School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.

MON-498

Background:
Molecular testing of thyroid nodules classified as indeterminate on fine-needle aspiration (FNA) is used for patient management. ThyroSeq® v3 genomic classifier is a commercially available test that examines a wide spectrum of genomic alterations in a thyroid FNA sample based on algorithmic analysis and reports test results as either negative (including currently negative) or positive. This study reviews our institutional experience with Thyroseq® V3 to distinguish between benign disease versus cancer in thyroid nodules diagnosed as Bethesda III or IV on cytology.
Methods:
Thyroid nodules with Bethesda III or IV cytology diagnoses and available Thyroseq® V3 results from 12/17 to 8/19 were retrieved from the pathology database. Cytopathology diagnoses were correlated with molecular testing and histopathology.
Results:
416 cases (Bethesda III n=252, Bethesda IV n=164) were retrieved: 295 (71%) were reported as Thyroseq® V3 negative and 121 (29%) as positive. The 82.1% (207/252) benign call rate (BCR) of Thyroseq® v3 for Bethesda III was significantly higher (p<0.001) than that for Bethesda IV, BCR 54% (88 /164). Histopathologic follow-up was available for 128 cases (96 ThyroSeq® v3 positive, 32 ThyroSeq® v3 negative): 57 benign and 71 malignant (including NIFTP). For Bethesda III and IV diagnoses respectively, the test demonstrated 91.7 % (95% Cl 73%-99%) and 91.5% (95% Cl 80%-98%) sensitivity, 94% (95% Cl 90%-97%) and 82.4% (95% Cl 74%-89%) specificity, 99% (95% Cl 96%-99%) and 95% (95% Cl 89%-98%) negative predictive value and 63% (95% Cl 50%-74%) and 70.5% (95% Cl 61%-79%) positive predictive value, given malignancy rates 10% Bethesda III; 32% Bethesda IV. 45 unique combinations of genetic alterations were detected in the 96 operated ThyroSeq® v3 positive cases—34 combinations (76%) were present in <2 cases and only 3 combinations occurred 7 or more cases. Forty-six (48%) nodules had RAS mutations, either combined with other mutations 31% (23/30, 77% malignant) or alone, 17% (10/16, 63% malignant), followed by
THADA/IGF2BP3 gene fusion changes,11.5% (10 /11 malignant). Three cases with BRAF mutations (1 V600E, 1 K601E, 1 K601N) were malignant. Copy numbers alterations alone were present in 10 (5/ 10 malignant) and the gene expression profile alone was positive in 5 cases (all malignant). Mutations that were associated with benign pathology were PTEN, DICER1, E1F1AX and TP53. There were 6 false negative cases, 5 low risk cancers by American Thyroid Association criteria and 1 NIFTP.
Conclusion:
The high BCR of Thyroseq® v3 for Bethesda III category avoids surgery for majority of patients. A more comprehensive mutational and fusion panel reveals the complexity of the genetic signature of indeterminate nodules. Future larger and likely multicenter studies will be required to define the associated cancer risk and potential prognosis associated with adjunct molecular testing.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Rates of Illnesses in Patients with Congenital Adrenal Hyperplasia

Ashwini Mallappa, MD, MHSc[1], Ninet Sinaii, PhD[1], Diala El-Maouche, MD, MS[2], Padmasree Veeraraghavan, RN[1], Elizabeth Joyal, FNP[1], Courtney J. Hargreaves, BS[1], Deborah P. Merke, MD, MS[3].
[1]NIH, Rockville, MD, USA, [2]National Institutes of Health Clinical Center, Rockville, MD, USA, [3]NIH, Bethesda, MD, USA.

MON-158

Background: Classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is the most common cause of primary adrenal insufficiency during childhood and patients are at risk for life-threatening adrenal crisis. In a recent study from our group, we reported gastrointestinal and upper respiratory tract infections as the two most common precipitating events for adrenal crises and hospitalizations across all ages. We also reported 11 incidents of life-threatening hypoglycemic events in children, sometimes accompanied by seizures.
Objective: To evaluate the annual rates of illnesses in patients with CAH.
Methods: We retrospectively reviewed longitudinally collected data over 23 years from 156 CAH patients enrolled in our CAH natural history study (www.clinicaltrials.gov #NCT00250159). Incidence of illnesses and occurrence of stress-dose days were computed per person-years. Incidence rate ratio (IRR) with 95% confidence intervals (CI) were calculated for comparisons.
Results: A total of 2298 visits (1909 for children and 389 for adults) were available for evaluation among the 156 patients (21-OHD: 97.4%). A total of 1870 illness events (1664 in children) were observed in 143 patients (121 children) and 2710 stress-dose days (2460 in children) were observed in 141 patients (120 children) during the study period. The incidence rate of illnesses was higher in children than adults (1.5 *vs.* 0.5 illnesses/person-years, IRR = 3.1, 95% CI 2.7 - 3.6; *P*<.0001) with incidence highest in young patients: 2.5 illnesses/person-years in <3 year olds. Similarly, the stress-dose days were higher in children than adults (2.2 *vs.* 0.6 days/person-years, IRR = 3.8, 95% CI 3.3 - 4.3; *P*<.0001).
Conclusions: Patients with CAH do not appear to have higher rates of infectious illnesses than expected, but remain at risk for life-threatening adrenal crises. As expected, illness rates are higher during childhood than adulthood. Prevention of adrenal crisis is crucial and is best accomplished through repeated age-specific education of patients and caregivers.
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Adrenal

ADRENAL CASE REPORTS II

Primary Adrenal Insufficiency Caused by Underlying Tuberculosis

Umara Zahir Jamal, MD.
The University of Texas Medical Branch, Galveston, TX, USA.