BK virus and a new type of JC virus excreted by HIV-1 positive patients in rural Tanzania


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Summary. HIV-1 positive patients from Tanzanian villages near Shirati were examined for urinary excretion of the human polyomaviruses JC and BK using the polymerase chain reaction (PCR). BK virus (BKV) was detected in 11 of 23 individuals tested. The BKV DNA sequences were all closely related to prototype Gardner strain and BKV (DUN). In contrast, a new type of JCV, termed Type 3 [or JCV (Shi)], was identified in seven of these same 23 individuals by comparison with Type 1 and Type 2 sequences of the VP1/intergenic/T antigen region of U.S., European and Asian strains. This suggests that JCV and BKV, although closely related, have different evolutionary histories within the African population. The six BKV regulatory regions amplified all showed the archetypal configuration. However, two of the seven JCV regulatory regions showed rearrangements: a small deletion and an inverted repeat. JCV causes a fatal demyelinating disease, progressive multifocal leukoencephalopathy (PML), in about 5% of AIDS patients in Europe and the U.S.A., but only one case has been reported in Africa. Our results suggest that this rarity of PML is not due to the absence of JCV in the African population.

Introduction

BK virus (BKV) and JC virus (JCV) are closely related human polyomaviruses isolated independently in 1971 from urine [14] and brain [29], respectively. Although 60–80% of the adult population has developed a specific antiviral immune response to BKV and/or JCV, no known symptoms are correlated with the primary infections. Following the initial infection, either virus may persist in
the kidneys (and possibly other internal organs), and be shed in the urine without disease symptoms [3]. However, reactivation of JCV in oligodendrocytes and astrocytes of the brain during immunosuppressive disease causes progressive multifocal leukoencephalopathy (PML) [42]. Initial clinical symptoms of this fatal demyelinating condition vary from slight impairment of intellectual functions to motor and visual deficits which usually progress to severe dementia and death within three to six months. In AIDS patients the incidence of PML is markedly increased. In Europe and the USA about 4–7 % of AIDS patients develop PML or present with it [7]. In addition to the effects of immune system impairment, a transactivating effect of HIV-1 Tat might directly stimulate JCV late region transcription [8]. In contrast to the neurologic disease caused by JCV, BKV is not known to be neurovirulent. A single case of BKV associated meningitis in a patient with immunosuppression has been reported [41].

The small, circular, supercoiled genome (5 kb) of these double-stranded DNA viruses is divergently transcribed from overlapping signals in a non-coding regulatory region. Large T antigen is a regulatory protein required for initiation of DNA synthesis and late region transcription. The structural proteins (capsid proteins VP1-3) coded by the late region represent the major antigenic sites for immunorecognition. The non-coding regulatory region of JCV amplified from PML tissue shows unique rearrangements generated by a process of deletion and duplication [5, 47]. JCV and BKV DNAs amplified directly from urine show predominantly a stable, unrearranged regulatory region designated “archetypal” [30, 47].

JCV and BKV are thought to have a world wide distribution, but the viruses characterized to date have been largely those found in Europe [19, 22], the U.S.A. [12, 31] and Asia [34, 47]. A BKV strain (MG) has been isolated in South Africa [21]. Moreover, while PML has been described on all continents, only one case has been reported in an African dying in Africa [23], despite the intensity of the AIDS epidemic there. Among European, Asian and American strains of JCV, two genotypes have been described [4, 46]. Both Types 1 and 2 are found in Europe and the U.S.A., while only Type 2 is found in Asia. Whether one of these or a new type exists in Africa has not been previously studied.

The taxonomy of BKV is based on four serologically defined types [15, 20]. The serological differences are mainly due to variability in the middle portion of the BKV capsid protein VP1 gene [18, 19]. The worldwide distribution of its types is not yet defined. However, a majority of strains are similar to the Gardner (prototype) and Dunlop strains of BKV [18, 31, 44]. Again, the type or types of BKV represented in the interior of Africa has not been explored.

We wished to determine whether JCV and BKV are detectable in a rural African population and if so, whether unique African types of either virus exist. Reasoning that HIV-1 positive patients may have a higher incidence of reactivation of latent polyomaviruses in the urinary tract, we studied urines obtained from 23 HIV-1 positive patients in rural Tanzanian villages near Lake Victoria. The identification of BKV (DUN)-like sequences and a new, third type of JCV is reported.