

Short Review

Vaccinia Virus: It's Use in Smallpox Vaccine and Epidemiology

Marina Gea Peres¹, Jane Megid^{*1}

¹UNESP-Faculdade de Medicina Veterinária e Zootecnia-Departamento de Higiene Veterinária e Saúde Pública-Botucatu-SP, Brasil

*Corresponding author: Dr. Jane Megid, UNESP-Faculdade de Medicina Veterinária e Zootecnia-Departamento de Higiene Veterinária e Saúde Pública-Botucatu-SP, Brasil, Email:jane@fmvz.unesp.br

Received: 10-24-2014

Accepted: 03-20-2015

Published: 04-02-2015

Copyright: © 2015 Jane

Introduction

Vaccinia virus (VACV), the prototype of Orthopoxvirus, was widely used in Smallpox vaccines in Brazil during the world vaccination campaign of World Health Organization [1]. But the history of Smallpox vaccines began with finds of Edward Jenner [2]. The finds of Edward Jenner was later named immunological cross-reaction of Orthopoxvirus genus [3]. These Orthopoxvirus properties allow the use of VACV in Smallpox vaccines.

After ends of world vaccination campaign in Brazil in 1980, zoonotic Vaccinia outbreaks has been recorded in several regions of the country [4-9]. It is believed that the VACV used in the world vaccination campaign in Brasil from 1960 to 1970 was involved in the re-emergence of the disease [10]. But some research has shown that the origin of VACV isolated in outbreaks is distinct of the VACV from vaccines [11,12].

The origin of outbreaks remains unknown in Brazil, but the most accepted theory assumes that there is a populations of VACV genetically diverse circulating in still unknown natural reservoirs, and according on biological and geographical conditions are transmitted to cows and human beings [11-13].

Subheadings

There is little information about natural reservoirs of VACV. It is believed that some species of Rodent Order act as VACV natural reservoirs [14,15]. Accordingly, a serological study was conducted in areas with and without official VACV zoonotic outbreak, and the statistical analysis show low likelihood of wild rodents studied are acting as VACV reservoirs in this area [16]. Although, studies has demonstrated the

possible of transmission of VACV from mice experimentally infected to cow [15,17,18]. But this interaction has not yet been proven in natural environment.

Interestingly VACV outbreaks affecting other mammals species beyond cows was described in Brazil. In this outbreak, fourteen creole horses were affected and showed characteristics lesions in muzzle, nostrils, internal and external areas of the lips. Molecular analysis of VACV isolated in this outbreak shows two distinct VACV viruses. This finds corroborates the previous finds of two distinct VACV affecting cows in the same outbreak [7].

The most important find of Brazilians VACV diversity is the genetic and biologic dichotomy between then [8,11-13]. Through molecular analysis of A56R gene, the gene that encodes the viral hemagglutinin (HA), it was observed a deletion of six amino acids at 251 position of the gene, and VACV that present this deletion was grouped in one group while VACV that don't present this deletion was grouped in another group [11,12]. Biologically there are also differences between virus frons two groups, mice experimentally infected with VACV that show this deletion in the gene A56R didn't presented clinical signs while mice infected whit VACV that don't show this deletion developed clinical signs and evolved to death [13].

Aiming to analyze the similarity between the viruses isolated over the years in Brazil and those used during Smallpox eradication, phylogenetic analyzes of vaccines viruses were compared to VACV isolated in outbreaks, and the result obtained was that Brazilians VACV are not grouped with vaccines viruses, making it clear that the natural history of VACV is distinct from the vaccine viruses used in Brazil [8,11,12].

Discussion

According to Abrahão [15], each of viruses isolated in the outbreaks is the result of a new introduction of a virus from wild reservoir to bovine and human populations, which probably is related to intensification of anthropogenic activity. It is known that anthropogenic disturbances in ecosystems such as deforestation and habitat fragmentation increase the contact of wildlife with rural populations, changing patterns of diversity and abundance of species, which directly influences the natural dynamics of wild cycles of infectious agents.

However, anthropogenic disturbances in the environment does not explain the findings of Peres [16], that showed a high serum prevalence of antibody against Orthopoxvirus in dogs without clinical signs from areas with and without official records of VACV outbreaks. May dogs acting as disseminators of the virus to the environment or be only accidental hosts? These important issues were raised and remain unanswered [16].

A hypothetical model of transmission proposed suggests that peridomestic rodents act as link between wild and domestic animals in rural [15,17,18]. This hypothetical model of transmission meets the reports of transmission of Cowpox from *Rattus norvegicus* or mice kept as a pet, for humans, domestic animals especially cats, and wildlife, in Europe. Considering the habit of dogs preying peridomestic rodents, it would be a good explanation for the high prevalence of antibodies against Orthopoxvirus in dogs without clinical signs [16]. But from 103 rodents captured for this study none was peridomestic, and statistical analysis of results of wild rodents showed low likelihood of species studied are acting as VACV reservoirs in the study area [16].

Conclusion

The origin of Vaccinia virus outbreaks in Brazil remains unknown as well as the reservoir of the virus, but phylogenetic studies of the vaccine virus and outbreaks virus have led to a breakthrough in the search for the origin of VACV in Brazil, allowing rule out the possibility of vaccine escape during the campaign the World Health Organization. Because it is a disease underreported, it is possible that there are other factors involved in transmission to cows and those to humans that deserve to be investigated.

References

1. Fernandes T. The smallpox vaccine: its first century in Brazil (from the Jennerian to the animal vaccine). *Hist Cienc Saude Manguinhos*. 1999, 6(1): 29-51.
2. Jenner E. The Three Original Publications on Vaccination Against Smallpox. Vol. XXXVIII, Part 4. The Harvard Classics. New York: P.F. Collier & Son, 1909-1914; Bartleby.com, 2001.

3. Buller RM, Palumbo GJ. Poxvirus pathogenesis. *Microbiol Rev*. 1991, 55(1): 80-122.
4. Damaso CR, Esposito JJ, Condit RC, Moussatché N. Na Emergent Poxvirus from Humans and Cattle in Rio de Janeiro State: Cantagalo Virus may derive from Brazilian Smallpox Vaccine. *Virology*. 2000, 277(2):439-449.
5. de Souza Trindade G, da Fonseca FG, Marques JT, Nogueira ML, Mendes LC et al. Araçatuba Vírus: A Vaccinia-like Virus Associated with Infection in Humans and Cattle. *Emerg Infect Dis*. 2003, 9(2):155-160.
6. Juliana A. Leite, Betânia P. Drumond, Giliane S. Trindade, Zélia I.P. Lobato, Flávio G. da Fonseca et al. Passatempo Vírus, a Vaccinia Virus Strain, Brazil. *Emerg Infect Dis*. 2005, 11(12): 1935-1941.
7. Trindade GS, Lobato ZI, Drumond BP, Leite JA, Trigueiro RC et al. Short Report: Isolation of two Vaccinia Virus Strain from a single Bovine Vaccinia Outbreak in a Rural area from Brazil: Implications on the Emergence of Zoonotic Orthopoxviruses. *Am J Trop Med Hyg*. 2006, 75(3): 486-490.
8. Giliane de Souza Trindade, Betania Paiva Drumond, Maria Isabel Maldonado Coelho Guedes, Juliana Almeida Leite, Bruno Eduardo Fernandes Mota et al. Zoonotic Vaccinia Virus Infection in Brazil: Clinical Description and Implications for Health Professionals. *J Clin Microbiol*. 2007, 45(4): 1370-1372.
9. Trindade GS, Guedes MI, Drumond BP, Mota BE, Abrahão JS et al. Zoonotic Vaccinia Virus: Clinical and Immunological Characteristics in a Naturally Infected Patient. *Clin Infect Dis*. 2009, 48(3):e37-40.
10. Moussatché N, Damaso CR, McFadden G. When good vaccines go wild: Feral Orthopoxviruses in developing countries and beyond. *J Infect Dev Ctries*. 2008, 2(3):156-173.
11. Giliane S Trindade, Ginny L Emerson, Darin S Carroll, Erna G, Inger K Damon. Brazilia Vaccinia Viruses and Their Origins. *Emerging Infectious Diseases*. 2007, 13(7).
12. Drumond BP, Leite JA, da Fonseca FG, Bonjardim CA, Ferreira PC et al. Brazilian vaccinia virus strains are genetically divergent and differ from the Lister vaccine strain. *Microbes Infect*. 2008, 10(2):185-197.
13. Ferreira JM, Drumond BP, Guedes MI, Pascoal-Xavier MA, Almeida-Leite CM et al. Virulence in Murine Model Shows the Existence of Two Distinct Population of Brazilian Vaccinia Virus Strains. *PloS One*. 2008, 3 (8): e304.
14. Fonseca FG, Lanna MC, Campos MA, Kitajima EW, Peres JN et al. Morphological and molecular characterization of the poxvirus BeAn58058. *Arch Virol*. 1998, 143(6):1171-1186.

15. Abrahão JS, Guedes MIM, Trindade GS, Fonseca FG, Campos RK et al. One More Piece in the VACV Ecological Puzzle: Could Peridomestic Rodents Be the Link between Wildlife and Bovine Vaccinia Outbreaks in Brazil? *Plos one*. 2009, 4 (10): e 7428.
16. Marina Gea Peres, Thais Silva Bacchiega, Camila Michele Appolinário, Acácia Ferreira Vicente, Susan Dora Alendorff et al. Serological study of vaccinia virus reservoirs in areas with and without official reports of outbreaks in cattle and humans in São Paulo, Brazil. *Arch Virol*. 2013, 158(12): 2433–2441.
17. Ferreira JM, Abrahão JS, Drumond BP, Oliveira FM, Alves PA et al. Vaccinia virus: shedding and horizontal transmission in a murine model. *J Gen Virol*. 2008, 89(Pt 12): 2986-2991.
18. D’Anunção L, Guedes MI, Oliveira TL, Rehfeld I, Bonjardim CA et al. Filling one more gap: Experimental Evidence of Horizontal Transmission of Vaccinia Virus Between Bovines and Rodents. *Vector Borne Zoonotic Dis*. 2012, 12(1):61-64.