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Correspondence

Comparison of thyroid transcription factor-1 expression by 2 monoclonal antibodies in schwannomas: the chosen clone matters

To the Editor:

We have read with great interest the recently published study by Wang et al [1] on aberrant expression of thyroid transcription factor-1 (TTF-1) in schwannomas. The authors described nuclear TTF-1 in 109 (67.7%) schwannomas, including 102 of 132 (77.9%) conventional, 1 of 20 (5%) cellular, and 6 of 10 (60%) plexiform schwannomas. Nuclear staining was not identified in normal peripheral nerves and nonschwannoma peripheral nervous system lesions.

However, the authors used in this study the monoclonal anti–TTF-1 antibody clone SPT24 and did not explore the difference between the SPT24 clone (Leica/Novocastra, Newcastle upon Tyne, UK) and the other main commercially available anti–TTF-1 antibody 8G7G3/1 clone (Dako, Santa Clara, CA, USA). There is strong evidence in the literature that an important factor influencing the prevalence of TTF-1 expression in tumors (other than those of pulmonary or thyroid origin) is the type of clone that is used [2,3]. This has also been demonstrated in publications documenting TTF-1 immunoreactivity in glial neoplasms [4,5], gynecologic carcinomas [6], breast carcinomas [3], and colorectal carcinomas [7,8].

Therefore, we analyzed TTF-1 expression in 60 additional schwannomas (including 44 conventional and 13 cellular subtypes) and compared the results obtained with the 8G7G3/1 and SPT24 TTF-1 clones (Tables 1 and 2). We also included in our study 3 cases of epithelioid schwannoma, a rare subtype of schwannoma, which was not tested in the current study by Wang et al [1]. We used the same combined scoring system to evaluate the intensity and distribution of nuclear TTF-1 staining as described by Wang et al. Notably, the SPT24 clone detected a much higher number of positive cases in both the conventional and cellular subtypes. In conventional schwannomas, positivity with the SPT24 clone was detected in 37 of 44 (83%) cases as opposed to the 8G7G3/1 clone, which showed expression in 25 of 44 (56%) cases. With the SPT24 clone, strong and diffuse SPT24 staining for TTF-1 (score 8-9) was observed in 14 (44%) conventional schwannomas. On the contrary, none of the cases showed a diffuse and strong staining with the 8G7G3/1 clone, and in most of the 8G7G3/1-positive cases, only focal and weak staining (score 2-5) was seen. Eight of 13 (61%) and 3 of 13 (23%) cellular schwannoma cases were only focally and weakly positive with the SPT24 and 8G7G3/1 clone, respectively. Compared to the results of Wang et al, we observed SPT24 anti–TTF-1 clone positivity in a higher percentage of cellular schwannoma cases. However, all positive cases of cellular schwannoma in our study showed only very focal and weak positivity (scores 2-3). Three epithelioid schwannomas, tested with both anti–TTF-1 antibody clones, were completely negative.

In summary, this comparative study of TTF-1 expression in schwannomas by 2 widely used anti–TTF-1 antibody clones, 8G7G3/1 and SPT24, showed TTF-1 expression with both clones, albeit expression with the 8G7G3/1 clone was seen in a much lower percentage of cases and was weaker in intensity and more focal in distribution compared to the SPT24 staining. With both antibody clones, TTF-1 expression was more prevalent in conventional schwannomas and was not seen in the rare epithelioid subtype. These findings further underscore the literature data that the sensitivity and specificity of TTF-1 staining are dependent on the antibody clone used [3,9].

Table 1 TTF-1 expression in conventional schwannomas

TTF-1 expression	Wang et al [1]	Ghent study	
	SPT24-clone, n (%)	SPT24-clone, n (%)	8G7G3/1-clone, n (%)
Negative	29/131 (22%)	7/44 (17%)	19/44 (44%)
Weak	31/131 (24%)	12/44 (27%)	20/44 (45%)
Moderate	45/131 (34%)	11/44 (25%)	5/44 (11%)
Strong	26/131 (20%)	14/44 (31%) [a]	0/44 (0%)

[a] Eleven of the 14 strongly staining cases had score of 8.

Table 2 TTF-1 expression in cellular schwannomas

TTF-1 expression	Wang et al [1]	Ghent study	
	SPT24-clone, n (%)	SPT24-clone, n (%)	8G7G3/1-clone, n (%)
Negative	19/20 (95%)	5/13 (39%)	10/13 (77%)
Weak	1/20 (5%)	8/13 (61%) [a]	3/13 (23%)
Moderate	0/20 (0%)	0/13 (0%)	0/13 (0%)
Strong	0/20 (0%)	0/13 (0%)	0/13 (0%)

[a] Five of the 8 weakly staining cases had a low score of 2 or 3.

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Comparison of thyroid transcription factor-1 expression by 2 monoclonal antibodies in schwannomas: the chosen clone matters—reply

Dear Editor,

We thank Dr Creytens and colleagues for their interest in our manuscript on expression of thyroid transcription factor-1 (TTF-1) in schwannomas and comparison of TTF-1 expression by 2 monoclonal antibodies. We appreciate the opportunity to reply and further explain some of our observations.

In this comparative study, the authors explored TTF-1 expression with 2 widely used antibodies: SPT24 and 8G7G3/1 clones. They found that TTF-1 expression with the 8G7G3/1 clone was seen in a much lower percentage of cases and was weaker in intensity and more focal in distribution compared to the SPT24 staining.

Although the results were not shown in our previous article, we also have compared the expression of TTF-1 with the 2 monoclonal antibodies in schwannomas with the same materials and methods [1]. Similar to the results of Creytens et al, in our study, nuclear TTF-1 expression was observed in 87 (54.0%) cases using the 8G7G3/1 clone (Dako, Glostrup, Denmark; 1:100 dilution; EDTA at pH 9.0 antigen retrieval). The 2 antibodies were concordant in 87 TTF-1–positive cases and 52 TTF-1–negative cases. However, 22 cases were TTF-1 positive with the SPT24 clone but TTF-1 negative with the 8G7G3/1 clone. In the positive cases, strong and diffuse staining (score 8–9) was not observed in any case with the 8G7G3/1 clone either. Most cases showed weakly focal to moderately partial staining (score 2–5) with the 8G7G3/1 clone (n = 76, 87.4%).

Our study showed that the SPT24 clone exhibited stronger staining intensity and more diffusely positive cells and suggested that the SPT24 clone is more sensitive to TTF-1 expression in schwannomas. Other comparative studies also revealed that the SPT24 clone is more sensitive and less specific than the 8G7G3/1 clone [2,3]. In addition, some tumors, such as squamous cell carcinoma of the lung and gliomas, are positive for SPT24 but negative for 8G7G3/1 [4,5]. The hypothesis that SPT24 has a higher affinity for TTF-1 protein than 8G7G3/1 may provide insight into these differences [2]. However, it is worth noting that the cross-reaction of TTF-1 antibodies with another nuclear protein could not be excluded because immunohistochemistry does not provide the information such as the molecular weights or sequences of the detected proteins [6]. In our study, we observed TTF-1 positivity in a smaller percentage of cellular schwannoma cases. The reason might be the positive cells of cellular schwannomas were too faint staining or in too small amounts to be detected for our laboratory.

In conclusion, TTF-1 staining with the SPT24 clone was much stronger and more dispersed than that with the 8G7G3/1 clone. However, it should be necessary to verify the expression of TTF-1 by another method, particularly in the case of aberrant expression with a low positive rate and/or only one antibody expression.

Sincerely,

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