A RETROSPECTIVE STUDY OF THE INFLUENCE OF A GENE EXPRESSION SIGNATURE ON THE TREATMENT OF MELANOCYTIC TUMORS

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BACKGROUND

- Ambiguous diagnoses of melanocytic lesions create difficult treatment decisions for both the physician and patient.
- Traditional pathology techniques alone can be insufficient to reliably identify malignant melanoma in biopsies of suspicious pigmented lesions.
- Therefore, adjunctive diagnostic methods that provide objective and reproducible information to inform medical management decisions by dermatologists.

DESIGN

- Representative sections of 632 difficult to diagnose melanocytic lesions were submitted by 3 separate dermatopathology practices to a clinical laboratory for gene expression testing.
- Diagnoses and recommendations for treatment of the lesions were documented by the dermatopathologist before and after testing.
- Melanoma diagnostic scores (MDS) were determined for each sample using the 23-gene expression signature and were classified as shown in Table 1.

Table 1. MDS reporting ranges and classifications

<table>
<thead>
<tr>
<th>MDS</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>-16.7 → -2.1</td>
<td>Benign</td>
</tr>
<tr>
<td>-2.0 → 0.1</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>0.0 → 11.1</td>
<td>Malignant</td>
</tr>
</tbody>
</table>

- Retrospective chart reviews were performed for 315 of these cases from 32 dermatologists. The actual treatment carried out for each patient was documented.
- Changes in treatment decisions were measured from the pre-test treatment recommendations recorded by the dermatopathologists to the actual treatment carried out for patients by dermatologists.

RESULTS

- Table 2 shows the pre-test treatment recommendations made by dermatopathologists and the actual treatment carried out by dermatologists, stratified by MDS classifications.

Table 2. Treatment Decisions

<table>
<thead>
<tr>
<th>Pre-Test Treatment Recommendation by Dermatopathologist</th>
<th>Benign (n=214)</th>
<th>Malignant (n=92)</th>
<th>Indeterminate (n=9)</th>
<th>Total (n=315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excision</td>
<td>150 (70.1%)</td>
<td>83 (90.2%)</td>
<td>4 (44.4%)</td>
<td>237 (75.2%)</td>
</tr>
<tr>
<td>No Excision</td>
<td>64 (29.9%)</td>
<td>9 (9.8%)</td>
<td>5 (55.6%)</td>
<td>78 (24.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Actual Treatment by Dermatologist</th>
<th>Excision</th>
<th>105 (49.1%)</th>
<th>60 (65.2%)</th>
<th>169 (53.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Excision</td>
<td>98 (45.8%)</td>
<td>11 (12.0%)</td>
<td>3 (33.3%)</td>
<td>112 (35.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (3.3%)</td>
<td>21 (22.8%)</td>
<td>2 (22.2%)</td>
<td>30 (9.5%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (1.9%)</td>
<td>0</td>
<td>0</td>
<td>4 (1.3%)</td>
</tr>
</tbody>
</table>

- Table 2 shows the pre-test treatment recommendations made by dermatopathologists and the actual treatment carried out by dermatologists, stratified by MDS classifications.

- Excisions were reduced by 33.1% (45/136) in cases where a treatment change occurred after a benign MDS was reported (Figure 1).
- In 36.2% (21/58) of cases where a treatment change occurred after a malignant MDS was reported, other treatments such as additional surgery and referrals to a cancer center were provided (Figure 1).

LIMITATIONS

- Long-term clinical follow-up is not available to confirm the most accurate diagnosis of the 315 cases studied.
- Beyond the treatment provided by the dermatologist, the 315 patients were not followed clinically to determine whether treatment changes were safe and efficacious over time.

CONCLUSIONS

- In this cohort, treatment decisions were changed after review of the gene expression signature results.
- Integration of this test into current practice has the potential to improve patient care by providing additional information to inform medical management decisions by dermatologists.
- Long-term clinical follow-up to assess patient outcomes would provide additional guidance in determining the optimal approach to integrating test results into clinical decision-making.
- Abstract # 0608-000467, presented at the Fellows Presentation, provides an initial assessment of the test's performance compared to clinical outcomes, with results supporting the currently published sensitivity and specificity values.

Case Study

**Dysplastic nevus with ‘balloon cells’ vs. Melanoma**

33 year old female, pigmented lesion on the mid-upper back

**Histopathologic Interpretation:** Indeterminate

Pre-test diagnosis of nevus based on the overall architecture and banal cytologic features (Fig. 2A). It was also noted that the lesion was transected at one edge (Fig. 2B) and that both architecturally and cytologically the left and right sides of the lesion (Fig. 2C) varied somewhat. This led to an indeterminate diagnosis by the submitting dermatopathologist.

**MDS:** -6.8 (benign)

**Final Diagnosis:** Benign

The dermatopathologist’s report indicated that no further treatment for the lesion was necessary and the clinician elected to forego re-excision in favor of simple clinical surveillance.