

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

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Abstract

Vaccinia Virus (VACV) was widely used in smallpox vaccines in Brazil during the world vaccination campaign of World Health Organization. After ends of this campaign in Brazil in 1980, zoonotic Vaccinia outbreaks have been recorded in several regions of the country. Researches believed that the VACV used in the world vaccination campaign in Brazil was involved in the re-emergence of the disease. To analyze the similarity between the viruses isolated from outbreaks 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. The origin of outbreaks remains unknown in Brazil, but the most accepted theory assumes that there is 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. There is little information about natural reservoirs of VACV. It is believed that some species of Rodent Order act as VACV natural reservoirs. Although, studies have demonstrated the possible of transmission of VACV from mice experimentally infected to cow, this interaction has not yet been proven in natural environment. There are two genetically distinct groups of VACV circulating in Brazil. Experimentally these two groups also differ biologically, but no difference in clinical signs was observed during outbreaks. This review analyzed VACV natural history and epidemiological studies conducted in the last years in Brazil.

Keywords: Orthopoxvirus; Smallpox virus; Vaccinia virus; Epidemiology; Natural history; Origins

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 Edwar 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 [4-12]. It is believed that the VACV used in the world vaccination campaign in Brazil from 1960 to 1970 was involved in the re-emergence of the disease [13]. But some research has shown that the origin of VACV isolated in outbreaks is distinct of the VACV from vaccines [14,15].

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 [14-16].

There is little information about natural reservoirs of VACV. It is believed that some species of Rodent Order act as VACV natural reservoirs [4,17]. 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 [18]. Although, studies has demonstrated the possible of transmission of VACV from mice

experimentally infected to cow [4,19,20]. 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 was 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 [10].

The most important find of Brazilians VACV diversity is the genetic and biologic dichotomy between them [11,15,19]. 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 [12,15]. 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 [19].

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 [11,15].

Discussion

According to Abrahão (2009a), 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 [18] 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 [18].

A hypothetical model of transmission proposed suggests that peridomestic rodents act as link between wild and domestic animals in rural [4,16,20]. 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 [18]. 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 [18].

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 of 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.

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