AUTOMATIC IDENTIFICATION OF HÜRTHLE CELLS AND HÜRTHLE NEOPLASIA BY TWO CLASSIFIERS THAT COORDINATE WITH THE CORE AFIRMA GSC CLASSIFIER

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Cytologically indeterminate thyroid nodules with Hürthle cells pose cytological and molecular challenges. Two Hürthle classifiers interface with the core GSC classifier to assess every FNA. We investigated how they performed among Bethesda III, GSC Suspicious nodules that were negative for mutations and fusions in a large RNA panel [the Xpression Atlas (XA)]. The Hürthle index (HI) classifier determines if the specimen contains Hürthle cells. If HI is negative, then the core GSC classifier renders a benign or suspicious result. If HI is positive for Hürthle cells, then the Hürthle neoplasm Index (NI) classifier determines if the specimen is neoplastic. If neoplastic, then the core GSC classifier renders a benign or suspicious result. However, if NI is negative for neoplasia, then the core GSC classifier uses an adjusted threshold that allows more GSC benign results.

Cleveland Clinic samples submitted for GSC testing were reviewed with Veracyte to identify all that were Bethesda III, GSC Suspicious, HI positive, NI positive, and XA negative. Two cases were identified. Case 1. Initial FNA = AUS. Hürthle cells with cytologic atypia and background lymphocytes. [cytology comment: In a patient with Hashimoto’s thyroiditis, this may represent Hürthle cell hyperplasia. Hürthle cell neoplasm cannot be entirely exclude.] No GSC submitted. Repeat FNA = AUS. Predominant oncocyctic population. Minimal colloid. [cytology comment: Differential diagnosis includes hyperplastic oncocyctic nodules vs oncocyctic neoplasm.] GSC Suspicious, XA negative. Surgical histology: 2.3 cm PTC, oncocyctic variant.

Case 2. Initial FNA = AUS. Hürthle cells with some background lymphoid cells. [cytology comment: In the right clinical context, this raises the possibility of lymphocytic thyroiditis.] GSC Suspicious, XA negative. Surgical histology: 0.9 cm PTC, oncocyctic variant and chronic lymphocytic thyroiditis. In both cases the HI and NI classifiers were correct given the Hürthle cell cytology and neoplastic surgical histology, respectively. The presence of malignancy, despite the lack of mutation or fusion on the 511 gene Xpression Atlas, supports that the GSC has high sensitivity, despite its significantly increased benign call rate.