Monkeypox Virus in Nigeria

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Monkeypox is a zoonotic disease caused by monkeypox virus (MPXV), which is a member of orthopoxvirus genus. The reemergence of MPXV in 2017 (at Bayelsa state) after 39 years of no reported case in Nigeria, and the export of travelers' monkeypox (MPX) from Nigeria to other parts of the world, in 2018 and 2019, respectively, have raised concern that MPXV may have emerged to occupy the ecological and immunological niche vacated by smallpox virus. This review X-rays the current state of knowledge pertaining the infection biology, epidemiology, and evolution of MPXV in Nigeria and worldwide, especially with regard to the human, cellular, and viral factors that modulate the virus transmission dynamics, infection, and its maintenance in nature.

Keywords: Poxviridae ; orthopoxviruses ; monkeypox viruses ; epidemiology ; Nigeria ; signaling ; phylogeny ; gene loss ; recombination ; antiviral drugs

1. Introduction to Family Poxviridae

Poxviruses belong to family *Poxviridae*, a large and diverse family of double-stranded DNA viruses that multiplies in the cytoplasm of infected cells [1][2]. The poxviruses are known to have brick-shaped or oval structures measuring 200–400 nm when viewed with electron microscopy [3]. The wide host range of poxvirus, as well as their successful evolution, is partly due to their manipulation and modulation of host immune responses. The poxviruses are also called ancient viruses because they have been found in insects, reptiles, birds, and mammals. It is believed that these viruses, before the divergence of invertebrates and vertebrates, form visible "pox" [4][5][6].

The family *Poxviridae* is subdivided (based on their animal hosts) into two subfamilies, namely *Chordopoxvirinae* and *Entomopoxvirinae*. The former subfamily is known to infect vertebrates, and it is differentiated into 18 genera, including *Avipoxvirus*, *Capripoxvirus*, *Cervidpoxvirus*, *Leporipoxvirus*, *Molluscipoxvirus*, *Orthopoxvirus*, *Parapoxvirus*, *Suipoxvirus*, and *Yatapoxvirus*, while the latter subfamily is known to infect invertebrates, and it is grouped into four genera (*Alphaentomopoxvirus*, *Betaentomopoxvirus*, *Deltaentomopoxvirus,* and *Gammaentomopoxvirus*) [7]. The subfamilies of *Poxviridae* were each divided into its genera based on the shared antigenic similarity, induction of immunological cross protection, and phylogenetic grouping [4].

Although the infection biology and epidemiology of MPXV have been widely studied and published, there is still paucity of data and published results on the occurrence, distribution and virus transmission dynamics in Nigeria. Thus, the objective of this paper is to review the current state of knowledge concerning the infection biology, epidemiology, and evolution of MPXV in Nigeria. In addition, this review also chronicles and explores the knowledge gaps as they pertain to MPXV reservoir hosts and the ecological dynamics that modulate the maintenance of the virus in nature, as well as their spillover into human populations and subsequent human-to-human transmission.

2. History of Monkeypox

Monkeypox virus was first reported in 1959 as an outbreak of a pox-like disease in monkeys kept at a research institute in Copenhagen, Denmark [8]. The first human MPXV case in medical history was recognized when, on September 1, 1970, a nine-month-old child was admitted to the Basankusu Hospital in the Democratic republic of Congo (at that time, known as the Republic of the Congo). The boy had a smallpox-like disease from which MPXV-like virus was isolated [8][9][10][11]. Six cases of human MPXV were described in Liberia, Nigeria, and Sierra Leone between October 1970 and May 1971. The first index MPXV case in Nigeria was recorded in 1971, and 10 MPXV cases were reported between 1971 and 1978 [12]. Since then, several thousand human cases of monkeypox have been confirmed in 15 different countries, with 11 of them in African countries. Monkeypox was imported to the United Kingdom, the USA, Israel, and Singapore [13].

3. Monkeypox Virus: Morphology, Genome Organization, and Morphogenesis

Having the same morphological characteristics as other orthopoxviruses the morphology of MPXV reveals that virions are ovoid or brick-shaped particles which are enclosed by geometrically corrugated lipoprotein outer membrane. MPXV size ranges are known to be 200 by 250 nm [14][15]. Membrane bond as well as densely packed core containing enzymes, a double-stranded DNA genome, and transcription factors are protected by the outer membrane. Due to an electron microscopy fixation artifact, the core is being described as biconcave, and it has lateral body on each side [16][17].

The MPXV genome consists of a linear double-stranded DNA (≈197 kb) [18] covalently joined at its ends by palindromic hairpins, and the inverted terminal repeats (ITRs) are made up of hairpin loop, tandem repeats, and some open reading frames (ORF). Although MPXV is a DNA virus, its entire life cycle occurs in the cytoplasm of infected cells. All the proteins required for viral DNA replication, transcription, virion assembly, and egress are encoded by the MPXV genome. The genes encoding for housekeeping functions are highly conserved among OPVs and are present in the central region of the genome while those that encode for the virus–host interactions are less conserved and are located in the termini region [19][20][21][22][23]. In VACV (and most in likely MPXV) intracellular mature virus (IMV) and extracellular-enveloped virus (EEV) are two forms of infectious virions produced in poxvirus-infected cells. IMV is released on cell lysis, while EEV is released from cells via interaction with actin tails, and this is said to be the cause of rapid long distance spread of the virus within the infected host. Although the aforementioned features are for VACV, it is likely that these features are common to all OPVs [22]. However, cell-associated virions (CEVs) are formed following the microtubule-mediated transport of intracellular enveloped virus (IEV) to the cell periphery, in which the outer membrane of IEV fuses with the plasma membrane and remains attached to the cell surface. CEVs are mostly responsible for cell-to-cell spread [24]. IEV is formed when IMV is wrapped by a double membrane derived from early endosomal component [17] or the trans-Golgi network (TGN) [25]. However apart from IEV exocytosis, an alternative route for the formation of EEV is by the budding of IMV through the plasma membrane [26]. In the prototype VACV, virion morphogenesis can be defective resulting in non-infectious dense particles (DPs) [26][27], but this has not yet been reported for MPXV. In addition, unlike some strains of CPXV in which IMVs are occluded within A-type inclusions (ATI) [28][29], MPXV do not form ATIs or sequester IMVs into ATIs because of truncation in the *ATIP* gene [30].

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