SAT-205

Comparison of Local Histopathology and a Central Pathology Panel in Diagnostic Thyroid Nodule Surgery from a Multicenter, Blinded Study

Michael Shanik, MD,[1] Thomas C Blevins, MD,[2] Paul Y Casanova-Romero, MD,[3] Jonathan Lokey, MD,[4] Justin W Fontenot, MD,[5]
Alexander L Shifrin, MD,[6] Krishnakumar Rajamani, MD,[7] Urooj Imtiaz,[8] Katie Beliveau,[8] and Neil M Barth, MD[9]

(1) Endocrine Associates of Long Island, Smithtown, NY (2) Texas Diabetes and Endocrinology, Austin, TX (3) Palm Beach Diabetes & Endocrine Specialists, Wellington, FL
(4) Department of Surgery, University Medical Group; Greenville Health System, Greenville, SC (5) Lafayette Arthritis & Endocrine Clinic, Lafayette, LA
(6) Jersey Shore University Medical Center, Neptune, NJ (7) Rochester Regional Health, Rochester, NY
(8) Clinical Affairs, Veracyte Inc., South San Francisco, CA (9) Medical Affairs, Veracyte Inc., South San Francisco, CA

Speakers: Shanik, Lokey; Study Investigators: Shanik, Blevins, Shifrin, Lokey; Veracyte Employees: Cleveland, Imtiaz, Barth

BACKGROUND

The majority of thyroid nodules with indeterminate cytology (Bethesda III, IV) and suspicious results on the 167 gene classifier (GEC) or, cytologic interpretation of suspicious for malignancy (Bethesda V) or malignant (Bethesda VI), undergo surgical resection. Additionally, a minority of cytologically indeterminate nodules with benign results on the GEC and cytologically benign nodules (Bethesda II) undergo surgery. For all operated thyroid nodules the final histopathology diagnosis becomes critical in determining the future care of the patient, starting with benign or malignant histopathologic classification. We examined the concordance between local and central expert panel histopathology in patients undergoing diagnostic thyroid surgery.

METHODS

Evaluation of Thyroid FNA Genomic Signatures (ENHANCE) Trial is an IRB approved, 47 center study designed to accrue a comprehensive bio-repository of paired cytology, genomic and histopathology samples from patients with thyroid nodules. Complete sample and data sets were collected from 467 operated patients (492 nodules). A central panel of 3 expert thyroid histopathologists, blinded to local diagnosis and the clinical findings, reviewed slides for each case. To obtain subtype diagnoses, a final label process was developed using majority consensus by (a) stepwise 2 of 2 central panel agreement while blinded to each other, (b) 2 of 3 central panel agreement while blinded to each other, or (c) an un-blinded conferral of the 3 central pathologists. Here we rank the diagnostic confidence of these steps as (a) high confidence, (b) intermediate confidence, and (c) low confidence. The last two ranks, (b) and (c), represent the not high confidence category. This analysis compares the local diagnosis to central majority consensus for individual nodules.

RESULTS

Of the 492 nodules from 467 patients that underwent thyroid surgery, 194 (39.4%) operated nodules were classified as histopathologically malignant by the central panel with 78.7% at 2 of 2 agreement (high confidence). Local pathologists called 139 of these 194 operated nodules malignant for a 71.6% concordance (Figure 1). 298 (60.6%) operated nodules were classified as histopathologically benign on central review with 70.5% at 2 of 2 agreement (high confidence) (Figure 2). 279 (93.6%) of these were also called benign by the local pathologists. Overall, local pathologists diagnosed 158 (32.1%) of the operated nodules as malignant.

CONCLUSION

Overall concordance between local and central histopathology at the categorical level of malignant versus benign of 85% sheds light on the difficulty of accurate histopathological diagnosis of operated thyroid nodules particularly among those with indeterminate cytology. Agreement was higher among operated nodules diagnosed as benign by the central panel, than among those diagnosed as malignant ($p < 0.0002$). Genomic tools that provide biological insight in addition to histopathology may assist clinicians in patient management given the limitations of histopathologic certainty.

TABLE 1.

Demographics Table

Variable	Total
Patients	
Age — year, mean (range)	54 (19-93)
Gender Male — no. (%) Female — no. (%)	 121 (25.9%) 346 (74.1%)
Thyroid Nodules	
Cytology Bethesda III — no. (%) Bethesda IV — no. (%)	 358 (72.8%) 134 (27.2%)
Nodule size — mean (range)	2.5 cm (0.9-12 cm)

FIGURE 1.

Histopathological Concordance

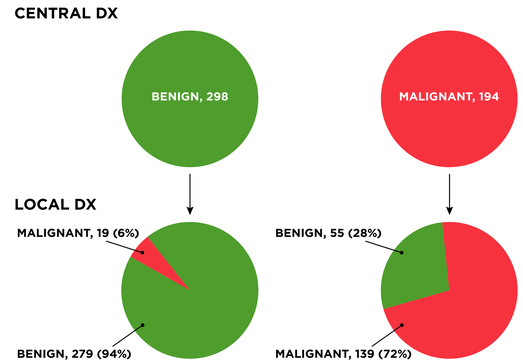

TABLE 2.

Central Panel Diagnostic Confidence by Sub-type

Subtype	Total Nodules	High Confidence	Not High Confidence
Follicullar Adenoma (FA)	121	85 (70%)	36 (30%)
Benign Nodule (BN)	104	71 (68%)	33 (32%)
Hürthle Cell Adenoma (HCA)	66	51 (77%)	15 (23%)
Parathyroid Adenoma (PTA)	3	3 (100%)	0 (0%)
Follicular Tumor of Uncertain Malignant Potential (FT-UMP)	2	0 (0%)	2 (100%)
Well-differentiated Tumor of Uncertain Malignant Potential (WDT-UMP)	2	0 (0%)	2 (100%)
Follicular Variant, Papillary Thyroid Carcinoma (FVPTC)	69	68 (99%)	1 (1%)
Papillary Thyroid Carcinoma (PTC)	54	51 (94%)	3 (6%)
Noninvasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP)	23	22 (96%)	1 (4%)
Hürthle Cell Carcinoma (HCC)	23	20 (87%)	3 (13%)
Follicular Carcinoma (FC)	16	11 (69%)	5 (31%)
Medullary Thyroid Carcinoma (MTC)	5	5 (100%)	0 (0%)
Poorly Differentiated Carcinoma (PDC)	3	3 (100%)	0 (0%)
Other Malignant (OM)	1	1 (100%)	0 (0%)