Low Proliferative Activity in Common Dermatofibroma Does Not Necessarily Guarantee a Low Proliferation in All Dermatofibroma Variants

To the Editor.—I have read with interest the report about the use of proliferation rate in the differential diagnosis of dermatofibroma (DF) versus certain malignant fibrohistiocytic tumors, such as atypical fibroxanthoma, malignant fibrous histiocytoma, and dermatofibrosarcoma protuberans. I agree with Hanly et al concerning their cases of fibrohistiocytic tumor, malignant fibrous histiocytoma, and dermatofibrosarcoma protuberans.

However, I would like to point out that I think that it is not true that in DFs the mitotic rate is usually lower than 10%. The mitotic count in a cellular DF can be up to 10 mitoses per 10 high-power fields. Even more, in deep penetrating areas of pathology in which mitotic counts are performed only in areas of central necrosis or infarction, high levels of mitotic activity are frequently seen in proximity to areas of central necrosis or infarction in both benign and malignant tumors. This level of mitotic activity is typically not seen at a distance from areas of necrosis. Consequently, there exists the potential for high mitotic counts to be reported if counts are performed only in areas of high mitotic activity related to necrosis and the full spectrum of mitotic activity within a lesion is not studied. This is more apt to occur when mitotic activity is reported rather than staining with MIB-1, as regional variation within tumors is far more easily recognized when MIB-1 staining is used. Although an article on CBFH does indicate that mitotic activity relates to cellularity, it fails to indicate whether the cases with high mitotic activity and high cellularity were related to tumors with necrosis. Furthermore, it is not stated how mitotic counts were calculated. If the tumors with central necrosis or infarction had high mitotic activity only within the vicinity of areas of central necrosis, and not in areas distant from the necrosis,


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In Reply.—Dr Fernandez-Flores' discussion centers predominantly on a subset of dermatofibroma (DF) referred to as cellular benign fibrous histiocytoma (CBFH). He implies that because CBFHs demonstrate some degree of mitotic activity, CBFHs would also be expected to show high proliferative activity if studied with MIB-1. This assumption is based on the statement that cases of CBFH show counts of up to 10 mitoses per 10 high-power fields. Furthermore, he speculates that this level of mitotic activity is somehow guaranteed to correlate with MIB-1 counts greater than 10% and therefore a high proliferative activity.

The problem is that Dr Fernandez-Flores fails to state that the mean mitotic count of CBFH was 3 mitoses per 10 high-power fields and therefore his subsequent speculation based on counts of up to 10 mitoses per 10 high-power fields is misleading. Also, 12% of cases of CBFH demonstrated areas of central necrosis or infarction. High levels of mitotic activity are frequently seen in proximity to areas of central necrosis or infarction in both benign and malignant tumors. This level of mitotic activity is typically not seen at a distance from areas of necrosis. Consequently, there exists the potential for high mitotic counts to be reported if counts are performed only in areas of high mitotic activity related to necrosis and the full spectrum of mitotic activity within a lesion is not studied. This is more apt to occur when mitotic activity is reported rather than staining with MIB-1, as regional variation within tumors is far more easily recognized when MIB-1 staining is used. Although an article on CBFH does indicate that mitotic activity relates to cellularity, it fails to indicate whether the cases with high mitotic activity and high cellularity were related to tumors with necrosis. Furthermore, it is not stated how mitotic counts were calculated. If the tumors with central necrosis or infarction had high mitotic activity only within the vicinity of areas of central necrosis, and not in areas distant from the necrosis,
then there remains the possibility that the higher levels of mitotic activity reported in this article may have been regionally related to necrosis or infarction and not reflective of a uniform high proliferative rate for this subset of CBFH. As this information is not presented, we cannot further evaluate this line of reasoning. I raise this issue as I believe that expecting a large series of DFs without necrosis to show mitotic counts of 10 per 10 high-power fields is somewhat suspect and therefore the whole presumption of Dr Fernandez-Flores’ discussion becomes moot.

The author also raises an issue with our study based on our selection of typical storiform dermatofibromas and not CBFHs. The DFs in our study demonstrated a storiform pattern and were otherwise typical. Whether some of our cases would be considered CBFH or not by independent observers is difficult to predict as acceptable scientific criteria are neither established nor uniformly accepted to allow for separation of storiform DF from CBFH. In their article on CBFH, Calonje et al state, “Although the cutoff from ordinary dermatofibroma is not sharp, we regard high cellularity and numerous mitoses as the minimum diagnostic criteria for the cellular variant.” The cutoff is not sharp, what denotes high cellularity is not clarified, and what numerical value equates with “numerous mitoses” is not stated. We can only assume that separation of CBFH from storiform DF is completely subjective and consequently not ideal for the basis of a scientific study.

Dr Fernandez-Flores also reaches the conclusion and states the following with regard to our study: “Nevertheless, they do not perform any studies about the proliferation rate on any cases of dermatofibrosarcoma protuberans.” I can only assume that he failed to read large sections of our article with regard to the scientific methods used and that he completely ignored Table 2, where the immunohistochemical results of our study are presented, including a summary of MIB-1 staining in dermatofibrosarcoma protuberans.

In summary, we feel Dr Fernandez-Flores fails to establish sufficient argument to support his stated assumptions to a satisfactory level of certainty or to warrant further comment.

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