BK Virus-Associated Progressive Multifocal Leukoencephalopathy

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Objective

To describe a rare case of BK virus-associated progressive multifocal leukoencephalopathy.

Background

Progressive multifocal leukoencephalopathy (PML) is a fatal demyelinating disease of the central nervous system (CNS) seen almost exclusively in the setting of advanced immunosuppression. JC virus is the usual etiologic agent described for PML in the current literature. We report a rare case of BK virus-associated PML in an HIV patient. Like JC virus, BK virus also belongs to the *Polyomaviridae* family. Clinical disease with BK virus is mostly encountered in acquired immunodeficiency syndrome (AIDS) or transplant recipient patients. Kidney, lung, eye, liver and brain are the usually affected organs[1,2]. BK virus disease in the brain is uncommon and is mostly reported as causing encephalitis[1]. BK viral DNA has also been identified in several types of brain tumors but the significance of such association remains unclear [2].

Case Report

A 36 year-old female with a history of AIDS (CD4 count of 88 cells/mm^3), on tenofovir/emtricitabine and lopinavir/ritonavir, presented with memory impairment, progressive left-sided hemiparesis, urinary incontinence and new onset seizures.

MRI of the brain showed asymmetric diffuse increased T2 hyperintensity in the deep white matter of both hemispheres, also involving the corpus callosum (Fig 1). There was no enhancement with gadolinium. Her clinical and MRI findings were highly consistent with PML. Cerebrospinal fluid analysis showed 4 WBC/µL, glucose of 65 mg/dL, and a mildly elevated protein of 49.8 mg/dL. Interestingly, JC virus PCR was negative, but we found that the patient had evidence of BK virus replication in the CSF. Based on these findings, we diagnosed her with BK virus-associated PML. Two years after her initial diagnosis, she presented to the hospital again with increased seizures. Her CD4 count was 454 cells/mm^3 . MRI of the brain was unchanged from before. JC virus PCR remained negative. And BK virus was no longer detectable in the CSF.

Imaging

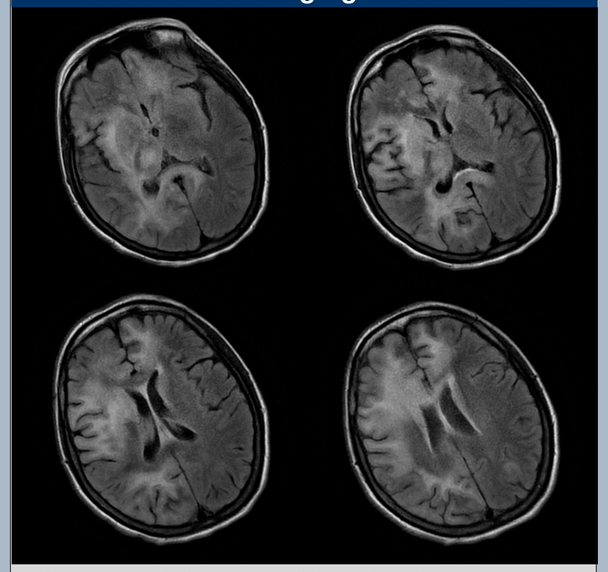

Figure 1. MRI of the brain showing diffuse confluent increased T2 signal in the deep white matter in the entire right hemisphere and in the left frontal lobe and deep gray matter. The corpus callosum is also involved.

Discussion

BK virus infection of the CNS is uncommon. To date, only 24 cases of BK virus-associated CNS disease have been reported and most of the cases have been encephalitis or meningoencephalitis[1]. There have only been 2 reported cases of BK virus-associated PML in the current literature. One case was described in a renal transplant patient [3] and the other in a patient who was on long term corticosteroid therapy [4].

This is the first reported case of BK virus-associated PML in an HIV patient. This case emphasizes the point that when assessing a patient with high suspicion of PML and a negative JC virus in the CSF, a work-up for BK virus should be considered.

BK virus infection of the CNS is likely under-diagnosed for a number of reasons. The BK viral DNA is present in very low copy numbers, from 1 to 20 genome equivalents per 200 cells, which can lead to false negative results [2]. Also, with cART treatment, it is possible to find negative BK virus or JC virus CSF PCR results in patients with AIDS. One postulated mechanism is that cART-induced recovery of the immune system can lead to decreased viral replication and to clearance of BK or JC virus DNA from CSF. Another consideration is that patients with PML stabilization with cART may also exhibit progressive decline in viral DNA levels.

In this case, the initial diagnosis of BK virus-associated PML was based on the patient's clinical history, imaging findings, and the presence of BK virus replication in the CSF. Although the repeat interval workup did not reveal the virus again, this is likely due to the reasons discussed earlier.

There is no specific anti-viral treatment for BK virus infection. Although cidofovir and leflunomide have been used with limited success in the treatment of BK virus nephropathy in transplant patients [5], we do not know whether such therapies would be effective in CNS infections too. The standard of care at present for JC virus-associated PML in HIV patients is cART with the goal of achieving immunological recovery and suppressing the HIV viral load.

Conclusion

Although, BK virus-associated PML is rarely described, it should be considered in patients with high clinical and radiological suspicion of PML but with a negative JC virus in the CSF.

References

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