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Clinical Commentary

Dengue fever in a multiple sclerosis patient taking ocrelizumab: Clinical commentary

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Dengue virus (DENV) is a mosquito-borne member of the *Flavivirus* genus and includes four serotypes, each of which is capable of the full spectrum of clinical manifestations, from asymptomatic infection to severe dengue disease (SDD). DENV is endemic to tropical and subtropical parts of the world.[1]

In this issue of the journal, Guerra et al.[2] reported a possible case of dengue fever in a patient with multiple sclerosis (MS) treated with ocrelizumab. Although the diagnosis of dengue is possible since this patient traveled to an endemic area, a positive serology is not enough for diagnosis, and other molecular biology techniques are mandatory for the confirmation.

The authors describe a favorable clinical outcome assuming the secondary dengue infection. It is known that SDD can be seen during primary infection but is more frequent following the secondary infection with a heterotypic DENV. The adaptive immune response to DENV infection contributes to resolution of infection and plays a key role in the memory response against reinfection. Conversely, it may also play a central role in the enhancement of disease severity. In most patients with SDD, high levels of virus replication have been detected during secondary infection with a heterotypic virus. This virus replication is thought to occur when non-neutralizing antibodies, present in the host from a previous DENV infection, bind to the virus during a subsequent heterotypic infection (antibody-virus complex, AVC).[3] The AVC gains access to monocytes via binding to the Fcγ receptors (FcγR), thereby facilitating the infection of FcγR cell types not readily infected in the absence of antibody. Regarding cell-mediated immune responses, the role of CD8+ T cell immunity is important in the clearance of acute viral infections, and therefore plays a minor role in protection against reinfection.[4] As such, a negative role of the humoral adaptive system is recognized for the development of SDD.

A previous report demonstrated that MS patients who are peripherally B-cell depleted after treatment with ocrelizumab can mount an attenuated humoral response to vaccines. Thereby, patients treated with ocrelizumab presented a lower booster effector than the control group.[5] In relation to this, the attenuated humoral response induced by ocrelizumab could be protective for the development of SDD. Only one previous study in Brazilian MS patients treated with fingolimod or natalizumab addressed this issue.[5] There were no complications of dengue fever or worse outcomes of MS in these patients.

Considering that there are few reports of dengue in patients with MS, it may be affirmed that the prevalence of MS is low in dengue-endemic regions. The highest age-standardized MS prevalence estimates per 100,000 population were North America and Western Europe, regions where dengue is not endemic.[6] More epidemiologic data are needed to improve our understanding of risk of SDD in MS patients infected with dengue.

Declaration of Conflicting Interests

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