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 data have been sought. Recently, a 23-gene expression signature has been clinically validated to differentiate benign nevi from malignant melanomas. The impact of this signature on treatment decisions requires further evaluation.

OBJECTIVE

Assess the change in treatment recommendations given by dermatopathologists before and after melanoma gene expression testing to the actual treatment carried out by the dermatologist.

METHODS

- Representative sections of 632 difficult to diagnose melanocytic lesions were submitted by 3 separate dermatopathology practices to a clinical laboratory for gene expression testing.
- Recommendations for treatment of the lesions were documented by the dermatopathologist before and after diagnostic testing.
- Melanoma diagnostic scores (MDS) were determined for each sample using the 23-gene expression signature.
- 32 dermatologists performed retrospective chart reviews for 315 of these cases and documented the actual treatment carried out for each patient.
- The percentage change was measured from the treatment recommendations recorded by the dermatopathologists to the actual treatment carried out for patients.

RESULTS

- Of the 315 dermatologist reviewed cases, 214 received a benign MDS, 92 received a malignant MDS, and 9 received an indeterminate MDS.
- The small number of indeterminate scores represents the introduction of an indeterminate reporting zone during the course of this study.
- After gene expression testing, only 4% of cases were diagnosed as indeterminate by the dermatopathologists. However, 21% of cases were diagnosed as indeterminate by the reporting dermatologist (Fig. 1).
- In 32.0% (65/203) of cases that received a benign MDS, patients received less invasive treatment (Fig. 2).
- In 39.4% (28/71) of cases that received a malignant MDS, patients received more invasive treatment (Fig. 2).

CONCLUSIONS

- The melanoma gene expression signature impacts the treatment of melanocytic lesions, as shown by clinical follow-up.
- Integration of this test into current practice has the potential to improve patient care by allowing more definitive diagnoses by dermatopathologists and optimized treatment decisions by dermatologists.
- Improved communication about melanoma diagnosis between dermatopathologists and dermatologists would further increase the impact of the gene expression signature.

CASE STUDY A

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. 3A). It was also noted that the lesion was transsected at one edge (Fig. 3B) and that both architecturally and cytologically the left and right sides of the lesion (Fig. 3C) 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.

CASE STUDY B

Dysplastic nevus vs. locally recurrent melanoma

- 61 year old male, pigmented lesion on his shoulder near the site of previously excised melanoma.
- Histopathologic Interpretation: Benign
- The submitting dermatopathologist's pre-test differential diagnosis included dysplastic nevus. There was significant concern for melanoma, particularly since the lesion was reportedly near the site of a prior melanoma excision (Fig. 4A). Most lesional melanocytes are relatively small, but many have hyperchromatic, angular nuclei, and a few are multinucleated (Fig. 4B).
- MDS: +3.1 (malignant)
- Final Diagnosis: Malignant
- The dermatopathologist concluded that this was malignant melanoma in situ (either a local recurrence of the prior melanoma or a 'second primary') and recommended wide local excision.

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