TTF-1 Positivity in Merkel Cell Carcinoma: The Chosen Clone Matters

To the Editor:

I have read with great interest the recently published article by Hughes et al[1] describing a case of a combined Merkel cell carcinoma associated with Bowen disease and squamous cell carcinoma that demonstrated strong and significant positivity for TTF-1 by immunohistochemistry, and I would like to make some additional comments. The authors used in this case study the monoclonal anti-TTF-1 antibody clone SP141 and did not explore the possible difference between the SP141 clone (Ventana) and the other main available anti-TTF-1 antibody clones, such as 8G7G31 (Dako) and SPT24 (Leica/Novocastra). Moreover, other published cases and case series of (combined) MCC with TTF-1 positivity did not mention which type of TTF-1 clone was used.[2–4] However, there is strong evidence in the literature that an important factor influencing the prevalence of TTF-1 expression in tumors is the type of clone that is used.[5,6] This has also been demonstrated in publications documenting TTF-1 immunoreactivity in glial neoplasms,[7] schwannomas,[8] breast carcinomas,[6] and colorectal carcinomas.[9] I want to illustrate this matter further with a recent case of a classical Merkel cell carcinoma, clinically presenting as a rapidly growing, firm, solitary nodule in the face of an 82-year-old woman. Histology showed a dermal-based lesion composed of monotonous small round cells with finely granular and dusty chromatin, inconspicuous nucleoli, and scanty cytoplasm ("small blue round cell" morphology). A membranous and paranuclear dot-like staining with cytokeratin 20 was observed. The tumor cells showed diffuse cytoplasmic staining with the neuroendocrine markers chromogranin and synaptophysin. The case was sent to me in consultation, given the strong expression with the TTF-1 antibody clones SP141 and SPT24 (Figs. 1A, B). Based on my findings in the recent published study on TTF-1 expression in schwannomas,[8] I performed an additional monoclonal anti-TTF-1 antibody clone 8G7G31 (Dako) on this peculiar case, which showed no expression (Fig. 1C). The difference in specificity according to the used anti-TTF-1 antibodies could be explained by a higher affinity of SP141 and SPT24 clones for TTF-1, which aberrantly expressed with a low level in Merkel cell carcinoma that it could not be detected by 8G7G31 clone. Other potential factors that can explain the difference include methodological issues such as antibody dilutions, antigen retrieval, and detection systems. This case further underscores the literature data that the sensitivity and specificity of TTF-1 staining is dependent on the antibody clone used, and attention should be given on using different clones of antibody raised against the same protein for diagnostic purpose.

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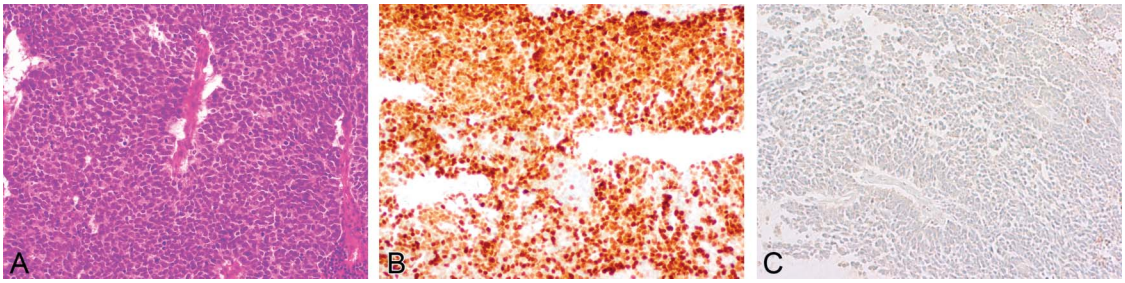

FIGURE 1. A, Hematoxylin and eosin staining of classical Merkel cell carcinoma (original magnification ×200). B, Strong nuclear TTF-1 positivity (clone SP141; original magnification ×200). C, No TTF-1 reactivity (clone 8G7G31; original magnification ×200).