E, Lecompte E, Koivogui L, Soropogui B, Doré A, Kourouma F, et al. Fluctuation of abundance and Lassa virus prevalence in *Mastomys natalensis* in Guinea, West Africa. *Vector Borne Zoonotic Dis.* 2007;7(2):119-128
12. Macher AM, Wolfe MS. Historical Lassa fever reports and 30-year clinical update. *Emerg Infect Dis.* 2006 May;12(5):835-7.
13. Unit for Surveillance and Communication, Unit for Preparedness and Response, Editorial team. E-alert 24 July: Case of Lassa fever imported into Germany from Sierra Leone. *Euro Surveill.* 2006;11(30):pii=3008. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3008>

This article was published on 16 October 2008.

Citation style for this article: Zeller H, Leitmeyer K, Varela Santos C, Coulombier D. Unknown disease in South Africa identified as arenavirus infection. *Euro Surveill.* 2008;13(42):pii=19008. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19008>