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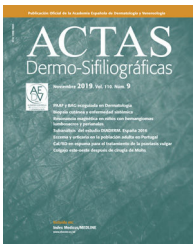

RESIDENT'S FORUM

RF - Polyomavirus Oncoprotein Antibodies in Merkel Cell Carcinoma: A Marker of Disease Progression and Prognosis☆

FR - Anticuerpos contra la oncoproteína del poliomavirus en el carcinoma de células de Merkel: marcador pronóstico y evolutivo

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Merkel cell carcinoma (MCC) is an aggressive cutaneous neuroendocrine carcinoma characterized by high mortality and a tendency to local recurrence and metastasis. Classically, MCC patients have been treated with combinations of surgery, radiotherapy, and intensive chemotherapy.[1] The Food and Drug Administration of the United States approved immunotherapy with the anti-programmed death-ligand 1 (PD-L1) agent avelumab and the anti-programmed cell death protein 1 (PD-1) agent pembrolizumab for the treatment of patients with MCC. While much MCC research has focused on immunotherapy, there have been important advances in patient follow-up, specifically focusing on Merkel cell polyomavirus antibodies.

In October 2010, Paulson and coworkers published 2 important findings in Cancer Research based on their comparison of 205 MCC cases and 530 controls.[2] First, they reported that MCC patients presented sustained increases in serum levels of antibodies against Merkel cell polyomavirus capsid proteins. However, the utility of these antibodies was limited by the fact that they were also detected in more than half of the healthy controls, indicating a previous Merkel cell polyomavirus infection. Furthermore, the authors found that antibodies against tumor-associated antigens (polyomavirus oncoproteins) were more specifically associated with MCC: these antibodies were detected in 0.9% of controls (and were of low titer) compared with 40.5% of MCC patients. They also observed differences in the levels of these antibodies depending on the disease course: titers were lower in patients without recurrence and higher in those in which the disease progressed.[2]

More recently, the same group published the results of a prospective validation study conducted in a cohort of 219 patients recently diagnosed with MCC and followed up for a median of 1.9 years. Seropositive patients (i.e. those

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with positive antibodies against polyomavirus oncoproteins) had less aggressive tumors, regardless of age, sex, staging, and immune status. In seropositive patients with a satisfactory response to treatment and without recurrence, titers of these antibodies decreased to below detectable levels within a median of 8.4 months. Furthermore, increases and decreases in antibody titers during follow-up had positive and negative predictive values for recurrence of 66% and 97%, respectively.[3]

Therefore, the determination of antibody titers against polyomavirus oncoproteins at baseline (before treatment initiation) and during evolution (in the case of seropositive patients) is useful for both prognosis and follow-up.[3,4] In fact, this serological test has been included in the 2018 National Comprehensive Cancer Network's MCC guidelines, which state the following: ''quantification of Merkel cell polyomavirus oncoprotein antibodies may be considered as a part of initial workup; seronegative patients may have a higher risk of recurrence; in seropositive patients, a rising titer may be an early indicator of recurrence''.[5]

Treatment and follow-up of MCC patients requires a multidisciplinary team, in which the dermatologist plays a fundamental role. Dermatological oncology reference centers could perhaps consider implementing serology for polyomavirus oncoprotein owing to its utility in the follow-up of these patients.

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