ABSTRACT

Background: We proposed recently that papillary thyroid carcinomas (PTCs) with V600E mutation are morphologically distinct. Here we investigate the accuracy and interobserver reproducibility of a defined set of histological criteria in predicting BRAF V600E mutation.

Design: We created a training set of 5 PTCs with and 5 without BRAF V600E mutation. The former group included classic, tall cell or subcapsular sclerosing variants, and showed well-developed nuclear features of PTC, tall or polygonal cells with moderate to abundant eosinophilic cytoplasm (plump pink cells), stromal fibrosis/sclerosis/desmoplasia, infiltrative tumor borders and psammoma bodies. The latter group, in general, included follicular variants with subtle nuclear features of PTC, and lacked most or all of the above mentioned histologic features of mutated PTCs. After self-training on the training set, two pathologists predicted the presence or absence of BRAF V600E mutation in 30 PTCs (test set) using the morphologic criteria learnt from the training set. The predictions were evaluated against BRAF V600E mutational analysis by single strand conformation polymorphism on tumor DNA.

Results: Table 1 shows the sensitivity, specificity, accuracy, and positive and negative predictive values of the histologic criteria for predicting BRAF V600E mutation by each pathologist. There was “excellent” (kappa 0.795) agreement between the two pathologists for predicting BRAF V600E mutation (concordance 27/30; 90%).

Table 2 and 3 summarize the results for accuracy and reproducibility between two pathologists. There was excellent (kappa 0.795) agreement between the two pathologists for predicting BRAF V600E mutation (concordance 27/30; 90%).

Table 3: Interobserver Agreement Between Two Pathologists in Predicting Presence or Absence of BRAF V600E Mutation

<table>
<thead>
<tr>
<th>Pathologist 1</th>
<th>Pathologist 2</th>
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<tbody>
<tr>
<td>BRAF V600E positive (n=15)</td>
<td>25/30 (83%)</td>
</tr>
<tr>
<td>BRAF V600E negative (n=15)</td>
<td>11/15 (73%)</td>
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CONCLUSIONS

• Histologic features can help predict BRAF V600E mutation in PTC with accuracy and good interobserver agreement. Recognizing the key morphologic features in routine surgical pathology practice may help triage tumors for the more labor intensive and expensive BRAF V600E mutational analysis.

REFERENCES