MicroRNA Expression Profiling Differentiated Parathyroid Lesions

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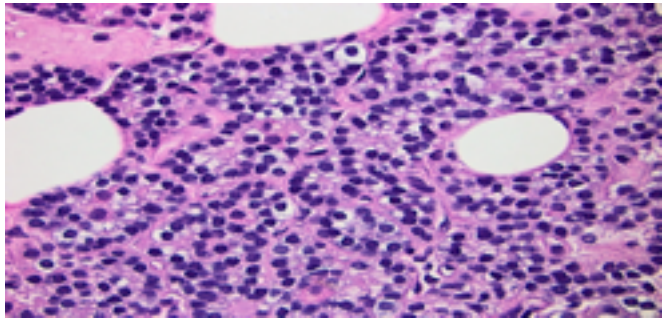
BACKGROUND

Thyroid nodules frequently undergo fine needle aspiration (FNA) to discriminate between benign versus malignant disease. Parathyroid processes in the form of hyperplasia (PH), adenoma (PA) and carcinoma(PC) can mimic thyroid nodular disease cytologically leading to indeterminate diagnosis. Molecular analysis, based on mutational analysis and/or RNA expression profiling, designed for thyroid neoplasia is often used as an ancillary tool. We sought discriminating features in thyroid molecular testing that would identify parathyroid tissue and indicate specific parathyroid disease states.

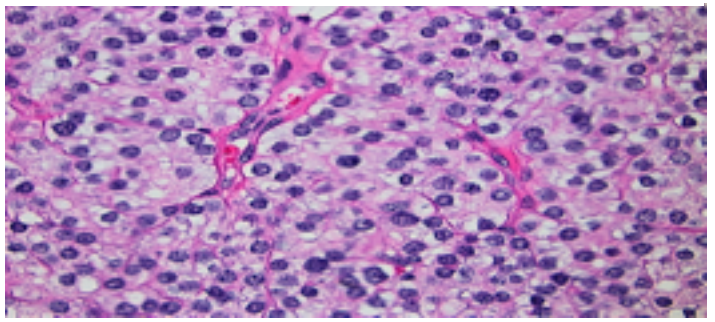
METHODS

8 FFPE tissue specimens representing pairs of normal, hyperplastic, adenomatous and carcinomatous parathyroid lesions underwent combined mutational & microRNA expression profiling designed to differentiate thyroid neoplasia. Mutational analysis targeted common thyroid mutations (BRAF, HRAS, KRAS, NRAS, PIK3CA, PAX8/PPAR and RET/PTC translocation) on next generation sequencing platform (Illumina). MicroRNA (miR) expression profiling targeted 10 specific miRs showing over and under expression in thyroid follicular cell neoplasia. Messenger RNA expression of PAX8 and NKX2.1, unique to thyroid follicular cells, was used as markers for thyroid origin of nucleic acid.

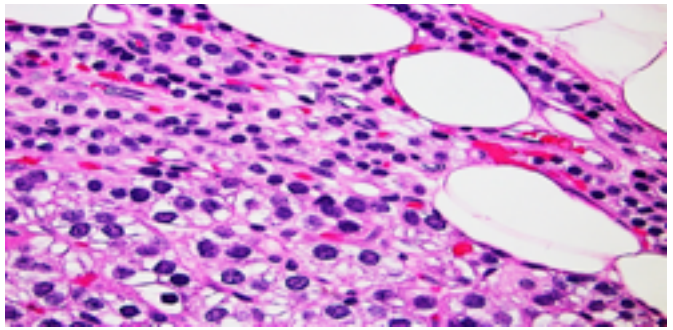
Normal parathyroid underexpressed miR138.



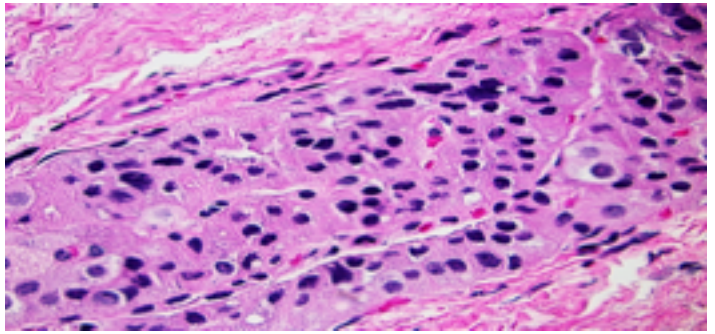
PH underexpressed miR31, 204 and 551.



PA overexpressed miR29b, 146 and 375.



PC showed hyperexpression of miR31, 204 and 551



RESULTS

Microdissected FFPE yielded adequate nucleic acid for this thyroid molecular testing approach. All parathyroid specimens lacked messenger RNA expression of PAX8 and NKX2.1 indicating absence of thyroid follicle lining cells. None of these parathyroid specimens manifest common somatic mutations seen in thyroid neoplasia. MicroRNA expression profiling, using criteria applied to thyroid follicular neoplasia, would have indicated thyroid malignancy if inappropriately assumed to be thyroid. Specific relative miR expression levels differentiated each of the parathyroid states.

CONCLUSIONS

Parathyroid lesion can confound FNA cytology diagnosis of nodules presumed to be of thyroid origin. In this initial study ancillary molecular testing can affirm parathyroid tissue origin (messenger RNA expression) and microRNA expression profiling appears capable of differentiating between parathyroid disease states supporting further confirmatory studies. The approach is effective on fixative treated specimens.